Statistical Robustness Study for Kinetic Models

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Kinetic models are nonlinear systems that depict the dependence between process variables and components or products where the process variables are usually assumed to be fixed. This is under the assumption that the process variables that govern the outputs are fully controllable. However, process variables are not always fully controllable and are more often hard-to-control during normal operation on a full-scale chemical production plant. This Article outlines the methodology of statistical robustness studies for kinetic models. Such an application is apparently new in engineering design and analysis. We illustrate the use of computer experiments and evaluate different response models and designs for determining optimum conditions, which are robust against the variability in the hard-to-control variables. The methodology is demonstrated with two examples, the main one being the ethoxylation of ethylene glycol in an inter cooled pipe reactor. The practical value of statistical robustness studies is that it quantifies the convoluted effect of model uncertainty and model input deviation.

Introduction

Ethylene glycol oligomers (ethylene glycol (EG), diethylene glycol (DEG), triethylene glycol (TEG), and higher ethylene glycols) are commonly used in a wide variety of applications including resins, films, fibers, antifreezes, aircraft anti-icer and deicers, heat transfer fluids, solvents, inks, and gas dehydration. Ethylene glycol oligomers are formed by reacting EG with ethylene oxide (EO). The market demand for the various oligomers may change, and it is therefore useful to be able to optimize the production of certain products. Di Serrio[1] published a kinetic model for predicting the reactions and selectivities for an ethylene glycol process. The reactions are dependent on, for example, temperature, feed ratio, and catalyst concentration.

The objective of the kinetic model for the ethylene glycole process is to explain the dependence between the process variables (temperature, feed ratio, etc.) and the products (DEG, TEG) according to the fundamentals of the reactions. However, in any design and operation of a chemical process, there are several parameters that have a degree of uncertainty and variability associated with them. Process variables, such as temperature and feed ratio in the ethylene glycol process, may be subjected to variability, which contributes to the variability in the products produced by the reactor. While it is critical to address these uncertainties during plant operation, it is also important that the variability in the process variables be taken into consideration in the reactor model development and design stage. The model parameters (rate constants, etc.) are generally estimated from experimental data, which are associated with random and normally distributed measurement errors. Methods for incorporating the variability in the model parameters into the design stage have received considerable attention in the chemical engineering literature.[2]

The process variables that govern the reactions are usually considered to be fully controllable during normal operation and are therefore treated as fixed in kinetic models. However, some process variables may also be subject to uncertainty and introduce variability into the outputs predicted by the reactor model. In the statistical literature, these variables are referred to as hard-to-control, and the effect of their variability on the predicted outputs is of interest. By incorporating the variability in the process variables at the model building and design stage, operability regions that are insensitive or robust to these uncertainties may be obtained. In addition, if the uncertainty in the outputs due to the variability in the inputs can be quantified, the convoluted effect of model uncertainty and model input deviation can be quantified, which will contribute to a more accurate and safer over design of equipment.

Any process is considered to be robust when it performs consistently on target and when it is insensitive to factors that are difficult or hard-to-control during normal operation. Statistical robustness studies is the methodology whereby experimental design, analysis, and model building are deployed to develop or improve a process or product to be insensitive to the variability transmitted to the outputs from factors or variables that are difficult or impossible to control when the process is operational.[3] The methodology of robustness studies is well documented for empirical studies,[3−5] but has not been utilized previously for fundamental or kinetic models.

The objective of robustness studies is to determine conditions on the process variables for which the process outputs are robust against the variability in the hard-to-control variables. Such a robustness study is one major contribution of the Taguchi method.[6] For this purpose, two response models are evaluated for the outputs of the process, that is, the mean response model and the variance response model. Performing statistical robustness studies entails the conducting of experiments or computer runs with the mean and variance models at different settings of the process variables. Therefore, we apply the methodology of the design and analysis of computer experiments to specify the variables' settings, and to construct approximation or surrogate models of the original computer code, facilitating the exploration of the design space, optimization, and continuous improvement.[7] Response surface and Kriging models are mainly used as approximation models.[8]

In this Article, we present the methodology of statistical robustness studies together with the design and analysis of computer experiments for kinetic models. We apply and demonstrate the advantages of the methodology to the ethylene

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glycol process. We illustrate how this methodology can be used in kinetic modeling for quantifying the variability or uncertainty effect that hard-to-control process variables has on the outputs of a process during normal operation. In addition, we show how the successful application of robustness studies leads to sustainable operating areas where the transmitted variability is minimized. The methodology also enables the estimation of the combined or interaction effects of the process variables on the mean and variance of the process. We evaluate several experimental designs for sampling the computer code for the kinetic and variance models. We compare response surface and Kriging models for approximating the input−output relationships for the kinetic and variance models, and make recommendations for application in industry.

Statistical robustness studies have not previously been applied to kinetic models, and neither have computer experiments been applied for robustness studies. This Article is outlined as follows. First, we present the methodology of statistical robustness studies for both linear and nonlinear models. Thereafter, the design and analysis of computer experiments are discussed. The application of the methodology to two examples is then discussed in detail, the main one being the kinetic model for the ethylene glycol process.

Methodology of Process Robustness Studies

Linear Models. In this section, we present a brief introduction to linear models because it is a prerequisite for the discussion of nonlinear models in the next section. Suppose that a relationship exists between a response Y and $q = r + s$ process variables, that is, $x = (x_1, x_2,..., x_r)^T$ and $z = (z_1, z_2,.., z_s)^T$. The variables x are considered to be controllable, and the variables z are the hard-to-control variables during normal operation. The model for the observations can be written as:

$$Y(x, z, \beta) = \eta(x, z, \beta) + \varepsilon \tag{1}$$

where $\eta(x, z, \beta)$ is a regression function, that is, the mean or expected response at (x, z) written as $E(Y(x, z, \beta)) = \eta(x, z, \beta)$. The parameters of the model are $\beta = (\beta_1, \beta_2,..., \beta_p)^T$, and the errors ε are considered to be normally distributed with mean 0 and common variance σ^2.

Let the mean and variance-covariance matrix of the hard-to-control variables, z, during normal operation be equal to μ_z and S_z, respectively, with $E(z_i) = \mu_{z_i}$ and $Var(z_i) = \sigma^2_{z_i}$, $Cov(z_i, z_j) = \sigma_{z_i z_j}$, $i \neq j = 1,..., s$. For the experimental design, it is assumed that the variables (x, z) belong to a design or experimental range $R = (R_x, R_z)$.

When little or no knowledge is available about the true functional relationship, then $\eta(x, z, \beta)$ can be approximated by a truncated Taylor series, that is, a polynomial in x and z of degree d, usually equal to 1 or 2, to produce a useful approximation. A second-order model contains linear, quadratic, and two-order interaction terms between the controllable and hard-to-control variables, for predicting the response surface of the performance variable of interest. The second-order response surface model is of the form 2:

$$\begin{aligned} Y(x, z, \beta) &= a^T\beta + \varepsilon \\ &= \delta_0 + \sum_{i=1}^{r} \delta_i x_i + \sum \sum_{i<j}^{r} \delta_{ij} x_i x_j + \sum_{i=1}^{r} \delta_{ii} x_i^2 \\ &+ \sum_{i=1}^{s} \gamma_i z_i + \sum_{i=1}^{r} \sum_{j=1}^{s} \gamma_{ij} x_i z_j + \varepsilon \end{aligned} \tag{2}$$

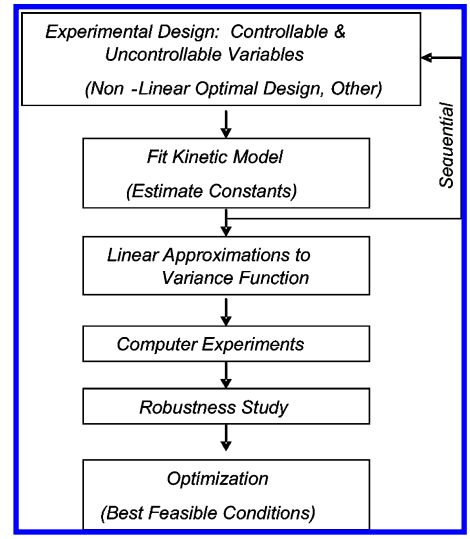

Figure 1. Schematic diagram of robustness studies utilizing the kinetic or fundamental model.

where a is the vector containing all of the terms in the model and β is the vector containing all of the parameters in the model. Model 2 is fitted to the experimental data to produce the estimates of β_u, for example, using least-squares estimation.

