On the Statistical Sensitivity Analysis of Models for Chemical Kinetics

The differential equations governing the propagation in time of the sensitivity matrix for a mathematical model given by a system of ordinary differential equations are derived. These equations are used to perform a statistical sensitivity analysis of models for chemical reactors. The behavior of the sensitivities at equilibrium is analyzed. It is shown that the sensitivity equations for linear kinetics may be solved using an analytic representation. The numerical solution of these equations is discussed, and illustrative examples are presented. The lognormal distribution is presented as being representative of errors in rate constants.

R. W. ATHERTON
R. B. SCHAINKER
and
E. R. DUCOT

Systems Control, Inc.
1801 Page Mill Road
Palo Alto, California 94304

SCOPE

Chemical reactors may be modeled in terms of a set of nonlinear, ordinary differential equations. Our knowledge of the parameters of such a model (rate constants, initial conditions, or transport coefficients) is less than perfect. As a result, these parameters are described as having noise, being uncertain, or possessing error. Determining the sensitivity of the model output variables to parameter uncertainties depends upon the structure of the model and the extent of knowledge of the statistics of the parameters. In this paper a means of assessing the effect of parameter uncertainties upon the model output variables is presented.

The approach, statistical sensitivity analysis, is based upon Taylor series approximations for the variance and expected value of the output variables of the model. The first partial derivatives of the output variables with respect to each parameter are determined from the model structure. Determination of these derivatives, the sensitivity matrix, is the key to application of the technique.

The derivation of the differential equations describing a complete sensitivity matrix for each output variable with respect to each parameter is based upon the process application studies of Stepner and Mehra (1973), Mehra (1969), and Schainker et al. (1973b). Sensitivity of the model output to initial conditions is a well studied problem in differential equations (Hille, 1969).

An attempt has been made to study the sensitivity of a set of chemical reactions to uncertainties in the rate coefficients through a Fourier analysis (Cukier et al., 1973; Schaibly and Schuler, 1973). This method requires lengthy computations and contains theoretical ambiguities (Atherton et al., 1974b). Another reference in the area is that of Tumovic and Vukobratovic (1972), where a deterministic treatment of second-order periodic systems is presented.

CONCLUSIONS AND SIGNIFICANCE

This paper presents a methodology for the calculation of the variance of the output of kinetic models subject to uncertainties in reaction rate coefficients, energies of activation, temperature, rate law exponents, and initial conditions. The parameters contributing the most to the uncertainty in the model results are identified by rank-ordering the contributions over the entire time interval of interest. This paper furnishes a thorough, systematic study of the sensitivity of models for chemical kinetics to the parameters of the model.

This work is motivated by a study of stratospheric photochemistry, which is described in terms of a large set of chemical reactions. The model possesses an even larger number of parameters, including the rate constants, energies of activation, temperature (in the case of an isothermal reactor), rate law exponents, initial conditions, and transport parameters. The numerical values of these parameters are known imprecisely, and it is necessary to explore the question of how the parameter uncertainties propagate into output-variable uncertainties. The answer to this question is derived from an interesting blend of mathematical physics and statistics and provides the methodology for a statistical sensitivity analysis of a system of nonlinear, ordinary differential equations.

As described in the first section, the methods detailed here are applicable to the study of industrial reactors in which the rate law exponents are of an empirical nature. For such a reactor model, the variance of the model output would indicate the reliability of such expressions and the importance of determining more accurate values for such parameters. We will next present the statistical formulas which provide insight into the results. Then the derivation of the differential equations for a sensitivity matrix will be presented, and analysis of the behavior of that matrix at equilibrium will be presented. These results are of a general nature. Some simple models for chemical reactors will be analyzed using the above techniques. Two specific examples will be treated to illustrate the technique.

Application to industrial problems will be indicated and the use of the lognormal distribution will be discussed.