The response surface model for the process mean is obtained by taking the expectation of the predicted model 2 over the prior distribution of the hard-to-control variables, that is, $E_z(\hat{Y}(x, z, \beta)) = \hat{Y}_{\mu|z}(x, z, \beta)$. This model is then used to optimize the process mean for the expected values or other of the hard-to-control variables z. The model for the process mean $\hat{Y}_{\mu|z}(x, z, \beta)$ can also be referred to as the first moment of the response variable $\hat{Y}$ about zero.

The variance function is obtained from the second moment of the response variable Y about the mean μ_z, that is, $E(\hat{Y}(x, z, \beta) - \mu_z)^2 = \hat{Y}_{\sigma|z}(x, z, \beta)^2$. The second moment is approximated by taking the conditional variance operator across the response surface model 2 over the prior distribution of the hard-to-control variables. Montgomery[3] gave a detailed discussion of robustness studies for empirical models. Coetzer and Keyser[9] developed second-order response surface models and applied statistical robustness studies to determine conditions of the process parameters that minimize the effect of the variability in the hard-to-control variables on gasifier performance.

Nonlinear Models. The main aim of fundamental or kinetic modeling is to explain the dependence between process variables and products according to the fundamental principles of the process under study. Figure 1 depicts the sequential process for iterative learning and scientific discovery for fundamental process robustness studies utilizing, for example, kinetic models. Fundamental modeling requires the sequential steps of selecting an experimental design, data collection, and model fitting for estimating the kinetic constants. However, for estimating nonlinear models, it is required to deploy a nonlinear optimal design to select the variable conditions for estimating the constants of the model most accurately. Atkinson and Donev[10] provided an excellent introduction to the theory of optimal design for nonlinear models. Atkinson et al.[11] presented optimum designs for estimating the kinetics of a reversible chemical reaction.

Because the fundamental model is a function of both the controllable and the hard-to-control variables, we recommend that the optimal design should contain both types of variables in a combined array. The kinetic model is fitted to the data using

an appropriate numerical routine for estimating the constants of the model. For kinetic experiments and model fitting, it is assumed that all of the variables that govern the process are fully controllable and therefore fixed. This is so because the first objective of such a study is to develop a kinetic model that can represent the fundamentals of the process. When this is done, experiments can be conducted with the model by running the computer code. The focus of this Article is not about model fitting but rather on how to use the kinetic model for process robustness studies.

Consider the model in (1) to be an accurate representation of the true fundamentals of the process under study; that is, model 1 is a nonlinear model or system of nonlinear equations, which is governed by controllable variables x and hard-to-control variables z. The kinetic constants are $\beta = (\beta_1, \beta_2, ..., \beta_p)^T$. Assume, as before, the mean and variance-covariance matrix of the hard-to-control variables, z, during normal operation are equal to μ_z and S_z, respectively, with $E(z_i) = \mu_{z_i}$ and $Var(z_i) = \sigma_{z_i}^2$, $Cov(z_i, z_j) = \sigma_{z_i z_j}$, $i \neq j = 1, ..., s$. For robustness studies, the kinetic model 1 is approximated through a second-order Taylor series expansion about the means of the hard-to-control variables μ_{z_i}. That is,

$$Y(x, z, \beta) = \eta(x, \mu_z, \beta) + \sum_{i=1}^{s} (z_i - \mu_{z_i}) \left(\frac{\partial \eta}{\partial z_i} \right) + \sum_{i=1}^{s} \sum_{j=1}^{s} \frac{1}{2} (z_i - \mu_{z_i})(z_j - \mu_{z_j}) \left(\frac{\partial^2 \eta}{\partial z_i \partial z_j} \right) + \varepsilon \quad (3)$$

From eq 3, the expected value of the model over the prior distribution of z can be approximated by:

$$Y_{\mu|z}(x, z, \beta) = E_z(Y(x, z, \beta)) = \eta(x, \mu_z, \beta) + \frac{1}{2} \partial I_z(x, z, \beta)^T S_z \partial I_z(x, z, \beta) \quad (4)$$

where $\partial I_z(x, z, \beta)$ is the vector of second-order derivatives of the model to the hard-to-control variables z. From approximation 3 and expectation 4, the second-order variance approximation of model 1 over the prior distribution of z can be specified as

$$Y_{\sigma|z}(x, z, \beta)^2 = Var_z(Y(x, z, \beta)) = E(Y(x, z, \beta) - Y_{\mu|z}(x, z, \beta))^2 \approx I_z(x, z, \beta)^T S_z I_z(x, z, \beta) + \sigma^2 \quad (5)$$

The constants β_u are replaced by their estimates b_u, $u = 1, 2, ..., p$, and σ^2 is replaced by its estimate $\hat{\sigma}^2$, for the predicted kinetic model. Therefore, two response models are constructed, that is, the mean response model and the variance response model, for conducting process robustness studies. The predicted kinetic model $\hat{Y}(x, z, \beta)$ in eq 1 is used for the mean response model, and the variance function in eq 5 is used for the predicted variance response model. The aim is to evaluate the effect of the variability in the hard-to-control variables on the model outputs for determining robust process conditions.

The kinetic model represents the system or process under study, and the variance response model represents the transmitted variability through the system due to the variability in the hard-to-control variables. Therefore, we recommend the use of the design and analysis of computer experiments for robustness studies on kinetic models. This methodology is deployed to sample the computer code and to construct approximation models of the mean response and the variance response as functions of the process variables. Lehman et al.[12] presented the design of computer experiments to determine robust variable conditions when uncontrollable variables are present in the system. They construct computer experiments by simulating random outputs or responses, and calculating the variance thereof, from the computer experiments based on a random distribution of the uncontrollable variables.

In contrast, we construct the variance function from the kinetic model directly and perform computer experiments on the variance model to determine robust control variables. The variance model is also considered to be deterministic and therefore permits the application of known computer experiments for sampling the computer code and for constructing the approximation models for the input−output relationships. It has a further advantage in that dual or multiple response surface optimization can be performed with the approximation models. We illustrate by way of two examples that the methodology presented in this Article is very efficient and easy to use for performing process robustness studies with the design and analysis of computer experiments.

Computer Experiments

Designs for Computer Experiments. Computer models are used extensively to predict the performance of real life complex engineering systems. However, these analyses may result in high computational costs, which limit their use in reliability analysis and design optimization. Therefore, the design and analysis of computer experiments were developed to reduce the computational expense of performing such computer analysis by providing a methodology for the sampling of the computer code and constructing approximation or surrogate models of the input−output relationships.[13] The approximation models are then used in lieu of the original analysis or simulation code, facilitating the exploration of the design space, optimization, and reliability analysis.[7]

The design and analysis of computer experiments were developed from the methodology of the design and analysis of physical experiments. However, the theory of the design of experiments (DOE)[14] and response surface (RS)[15] are based on the fact that an observation in a physical experiment is affected by variability due to the effect of a number of independent factors and random variability. In contrast, computer experiments are deterministic and yield the same result from repeated runs.

Therefore, space filling experimental designs are employed for computer experiments. Latin hypercubes, orthogonal arrays, and uniform designs (UD) are examples of different types of space filling designs.[16] Since uniform designs were introduced in the early eighties by Fang,[17] it became very popular. The design points of a uniform design are uniformly scattered on the experimental domain. It is a type of fractional factorial design with an added uniformity property. According to Fang and Lin,[16] the uniform design is superior to other designs because many other design criteria are simultaneously optimized together with minimization of the uniformity property.

A big advantage of uniform designs is that less information is required of the underlying model. A large number of different uniform designs are available at the Web site developed by Fang et al.,[18] and they are specified by the notation $U_n(q^s)$, where U stands for UD, n is the number of runs, s is the number of factors, and q is the number of levels. See Fang and Lin,[16] Fang et al.,[19] for the theory and application of uniform designs. However, other designs, such as the CCD and D-optimal designs, may also be employed for performing computer

experiments, although they were developed specifically for physical experiments and response surface modeling.[15]

Statistical Approximations of Computer Experiments

Statistical Modeling. To construct approximations of computer codes, statistical techniques are required: (a) choosing an appropriate experimental design to sample the computer analysis code, (b) choosing a model to describe the input−output relationships, and (c) fitting the model to the data.[8]

Response surface (RS) modeling of the form 2 can be used as an approximation method.[15] With "traditional" DOE, random variation is accounted for by replicating experiments and by spreading the sample points out in the design space. Because deterministic experiments lack random error, the "classical" notions of blocking, replication, and randomization are irrelevant; thus sample points should be chosen to fill the design space.[20] Therefore, a more appropriate method for approximating deterministic computer experiments might be the use of Kriging, which is an exact interpolation or "smoothing" of the data, and, consequently, its validity will not depend on the existence of random error. Kriging is discussed in detail in the next section.

Suppose that n_t number of points is sampled from the design space in the controllable and hard-to-control variables $R = (R_x, R_z)$ according to the experimental design for the computer code. The second-order response surface model is of the form 2, and the least-squares estimation produces the estimates b of β from:

$$b = (\mathbf{X}^T\mathbf{X})^{-1}\mathbf{X}^T Y \tag{6}$$

where $\mathbf{X}$ is the matrix of n_t sampled data points expanded to contain all of the terms in the second-order model. Note that the matrix $\mathbf{X}$ contains linear functions of the controllable and hard-to-control variables. Furthermore, dual response surface models are constructed, that is, one for the mean response and one for the variance response. Therefore, we obtain estimates b_μ from the approximation model of the mean response, and b_σ from the approximation model of the variance response. Polynomial response surface models can be easily constructed and allow quick convergence of noisy functions for optimization.

Kriging. Kriging is an interpolation technique that was originally developed in the field of geostatistics. Sacks et al.[20] initiated the application of Kriging to the design and analysis of computer experiments where it postulates a combination of a regression part and a stochastic part:

$$y(x) = f(x) + Z(x) \tag{7}$$

In eq 7, x are the design variables, $y(x)$ is the unknown response function, $f(x)$ is the known (usually polynomial) regression function of x, and $Z(x)$ is the realization of a stochastic process with mean zero, variance σ^2, and nonzero covariance. While $f(x)$ approximates the design space, $Z(x)$ creates "localized" deviations or departures so that the Kriging model interpolates the n_t data points.

In this Article, the design variables consist of controllable variables x and hard-to-control variables z. Therefore, eq 7 can be rewritten as $y(w) = y(x, z)$. The change in notation is necessary to emphasize the study in two types of design variables. Furthermore, we will fit dual Kriging models: one for the mean response $y_\mu(w)$ and one for the variance response $y_\sigma(w)$. However, in the discussion that follows, we will omit the subscripts because the estimation procedure is the same for both responses. The covariance matrix of $Z(w)$ is given by:

$$Cov[Z(w_i), Z(w_j)] = \sigma^2\mathbf{R}([R(w_i, w_j]) \tag{8}$$

where $\mathbf{R}$ is the correlation matrix, and $R(w_i, w_j)$ is the correlation function between any two of the sampled n_t data points w_i and w_j. $\mathbf{R}$ is a $(n_t \times n_t)$ symmetric matrix with ones along the diagonal. The correlation function $R(w_i, w_j)$ needs to be specified by the user. Several correlation functions can be used and are discussed by Sacks et al.[20] Throughout this Article, the Guassian correlation function 9 is employed:

$$R(w_i, w_j) = \exp[-\sum_{k=1}^{n_d} \theta_k |w_{ik} - w_{jk}|^2] \tag{9}$$

where n_d is the number of design variables, θ_k are the unknown correlation parameters used to fit the model, and w_{ik} and w_{jk} are the kth components of sample data points w_i and w_j.

Predicted values of the response $y(w)$ at untried values of w are given by:

$$\hat{y}(w) = \hat{\beta} + r^T(w)\mathbf{R}^{-1}(y(w) - f(w)\hat{\beta}) \tag{10}$$

where $y(w)$ is the column vector of length n_t, containing the sample values of the response, and $f(w)$ is a column vector with the same length that is filled with ones when $f(w)$ is taken as a constant. In (10), $r^T(w)$ is the correlation vector between an untried w and the sampled data points $\{w_1, ..., w_{n_t}\}$ and is defined as:

$$r^T(w) = [R(w, w_1), R(w, w_2), ..., R(w, w_{n_t})]^T \tag{11}$$

$\hat{\beta}$ in eq 10 is estimated using eq 12:

$$\hat{\beta} = (f(w)^T\mathbf{R}^{-1}f(w))^{-1}f(w)^T\mathbf{R}^{-1}y(w) \tag{12}$$

The variance ($\hat{\sigma}^2$) between the underlying model $\hat{\beta}$ and y is estimated as:

$$\hat{\sigma}^2 = \frac{(y(w) - f(w)\hat{\beta})^T\mathbf{R}^{-1}(y(w) - f(w)\hat{\beta})}{n_t} \tag{13}$$

The maximum likelihood estimates (MLEs) of θ_k in eq 9 used to fit the model are found by maximizing eq 14:

$$-\frac{[n_s \ln(\hat{\sigma}^2) + \ln|\mathbf{R}|]}{2} \tag{14}$$

Any values for θ_k will create an interpolative model, but the "best" Kriging model is found by solving the k-dimensional unconstrained nonlinear optimization problem given in eq 14.[8]

Simpson et al.[8] state that Kriging models have found limited application in engineering design, perhaps because of the lack of readily available software, the added complexity of fitting Kriging models, or the additional effort to use these models. Prediction with a Kriging model requires the inversion and multiplication of several matrices as compared to response surface models where prediction only requires the computation of a simple polynomial equation once the model has been fit.

Simpson et al.[8] made a comparison between response surface and Kriging models for the multidisciplinary design of an aerospike nozzle, which consists of a computational fluid dynamics model and a finite-element model. The RS and Kriging approximations yielded comparable results with minimal difference in predictive capability. Simpson et al.[7] compared four approximation model types in terms of their capability to generate accurate approximations for two engineering applica-

Table 1. Estimated Rate Constants for the Reactor Model

constant	ln A [cm^3/mol/min]	B [kcal/mol]
k_0	37.5 ± 2.6	21.7 ± 1.9
k	28.0 ± 1.4	15.8 ± 1.1

tions with typical engineering behaviors and a wide range of nonlinearity. They found that the Kriging and radial basis function models tend to offer more accurate approximations over a wide range of DOE types. Second-order response surfaces yielded average results and performed particularly well when approximating low-order nonlinear functions.