EXPRESSIONS FOR REACTION RATES

We begin by determining the context of this paper within the field of reactor design. In using the techniques presented in this paper, it is assumed that a set of chemical reactions has been chosen, that functional expressions for the rates $r_i(\mathbf{p})$ have been determined, and that the parameters $\mathbf{p}$ in these rate expressions have been identified. Then application of statistical sensitivity analysis determines the effect of errors in the parameters on the solution of the kinetic equations for the reactor model. In this discussion, we distinguish between reaction models r_i and reactor models given by Equation (1)

$$\frac{dc_j}{dt} = \sum_{i=1}^{R} \alpha_{ij}\, r_i(\mathbf{p}) \quad j = 1, \ldots N \tag{1}$$

Two very important steps not treated in this paper are the determination of the functional form for r_i, model discrimination, and the determination of values for the parameters $\mathbf{p}$, parameter identification. Both topics are treated in the text of Himmelblau (1970); and Kittrell (1970) has given a review of parameter identification for chemical reaction models. Both these steps are performed with the aid of experiments; consequently, the design of the experiments has great influence on the effort required. Box and Hill (1967) have presented a technique of sequential experimentation and model discrimination in which calculations made after each stage determine, for the next experiment, the process conditions that provide the most discrimination. A further refinement is given by Hill et al. (1968) in which both model discrimination and parameter estimation are performed sequentially with experiments. These techniques have been applied to pentane isomerization by Froment and Mezaki (1970).

Mezaki and Happel (1969) have pointed out the importance of using knowledge of physicochemical principles to postulate models that reflect the true physical processes. Otherwise the reaction model and parameters chosen may be statistically correct, but provide little insight into the physical processes. They thus discuss methods of formulating a set of rival models for the reaction rates.

To summarize, modeling of chemical reactors is the result of the sequential application and feedback of the following four steps:

1. Formulation of a set of rival reaction models.
2. Model discrimination.
3. Parameter identification.
4. Statistical sensitivity analysis.

STATISTICAL SENSITIVITY ANALYSIS

A statistical sensitivity analysis consists of computing the variance and the expected value of each model output and rank-ordering the contributions to the variance. The expected value $<X>$ of the output X can be represented by a Taylor series expansion for X about $\overline{X}$ its value at the mean value of the parameters (Hahn and Shapiro, 1967; Papoulis, 1965).

$$<X> = \overline{X} + 1/2 \sum_{i=1}^{n} \frac{\partial^2 X}{\partial p_i^2} \operatorname{var}(p_i) + \sum_{i} \sum_{\substack{j \\ i<j}} \frac{\partial^2 X}{\partial p_i \, \partial p_j} \operatorname{cov}(p_i, p_j) \tag{2}$$

where $\operatorname{var}(p_i) = \sigma^2(p_i)$

$$\operatorname{cov}(p_i, p_j) = <(p_i - <p_i>)\,(p_j - <p_j>)> \tag{3}$$

The variance of X may be represented similarly.

$$\operatorname{var}(X) = \sum_i \left(\frac{\partial X}{\partial p_i}\right)^2 \operatorname{var}(p_i) + 2 \sum_{i} \sum_{\substack{j \\ i<j}} \left(\frac{\partial X}{\partial p_i}\right)\left(\frac{\partial X}{\partial p_j}\right) \operatorname{cov}(p_i, p_j) + \sum_i \left(\frac{\partial X}{\partial p_i}\right)\left(\frac{\partial^2 X}{\partial p_i^2}\right) \mu_3(p_i) \tag{4}$$

where μ_3 is the third central moment.

In order to perform a statistical sensitivity analysis, we require the statistics of the parameters and the parameter derivatives of the model. The minimum information on the statistics of the parameters required for such an analysis is the mean value and standard deviation of each parameter. For parameters whose statistics are correlated, knowledge of the covariance matrix is required. Knowledge of higher central moments would allow computation of more terms in the approximation.

Values of the derivatives $\partial X/\partial p_i$ and $\partial^2 X/\partial p_i \, \partial p_j$ evaluated at the expected value of the parameter vector must be deduced from the mathematical structure of the model. When the relationship between the parameters and the function is given by an explicit algebraic relation, the statistical sensitivity analysis is very easy to perform. More complicated model structures as required for the chemical reactor preclude straightforward calculation of derivatives with respect to parameters.

Equation (4) may be simplified in two stages. If, for each parameter p_i, either $\mu_3(p_i)$ or $\partial^2 X/\partial p_i^2$ is zero or small in comparison with the leading terms, then the third term may be neglected and the approximation for the variance becomes

$$\operatorname{var}(X) = \sum_i \left(\frac{\partial X}{\partial p_i}\right)^2 \operatorname{var}(p_i) + 2 \sum_{i} \sum_{\substack{j \\ i<j}} \left(\frac{\partial X}{\partial p_i}\right)\left(\frac{\partial X}{\partial p_j}\right) \operatorname{cov}(p_i, p_j) \tag{5}$$