Error Analysis of Response Surface and Kriging Models. Because the approximation models interpolate the sample data, additional validation points are collected in the design variables' ranges to assess the accuracy of each approximation model over the region of interest. For each set of validation points, the error is defined as the difference between the actual response from the computer analysis and the predicted value from the RS or Kriging model. We define the root-mean-square error as:

$$\text{rmse} = \sqrt{\frac{\sum_{i=1}^{n_e} (y_i - \hat{y}_i)^2}{n_e}} \tag{15}$$

where n_e is the number of additional validation points. The rmse provides a good estimate of the "global" error over the region of interest.[7]

Example 1: The Branin Function. Lehman et al.[12] presented the design of computer experiments to determine robust variable conditions when uncontrollable variables are present in the system. They developed a sequential algorithm for the construction of designs by simulating random outputs or responses, and calculating the variance thereof, from the computer experiments based on a random distribution of the uncontrollable variables. Lehman et al.[12] used the Branin function[21] to illustrate their M-robust design, that is, maximizing or minimizing the mean response 4 subject to a limit on the variance function 5 (see criterion (22) of example 2). In this section, we also use the Branin function to first prove the reliability of the proposed methodology.

The Branin function is defined as:

$$z(w_1, w_2) = \left(w_2 - \frac{5.1}{4\pi^2}w_1^2 + \frac{5}{\pi}w_1 - 6\right)^2 + 10\left(1 - \frac{1}{8\pi}\right)\cos(w_1) + 10 \tag{16}$$

The true response function has four inputs and is defined to be

$$y(x_1, x_2, x_3, x_4) = \frac{1}{30}z(x_1, x_2)z(x_3, x_4) + (x_1 - \pi)^2 \tag{17}$$

with (x_1, x_2) being the control variables defined on the range $[-5, 10] \times [0, 15]$, and (x_3, x_4) are the hard-to-control or uncontrollable variables defined on the range $[-2, 1, 4, 7] \times [3.75, 7.5, 11.25]$. The joint distribution of the uncontrollable variables is given in Table 1 of Lehman et al.[12] The aim is to determine the control variable settings that minimize $y_{\mu l(x_3,x_4)}$ subject to $y_{\sigma l(x_3,x_4)} \leq 100$.

The joint distribution of the uncontrollable variables was used to calculate the $Var(x_3)$ and $Var(x_4)$, whereas $Cov(x_3, x_4)$ is equal to zero. Equation 5 was used to calculate $y^2_{\sigma l(x_3,x_4)}$. Figures 2 and 3 depict the true $y_{\mu l(x_3,x_4)}$ and $y_{\sigma l(x_3,x_4)}$, respectively.

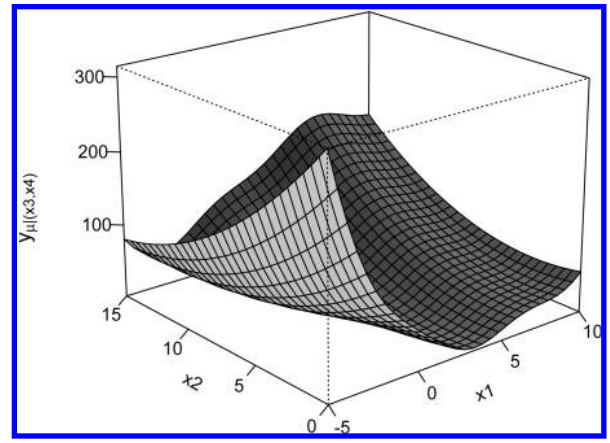

Figure 2. Surface plot for $y_{\mu l(x_3,x_4)}$.

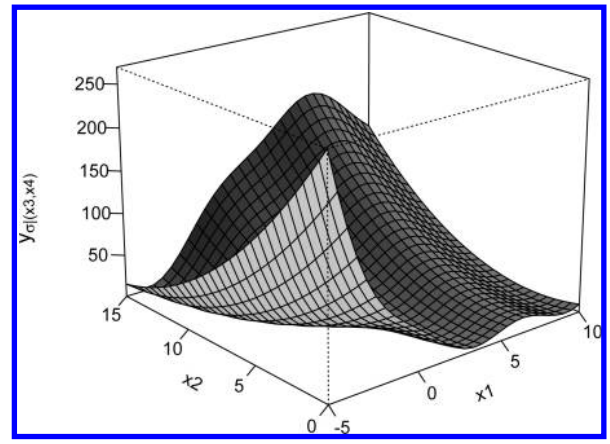

Figure 3. Surface plot for $y_{\sigma l(x_3,x_4)}$.

The $U_{52}(4^4)$ uniform design was used to sample the computer codes for both the $y_{\mu l(x_3,x_4)}$ and the $y^2_{\sigma l(x_3,x_4)}$ functions. A cubic RS model was fitted to the data and validated using a grid of 81 data points in the design ranges of the four variables. The rmse was equal to 9.207 and 5.520 for the $y_{\mu l(x_3,x_4)}$ and $y_{\sigma l(x_3,x_4)}$ approximation models, respectively. Clearly, the cubic models constructed on the data from the uniform design provide very accurate predictions of the original mean and variance functions.

Robustness studies can now be performed by determining the variables' settings for minimum $y_{\mu l(x_3,x_4)}$, which are robust against the variability in the uncontrollable variables. Figure 4 depicts the feasible area in x_1 and x_2 for $y_{\mu l(x_3,x_4)} < 17.205$ and $y_{\sigma l(x_3,x_4)} < 100$ obtained from overlaying contours of the cubic RS models. Note that the true optimum value in $(x_1, x_2) = (\pi, 2.275)$ is contained in the feasible area.[12] Therefore, similar results were obtained by utilizing the methodology of statistical robustness studies and the design and analysis of computer experiments. This example clearly illustrates that optimum variable conditions can be obtained by applying the methodology presented in this Article for nonlinear or kinetic models.

Example 2: Ethoxylation of Ethylene Glycol. Reactor Modeling. Ethoxylation and propoxylation are extensively used by industry to produce products such as polypropylene glycols and polyethylene glycols that are largely used as chemical intermediates, lubricants, and components for cosmetic formulations. Ethylene glycol oligomers are formed by reacting EG with ethylene oxide (EO). Di Serrio[1] published a kinetic model for predicting the reactions and selectivities for an ethylene glycol process. The ethoxylation of ethylene glycol (EG) has been selected as a test problem for applying the methodology of

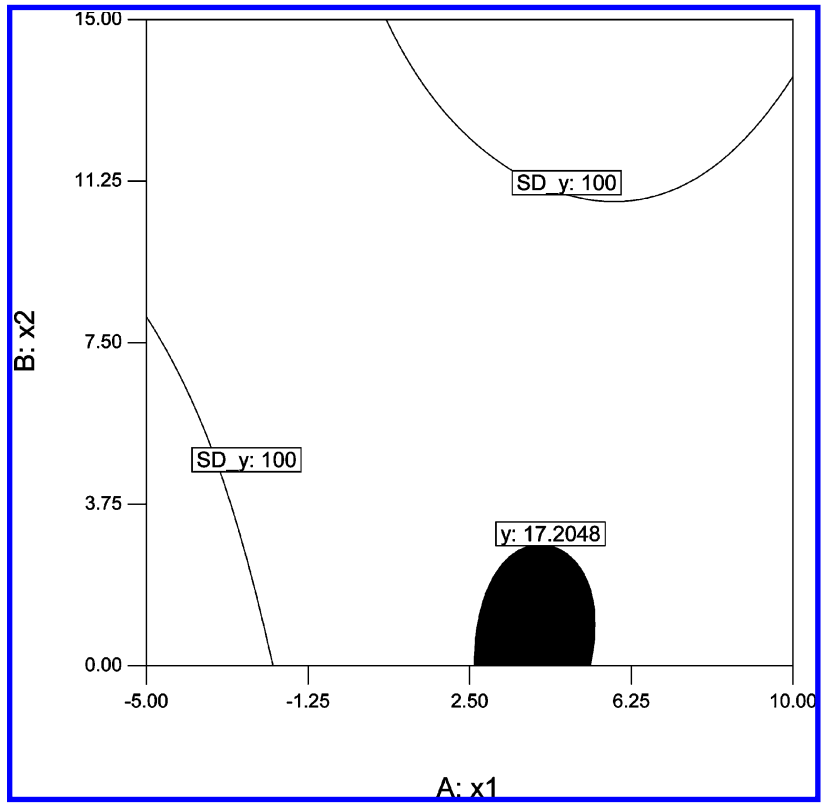

Figure 4. Feasible area for $y_{\mu l(x_3,x_4)} < 17.2\ 05$ and $y_{\sigma l(x_3,x_4)} < 100$ (feasible area in black).

robustness studies and for comparing the predictive capability of RS and Kriging models.

Although many more examples of determining kinetic models and estimating the parameters thereof exist in the literature,[22−26] the ethoxylation of EG was selected because the reaction mechanisms and the kinetic constants are published.[1] The kinetic model is nonlinear for which no analytical solution can be obtained. The model contains all of the characteristics of reactor modeling and analysis in the chemical industry and could therefore be used to illustrate the application and advantages of statistical robustness studies for kinetic models.

The reactor is modeled as an ideal plug flow reactor. Because the selectivities of the different products are temperature dependent, an option is included in the reactor to limit the maximum temperature increase by adding intercoolers as needed along the reactor length. This results in a sawtooth temperature profile that varies between the reactor inlet temperature and the specified maximum temperature.

The kinetic equations are integrated numerically using a fifth-order adaptive step Runge−Kutta method with Cash−Carp coefficients.[27] During integration, the temperature increase is calculated using heats of formation for the different components in the reactor. If a limit on the maximum temperature increase above the feed temperature has been specified, the temperature profile is monitored during integration until the difference between the current temperature and inlet temperature is exceeded. Linear interpolation is then used to calculate the location where the limit is exceeded, and the temperature is reset to the inlet temperature.

The inputs or design variables required to solve the model are: (1) inlet temperature (T(K)), (2) optional maximum temperature increase (ΔT(K)), (3) EG:EO feed ratio (EG:EO), (4) catalyst concentration (CC(mol %)), and (5) EO fractional conversion (%).

The model output included selectivities to DEG, TEG, heavies (components heavier than TEG), and the time to reach the target ethylene oxide conversion. For the linear approximation of the variance function 5, numerical derivatives of the outputs with respect to all input variables except EO fractional conversion were calculated using a perturbation of 1 K for inlet temperature and maximum temperature, 0.1 for the EG:EO ratio, and 0.001 mol % for the catalyst concentration. Numerical derivatives of the output with respect to the kinetic parameters were also calculated by perturbing the parameters by 1%, respectively.

Kinetic Modeling. The catalyzed oligomerization of EG with EO can be represented as follows:[1]

$$HOCH_2CH_2(EO)_iO^-K^+ + EO \rightarrow HOCH_2CH_2(EO)_{i+1}O^-K^+, i = 0, 1, ... \quad (18)$$

The cation of the catalyzed species can migrate to different hydroxyl groups via proton transfer. This is assumed to occur fast and is modeled as equilibrium reactions. The concentrations of all of the ionic species in solution can be calculated as follows:

$$[HOCH_2CH_2(EO)_iO^-K^+] = \frac{[HOCH_2CH_2(EO)_iOH]C^0}{[HOCH_2CH_2OH] + K_e \sum_{j=1,2,...} [HOCH_2CH_2(EO)_jO^-K^+]}, \quad i = 0, 1, 2, ... \quad (19)$$

The kinetic expression for reaction 18 is given by:

$$r_i = k_i[HOCH_2CH_2(EO)_iO^-K^+][EO], i = 0, 1, 2, ... \quad (20)$$

The changes in composition of the different components with time are given by:

$$\frac{d[HOCH_2CH_2OH]}{dt} = -r_0$$
$$\frac{d[HOCH_2CH_2(EO)_iOH]}{dt} = r_{i-1} - r_i, i = 1, 2, ... \quad (21)$$

Equations 19−21 describe the change in composition under reactive conditions with time. Because the conditions investigated in this work typically favor shorter oligomers, only reactions up to $i = 3$ were simulated. The catalyst equilibrium coefficient in eq 19 is $K_e = 3.5$, assuming that all of the k_i in eq 20 are constant and denoted by k. The rate constants were assumed to follow an Arrhenius temperature dependency, that is, $k = A \exp((-B)/(RT))$. The estimated kinetic constants together with their standard errors are depicted in Table 1.[1]

Application of the Design and Analysis of Computer Experiments to the Reactor Model. Computer Experiments. We applied the design and analysis of computer experiments to the kinetic model and the variance function of the model to sample the analysis code and to construct approximation models for the ethylene glycol process discussed in the previous section. We selected five different experimental designs to evaluate as alternatives for collecting the sample data points and for constructing the RS and Kriging models. The five designs are: (a) face centered central composite (CCD FC), (b) D-optimal design, and the following uniform designs: (c) $U_{32}(4^4)$, (d) $U_{24}(4^4)$, and (e) $U_{30}(3^4)$. Note the classical CCD FC and D-optimal designs were also evaluated in this study because they are very popular and well-known experimental designs in industry. Therefore, their ability in generating accurate approximation models was compared to that of the space-filling designs.

Experimental designs were constructed in the following four variables: inlet temperature (T), temperature increase in the reactor (ΔT), alcohol ratio (EG:EO), and catalyst concentration (CC). Temperature was varied between 393 and 423 K, ΔT between 5 and 60 K, EG:EO ratio between 5 and 7, and CC between 0.01 and 0.10 mol %. The selectivities of the products as well as the derivatives for calculating the variance model were obtained numerically as discussed in the previous section.

Approximation Models. The kinetic model predicts selectivity for the products DEG, TEG, and heavier components, which constitute the full product composition. Because the desired product is DEG, we evaluated the results in terms of the DEG:TEG ratio. Therefore, the aim is to determine the optimum or desired variable conditions, which yield high DEG:TEG ratio and simultaneously minimizes its variance transmitted through the kinetic model due to the variability in the hard-to-control variables.

Second-order RS and Kriging models were constructed for the selectivity to the product ratio (DEG:TEG), as well as for the square root of the variance function, that is, the standard deviation (SD) of the selectivity to the product ratio (DEG:TEG). For this example, we assumed that all of the design variables, that is, inlet temperature (T), temperature increase in the reactor (ΔT), alcohol ratio (EG:EO), and catalyst concentration (CC), may be hard-to-control variables during normal operation. From experience, values for $Var(T)$, $Var(\Delta T)$, and Var(EG:EO) were assumed to be 25 K, 25 K, and 0.1, respectively. Var(CC) was assumed to be negligibly small. The variance function was calculated using eq 5 and by incorporating the variability of all of the design variables.