If the parameters p_i are uncorrelated, then the second term may be neglected as well, and Equation (4) reduces to the equation

$$\operatorname{var}(X) = \sum_i \left(\frac{\partial X}{\partial p_i}\right)^2 \operatorname{var}(p_i) \tag{6}$$

For a vector of output variables X_i the matrix of derivatives is designated as the sensitivity matrix ϕ_{ij}

$$\phi_{ij} \equiv \frac{\partial X_i}{\partial p_j} \tag{7}$$

The variance of the output indicates the magnitude of the effect of uncertainty in the parameters. As a source of uncertainty each parameter, in the case of Equation (6), contributes an amount ν_{ij} given by Schainker et al. (1973a).

$$\nu_{ij} = \phi_{ij}^2 \operatorname{var}(p_j) \tag{8}$$

The relative effect of the uncertainty in each parameter is determined by ranking the contributions to the variance in the order of their magnitudes. Since ν_{ij} is positive, the

$\max_{j} \nu_{ij}$ indicates the key parameter for the ith variable.

Caution must be exercised in the choice of the very simple Equation (6) over Equation (5). The covariances are of overriding significance and are rarely negligible in real problems, especially chemical kinetics (Ware, 1974). At the completion of the parameter estimation stage of the analysis, the covariance matrix provided by the estimation procedure should be examined closely. Neglect of the covariances and use only of the variances, the diagonal terms, can result in a substantial error in the value obtained for the variance of the output. The uncertainty can be either much better or much worse when using the full covariance matrix than when using the variances alone.

THE SENSITIVITY MATRIX

A statistical sensitivity analysis for model output **c** requires knowledge of the matrix

$$\left[\frac{\partial c_i}{\partial p_j}\right] = \frac{\partial \mathbf{c}}{\partial \mathbf{p}} \tag{9}$$

The information provided by the model must be used to determine $\partial\mathbf{c}/\partial\mathbf{p}$. The class of models for chemical kinetics under study is described by the initial value problem for a set of ordinary differential equations for concentration **c**

$$\frac{d\mathbf{c}}{dt} = \mathbf{f}(\mathbf{c}, \mathbf{p}) \quad \mathbf{c}|_{t=0} = \mathbf{c}(0) \tag{10}$$

f need not be linear.

In order to calculate the sensitivity matrix, it must be related to the model. To do so, interchange the order of differentiation in the expression below and use Equation (10).

$$\frac{d}{dt}\left(\frac{\partial \mathbf{c}}{\partial \mathbf{p}}\right) = \frac{\partial}{\partial \mathbf{p}}\left(\frac{d\mathbf{c}}{dt}\right) = \frac{\partial}{\partial \mathbf{p}}\,\mathbf{f}(\mathbf{c}, \mathbf{p}) \tag{11}$$

Since **c** is a function of **p**, the right-hand expression is expanded to give

$$\frac{d}{dt}\left(\frac{\partial \mathbf{c}}{\partial \mathbf{p}}\right) = \left(\frac{\partial \mathbf{f}}{\partial \mathbf{c}}\right)\bigg|_{\mathbf{p}}\left(\frac{\partial \mathbf{c}}{\partial \mathbf{p}}\right) + \left(\frac{\partial \mathbf{f}}{\partial \mathbf{p}}\right)\bigg|_{\mathbf{c}} \tag{12}$$

The matrices of derivatives are defined in the usual manner as in Equation (9). For simplicity, we introduce ϕ_{ij} defined as in Equation (7). Equation (12) may be written in subscript notation as

$$\frac{d}{dt}\phi_{ij} = \sum_{l} \frac{\partial f_i}{\partial c_l}\phi_{lj} + \frac{\partial f_i}{\partial p_j} \tag{13}$$

To determine the initial conditions for Equation (12), we note that at $t = 0$

$$\frac{\partial c_i(0)}{\partial c_j(0)} = \delta_{ij};\ \frac{\partial c_i(0)}{\partial p_k} = 0 \tag{14}$$

These conditions are summarized as

$$\phi_{ij}(0) = \begin{cases} 0 & \text{if } p_j \text{ is not an initial condition} \\ \delta_{ij} & \text{if } p_j \text{ is an initial condition} \end{cases} \tag{15}$$

Equations (13) and (15) give a set of differential equations whose solution determines the sensitivity matrix as a function of time. The number of equations is the product of the size of the state and the number of parameters. Each equation is linear in the ϕ_{ij} and has variable coefficients which are determined by the state **c**.

Solution of the sensitivity equations gives a complete time history of the parameter derivatives and provides information necessary to determine the variance as given by Equations (5) or (6) and the contributions to the variance. In order to use the more general expression for the variance given in Equation (4), knowledge of $\partial^2 c_i/\partial p_k \partial p_j$ is required. A differential equation governing the time propagation of this array has been derived in a manner analogous to Equation (13). The derivation of the equations governing sensitivity is valid for an arbitrary set of differential equations.

To illustrate the simplicity and utility of the ideas involved, a statistical sensitivity analysis for a model of a single first-order reaction is given in Appendix A. Specific application to more general models is given in the following section.

LINEAR KINETICS IN GENERAL

The equations for the sensitivity matrix for the case of linear kinetics can be solved exactly. Let the kinetics of an independent set of reactions be described by

$$\frac{d\mathbf{c}}{dt} = \mathbf{A}\mathbf{c} \tag{16}$$

The dynamics of Equation (16) have been treated in detail by Wei and Prater (1962). Define a vector of sensitivities $\boldsymbol{\varphi}_j$ by

$$\boldsymbol{\varphi}_j = \frac{\partial \mathbf{c}}{p_j} \tag{17}$$

Then $\boldsymbol{\varphi}_j$ is governed by

$$\frac{d}{dt}\boldsymbol{\varphi}_j = \mathbf{A}\,\boldsymbol{\varphi}_j + \frac{\partial \mathbf{A}}{\partial p_j}\mathbf{c} \tag{18}$$

Note that both the state and the sensitivity are governed by the operator A. This result is an example of a more general theorem for linear operators (Atherton, 1974).

The solution for Equation (18) via the usual techniques (DeRusso et al., 1965) is

$$\boldsymbol{\varphi}_j = e^{\mathbf{A}t}\int_0^t e^{-\mathbf{A}\tau}\frac{\partial \mathbf{A}}{\partial p_j}\mathbf{c}\,d\tau + e^{\mathbf{A}t}\boldsymbol{\varphi}_j(0) \tag{19}$$

If the parameters consist of rate constants and initial conditions only, the solution can be simplified. If p_j is a rate constant, then its initial vector is zero, and the second term in the equation is zero.

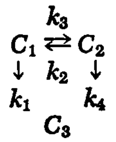
$$\boldsymbol{\varphi}_j = e^{\mathbf{A}t}\int_0^t e^{-\mathbf{A}\tau}\frac{\partial \mathbf{A}}{\partial p_j}\mathbf{c}\,d\tau \tag{20}$$

If p_j is an initial condition, then the integral is zero since its integrand is zero. Thus

$$\boldsymbol{\varphi}_j = e^{\mathbf{A}t}\boldsymbol{\varphi}_j(0) \tag{21}$$

LINEAR KINETICS—AN EXAMPLE

Consider the following set of four reactions in three components.



$$\begin{array}{ccc} & k_3 & \\ C_1 & \rightleftarrows & C_2 \\ \downarrow & k_2 & \downarrow \\ k_1 & & k_4 \\ & C_3 & \end{array} \tag{22}$$

An independent set of equations is given by

$$\frac{d}{dt}\begin{bmatrix} c_1 \\ c_2 \end{bmatrix} = \begin{bmatrix} -(k_1 + k_3) & k_2 \\ k_3 & -(k_2 + k_4) \end{bmatrix}\begin{bmatrix} c_1 \\ c_2 \end{bmatrix} \tag{23}$$

And the kinetic equation for c_3 is

$$\frac{dc_3}{dt} = k_1\, c_1 + k_4\, c_2 \tag{24}$$

Numerical values will be assigned to the rate constants and initial conditions.

$$\begin{aligned}(k_1, k_2, k_3, k_4) &= (1, 499.5, 499.5, 1)\\ \mathbf{c}(0)^T &= (2, 1, 0)\end{aligned} \tag{25}$$

The equations are in the form of Equation (16) where

$$A = \begin{bmatrix} -500.5 & 499.5 \\ 499.5 & -500.5 \end{bmatrix} \tag{26}$$

The particular choice of k's is designed to give a set of differential equations which is known to be stiff (Seinfeld, 1971), a point to be emphasized in a later section.

The problem has seven parameters, four rate constants and three initial conditions. The 21 sensitivities are given in Appendix B and illustrated in Figure 1. Note that the sensitivity function typically attains a maximum.