Note these variables are considered to be hard-to-control to illustrate the robustness concept. However, in practice it is not unreasonable to experience temperature fluctuations on an actual production plant due to changing ambient conditions, for example, a rain shower, poorly tuned control loops, fluctuating utility conditions, etc. The temperature increase in the reactor will be more difficult to control, specifically the inlet temperature to a heat exchanger. The reactor design selected for the example consists of pipe sections connected to heat exchangers. Therefore, once the reactor is built, the inlet temperature to the heat exchanger is fixed by the length of the pipe and the extent of the reaction up to the heat exchanger. If the reaction rate or the volumetric flow rate on the plant is different from design, then the adiabatic temperature rise before the heat exchanger will be different from design.

Table 2. Root-Mean-Square Error of Approximation Models for DEG:TEG Ratio and the Standard Deviation, SD(DEG:TEG Ratio)

	approximation models		SD(DEG:TEG ratio)	
design	Kriging	RS	Kriging	RS
CCD FC	0.43	0.46	2.63	2.62
D-Opt	0.67	0.67	1.66	1.66
$U_{32}(4^4)$	0.92	0.86	0.33	0.53
$U_{24}(4^4)$	1.20	1.20	0.32	0.32
$U_{30}(3^4)$	0.31	0.45	0.25	0.27

The parameter estimates were obtained through least-squares estimation on R[28] for the RS models. "DACE",[29] Design and Analysis of Computer Experiments, is a Matlab[30] toolbox for estimating Kriging models. Matlab was used to construct Kriging approximation models based on the same sample data points used to fit the RS models. The data were modeled using a constant term for the global model 7 and a Gaussian correlation function, eq 9, for the local deviations or departures determined by the correlation matrix, **R** in eq 9.

A grid of $3^4 = 81$ data points in the four variables' design ranges was used for the validation of the RS and Kriging models. The rmse for the five experimental designs are summarized in Table 2, for the product ratio, DEG:TEG, and the SD of the product ratio, SD(DEG:TEG), respectively. The Kriging and RS approximations yield comparable results with minimal difference in predictive capability for all of the designs evaluated. Based on this example, the $U_{30}(3^4)$ uniform design is superior in terms of its predictive capability for both the DEG:TEG ratio and the SD. The face centered CCD yielded very similar results as compared to the $U_{30}(3^4)$ design for the DEG:TEG selectivity ratio, but is much worse, that is, about 90%, as compared to the $U_{30}(3^4)$ design for the SD of the DEG:TEG ratio for both the RS and the Kriging models. The D-optimal design also performs very poorly as compared to the uniform designs for the SD of the DEG:TEG ratio, but performs better than the $U_{32}(4^4)$ and $U_{24}(4^4)$ designs for the DEG:TEG ratio. This seems to suggest that the four-level uniform designs do not perform well in computer experiments and in prediction with approximation models for the specific example. In summary, the $U_{30}(3^4)$ design outperforms the other designs and is therefore used for the robustness study discussed in the next section.

Robustness Study. The aim of process robustness studies is to determine settings of the design variables for which the outputs or products are insensitive to the variability transmitted to the outputs from the variables that are hard-to-control during normal operation. We evaluate the robustness of the process through the kinetic model, which is governed by the variables T, ΔT, EG:EO ratio, and CC. We assume that all of the design variables may be hard-to-control and determine the operating conditions that result in the most sustainable output, or smallest variability, of the DEG:TEG ratio and the heavier components

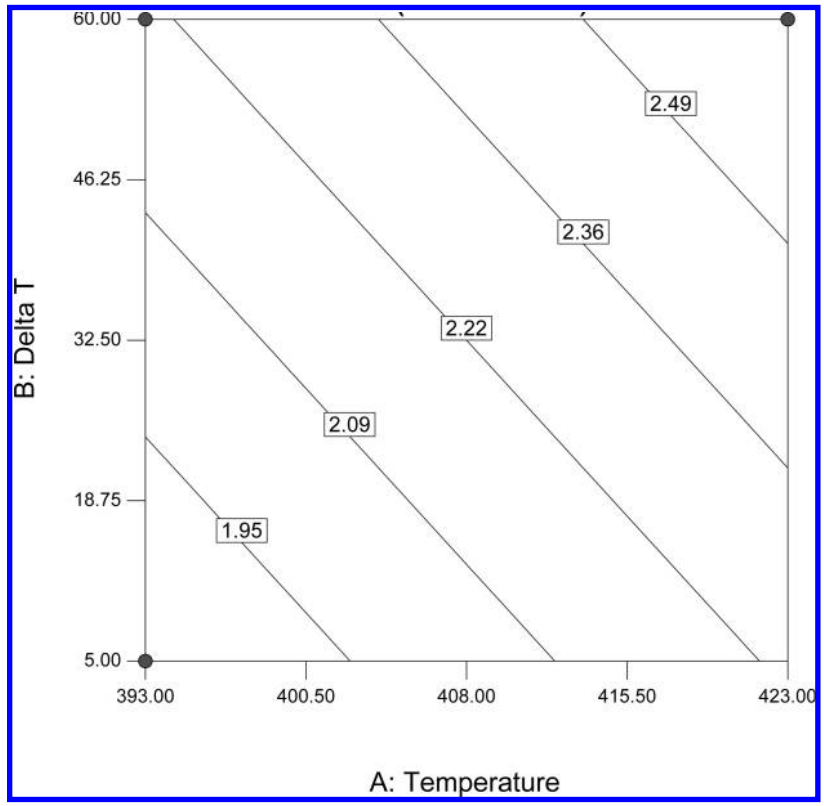

Figure 5. SD (DEG:TEG) as a function of T and ΔT for EG:EO = 6 and CC = 0.06.

(S-Heavies). The RS model obtained with the $U_{30}(3^4)$ design is used for the robustness study. The following points were observed:

Figure 5 depicts the predicted contours of the SD of DEG:TEG ratio as a function of T and ΔT. The SD reduces toward lower temperatures and lower ΔT. For interpretation purposes, EG:EO ratio and CC were fixed at their respective mean values. The smallest predicted SD is 28% less than the largest predicted SD, which indicates that there is a substantial amount of variability transmitted to the product ratio DEG:TEG due to the variability in T, ΔT, EG:EO ratio, and CC, at the specified conditions. This result has a huge practical implication becuase it quantifies the uncertainty, which can be used in the over design of the reactor.

Figure 6 depicts the predicted contours of the DEG:TEG selectivity ratio as a function of T and ΔT. High selectivities are observed at high temperatures and high ΔT.

However, due to the dual responses, that is, mean and variance responses, dual response optimization may be performed. For example, the following engineering objectives may be of interest:

$$Max_{x,z} Y_{\mu|z}(x, z, \beta) \text{ subject to } Y_{\sigma|z}(x, z, \beta) \leq c \qquad (22)$$

where c is specified by the engineer. Figure 7 depicts the feasible area for criterion (22) for $c = 2.32$, but with a DEG:TEG ratio greater than 40. The contour overlay plot indicates the most sustainable operating area for minimizing the variability or uncertainty due to the variability in T, ΔT, EG:EO ratio, and CC, as well as maximizing the selectivity toward the product ratio simultaneously, at the specified conditions. Notice that these criteria are arbitrarily chosen for the current example. The overlaying plots were created using Design-Expert.[31]

There are many dual response optimization criteria other than (22) available in the literature that may be applied to robustness studies for nonlinear models as discussed in this Article.[32−36] However, this is left for a future publication; the main aim of this Article was to present the methodology of process robustness studies for nonlinear models.

A similar analysis was done for the product S-Heavies. The overlaying of contour plots obtained from the different response surface analysis often provides workable solutions for process improvement and design. Figure 8 presents a feasible operating area produced from overlaying different predicted contour plots for the SD and selectivity of the different products. The feasible area is for the following optimization criteria: maximize the selectivity toward a product ratio range between [40, 50], minimize the selectivity toward S-Heavies to be <0.0004%, and minimize the SD of DEG:TEG to be <2.3223, and the SD of S-Heavies to be <0.00003%.

Although these different criteria are chosen arbitrarily, it indicates typical objectives that would be valuable to engineering studies and design. Incorporating the standard errors of the kinetic constants in Table 1 in the robustness analysis will affect the feasible area obtained according to the different criteria. Therefore, in practice, the standard errors of the constants can be used to generate a confidence region at a certain confidence level for the optimum variable settings, which optimize specific design criteria in terms of performance and robustness.[15] Furthermore, although it was not addressed in the current Article, the uncertainty in the kinetic constants can also be used in reactor design and development.[2] However, the aim of the current Article was to illustrate that statistical robustness studies and development of robust processes form a very important part of process design, development, and improvement.

Concluding Remarks

In this Article, we presented the methodology of statistical robustness studies for nonlinear or fundamental models. It was

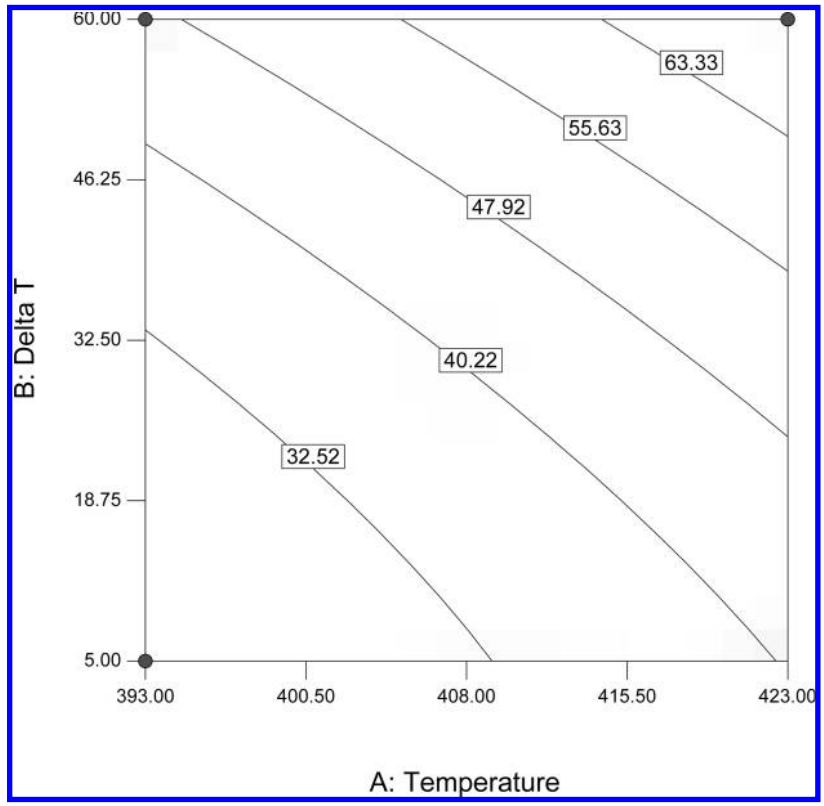

Figure 6. DEG:TEG selectivity ratio as a function of T and ΔT for EG:EO = 6 and CC = 0.06.

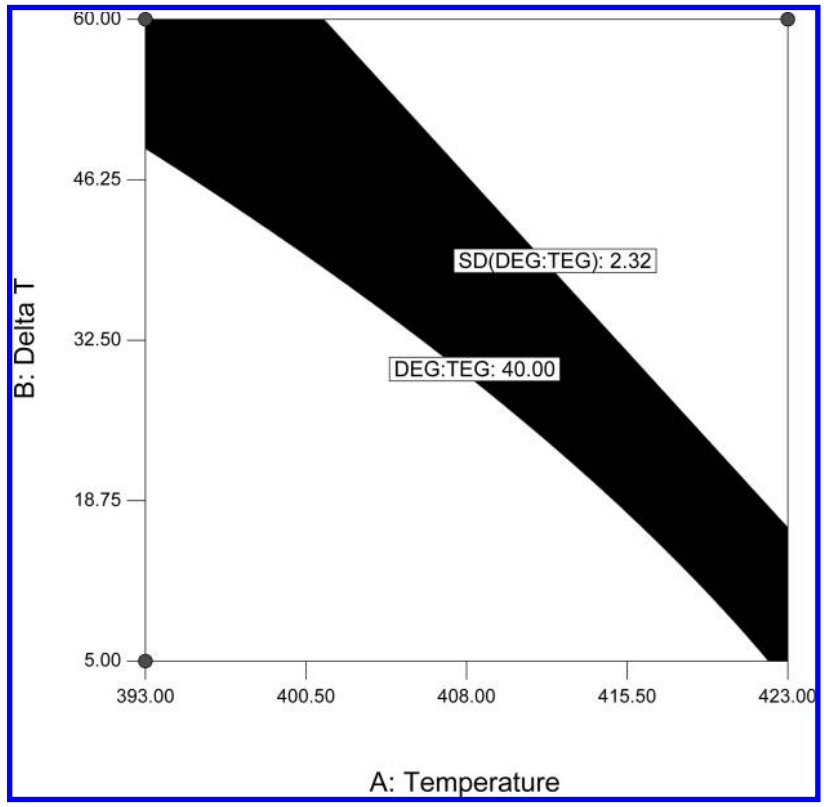

Figure 7. The feasible operating area for criterion (22) for $c = 2.32$, but with a DEG:TEG ratio greater than 40 (feasible area in black).

illustrated that process robustness studies can be utilized for processes not only described by models that are linear in the parameters, but also by models that are nonlinear in the parameters, such as kinetic models. Statistical robustness studies require the calculation of the variability transmitted to the outputs of the process or system due to the variability or uncertainty of the hard-to-control variables when the process is operational. We illustrated the use of computer experiments in combination with robustness studies and constructed approximation models for the mean response and the variance response models. We showed that Kriging and RS models perform similarly in terms of their predictive capability, but that

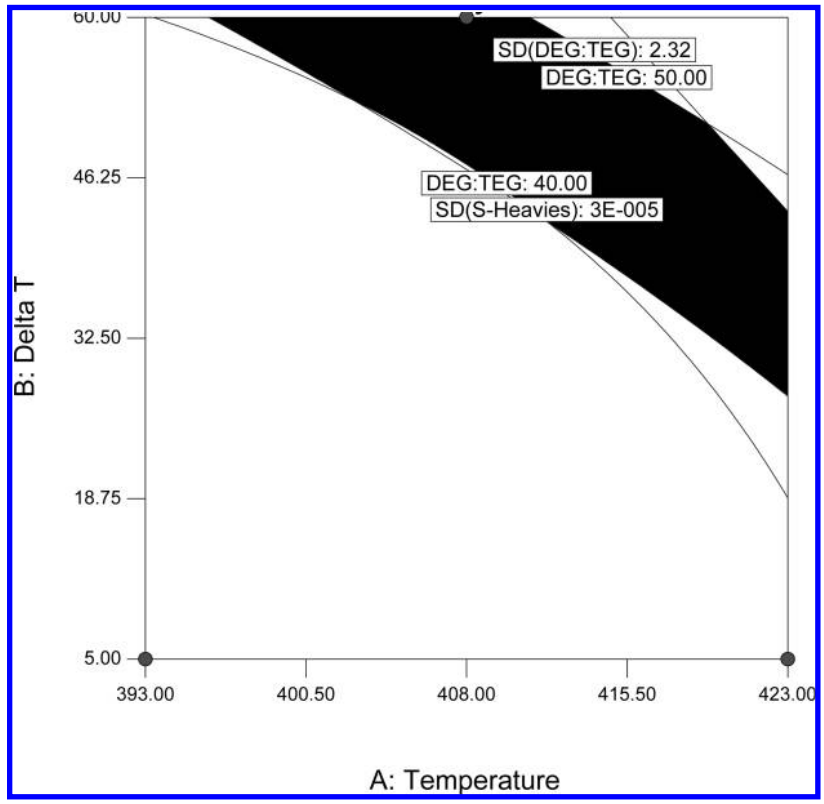

Figure 8. Contour overlay plot of the transmitted SD and selectivity of the calculated products, that is, DEG:TEG ratio and S-Heavies (feasible area in black).

the uniform designs outperform the CCD and the D-optimal design in the design and analysis of computer experiments.

The effective use of this methodology will result in quantifying the variability or uncertainty effect that hard-to-control process variables have on the outputs of processes during normal operation. This methodology, which makes use of kinetic equations, can lead to sustainable operating areas where the variability effect will be minimized. The methodology also enables interaction effects to be estimated. This is very valuable because the interactions between variables are not always easily identifiable from the form of the kinetic model. Interactions are also important in evaluating sustainable operating regimes.

An additional practical implication of statistical robustness studies is that it quantifies the convoluted effect of model uncertainty and model input deviation. The calculated uncertainty (SD) can then be used to over design equipment, rather than just using rules of thumb or gut feel to estimate the over design to incorporate. To effectively apply this analysis to real world problems would require that the standard deviation in process inputs be quantified. For instance, the EG:EO ratio in the case study could be controlled by two controllers controlling the flow rates of EG and EO to the reactor. The appropriate standard deviation to use would depend on the type of control equipment. Obviously, control equipment that allows tight control would result in less uncertainty or variability in the process; hence a smaller design contingency would be required. A SD analysis could then be used to quantify the cost of over design required versus different types of control systems, based on a known process model.

Topics for research can be identified following the methodology discussed in this paper. For example, the methodology, and the advantages, of statistical robustness studies must be more widely applied and published for engineering analysis and design. Alternative experimental designs may be developed for robustness studies, specifically, designs for dual response modeling for nonlinear models and complicated systems. Dual response optimization can be applied for robustness studies, and new methods may be developed that are more efficient for multiple optimization of responses generated from computer experiments.

Literature Cited

(1) Di Serrio, M. *Ind. Eng. Chem. Res.* **2002**, *41*, 5196–5206.
(2) Rooney, W.; Biegler, L. *Process Syst. Eng.* **2001**, *47*, 1794–1804.
(3) Montgomery, D. *The Statistician* **1999**, *48*, 159–177.
(4) Myers, R. *Communications in Statistics-Theory and Methods*; 1991; Vol. 20, pp 457−476.
(5) Lucas, J. *J. Quality Technol.* **1994**, *26*, 248–260.
(6) Taguchi, G. *Introduction to Quality Engineering*; UNIPUB: White Plains, NY, 1986.
(7) Simpson, T.; Lin, D.; Chen, W. *Int. J. Reliab. Appl.* **2002**, *2* (3), 209–240.
(8) Simpson, T.; Korte, J.; Mauery, T.; Mistree, F. 7th AIAA/USAF/NASA/ISSMO Symposium on Multidisciplinary Analysis and Optimization, AIAA-98-4755, 1998.
(9) Coetzer, R.; Keyser, M. *ORiON* **2004**, *20*, 89–108.
(10) Atkinson, A.; Donev, A. *Optimum Experimental Design*; Clarendon Press: Oxford, 1992.
(11) Atkinson, A.; Bogacka, B.; Bogacki, M. *Chemom. Intell. Lab. Syst.* **1998**, *43*, 185–198.
(12) Lehman, J.; Santner, T.; Notz, W. *Stat. Sinica* **2004**, *14*, 571–590.
(13) Isaacs, A. Sampling Strategies for Computer Experiments, Technical Report; Center of Aerospace Systems Design & Engineering, Indian Institute of Technology Bombay, Mumbai 400076, 2004.
(14) Montgomery, D. *Design and Analysis of Experiments*; John Wiley and Sons, Inc.: New York, 2001.
(15) Myers, R.; Montgomery, D. *Response Surface Methodology*; John Wiley and Sons, Inc.: New York, 1995.
(16) Fang, K.; Lin, D. Uniform experimental designs and their applications in industry. In *Handbook of Statistics*; Khattree, R., Rhao, C., Eds.; Elsevier Science: New York, 2003; Vol. 22, Chapter 4, pp 131−170.
(17) Fang, K. *Acta Math. Appl. Sinica* **1980**, *4*, 363–372.
(18) Fang, K.; Ma, C.; Maringer, D.; Tang, Y.; Winker, P. Available at http://www.math.hkbu.edu.hk/UniformDesign, 2003.
(19) Fang, K.; Lin, D.; Winker, P.; Zhang, Y. *Technometrics* **2000**, *42*, 237–248.

(20) Sacks, J.; Welch, W.; Mitchell, T.; Wynn, H. *Stat. Sci.* **1989**, *4*, 409–435.
(21) Dixon, L.; Szego, G. The global optimization problem: an introduction. In *Towards Global Optimization*; Dixon, L., Szego, G., Eds.; North Holland, Amsterdam, 1978; Vol. 2.
(22) Papadaki, M.; Gao, J. *Comput. Chem. Eng.* **2005**, *29*, 2449−2460.
(23) Katarel, S.; Bhan, A.; Caruthers, J.; Delgass, W.; Venkatasubramanian, V. *Comput. Chem. Eng.* **2004**, *28*, 2569–2581.
(24) Long, F.; Gevert, B. *Comput. Chem. Eng.* **2003**, *27*, 697–700.
(25) Xin, Y.; Vasquez, V.; Whiting, W. *Comput. Chem. Eng.* **2000**, *24*, 1269–1274.
(26) Kafarov, V.; Pisarenko, V.; Dallas, C.; Keil, F.; Duarte, L. *Comput. Chem. Eng.* **1998**, *22*, S663–S666.
(27) Press, W. *Numerical Recipes in Fortran*, 2nd ed.; Cambridge University Press: Cambridge, 1992.
(28) *R Development Core Team, R: A language and environment for statistical computing*; R Foundation for Statistical Computing: Vienna, Austria, 2004; ISBN 3-900051-00-3.
(29) Lophaven, S.; Nielsen, H.; Sondergaard, J. *DACE - A MATLAB Kriging Toolbox*; Technical University of Denmark, IMM-REP-2002-12, 2002.
(30) *MATLAB, R2009a*; The Mathworks, Inc.: Natick, Massachusetts, 2009.
(31) *Stat-Ease, "Design-Expert, Version 6.0.6*; Stat-Ease, Inc.: Minneapolis, MN, 2002.
(32) Coetzer, R.; Rossouw, R.; Lin, D. *Appl. Stat.* **2008**, *57*, 567–587.
(33) Vining, G.; Myers, R. *J. Quality Technol.* **1990**, *22*, 38–45.
(34) Lin, D.; Tu, W. *J. Quality Technol.* **1995**, *27*, 34–39.
(35) Kim, K.; Lin, D. *J. R. Stat. Soc., Ser. C (Appl. Stat.)* **2000**, *49*, 311–325.
(36) Kim, K.; Lin, D. *Eur. J. Operational Res.* **2006**, *169*, 133–145.

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