Since an explicit solution exists for linear kinetics, it might appear that the sensitivities could be obtained by direct differentiation; however, it is more difficult to differentiate the dependence of the eigenvalues and modal matrices on the rate constants than to calculate the sensitivity matrix using the methods of this paper. Attempting the first procedure on this example will illuminate this point (see Wei and Prater, 1962).

Naturally, the behavior of the sensitivity functions is strongly coupled to the behavior of the state. The properties of the sensitivities can be explained in terms of the behavior of the state. For instance, c_1 and c_2 attain equilibrium; after equilibrium is reached, the sensitivities are equal. The forms of $\partial c_1/\partial k_2$, $\partial c_2/\partial k_2$, $\partial c_1/\partial k_3$, $\partial c_2/\partial k_3$ are similar, and so are the forms of $\partial c_1/\partial k_1$, $\partial c_2/\partial k_1$, $\partial c_1/\partial k_4$, $\partial c_2/\partial k_4$.

Reasoning from the chemistry of the reaction set, c_3 does not depend upon k_2 or k_3; consequently, it is not surprising that the corresponding sensitivities are zero.

Because of its utility in atmospheric photochemistry, we have chosen to work in concentration units. To this point there is no ambiguity in considering the independent variable $\mathbf{c}$ as a mole fraction. We now make use of the fact that $\mathbf{c}$ is a concentration and note that conservation of mass yields the following seven consistency relations among the 21 sensitivity functions:

$$\frac{\partial(\sum\limits_i c_i)}{\partial k_j} = 0, \quad j = 1, 4 \tag{27}$$

$$\frac{\partial(\sum\limits_i c_i)}{\partial c_j(0)} = 1, \quad j = 1, 3 \tag{28}$$

There is redundancy in the equations, and the choice is between efficient computation and retaining a set of checks on the result. Indeed, use of Equation (27) and the values in Appendix B for the appropriate sensitivities for c_1 and c_2 results in the following:

$$\frac{\partial c_3}{\partial k_l} = -\left(\frac{\partial c_1}{\partial k_l} + \frac{\partial c_2}{\partial k_l}\right) = 0, \quad l = 2, 3 \text{ only} \tag{29}$$

Before leaving this example, we shall consider the effect of the covariance terms on the variance of the model output. Two covariance matrices are given in Equations (30) and (31).

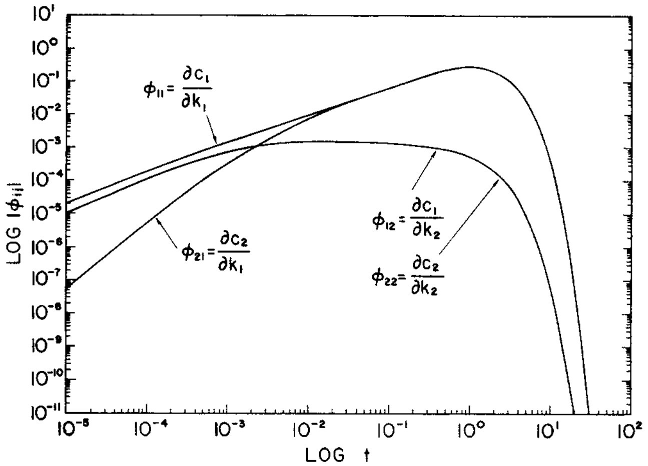


Fig. 1. Plot of $|\phi_{ij}|$ for linear kinetics example.

$$\text{cov}\,(k_i, k_j) = \begin{bmatrix} .04 & 0 & 0 & .01 \\ 0 & 4 \times 10^4 & 10^4 & 0 \\ 0 & 10^4 & 4 \times 10^4 & 0 \\ .01 & 0 & 0 & .04 \end{bmatrix} \tag{30}$$

$$\text{cov}\,(k_i, k_j) = \begin{bmatrix} .04 & 0 & 0 & -.01 \\ 0 & 4 \times 10^4 & -10^4 & 0 \\ 0 & -10^4 & 4 \times 10^4 & 0 \\ -.01 & 0 & 0 & .04 \end{bmatrix} \tag{31}$$

We consider three cases. The computation of Case I uses Equation (5) and the full covariance matrix as given in Equation (30). Case II uses only the diagonal terms of the covariance matrix and can be computed using Equation (6). Case III uses the full covariance matrix of Equation (31). It is obvious that Case I $\geqq$ Case II $\geqq$ Case III for all c_i and all time. For instance we calculate $\text{Var}(c_1)$ at $t = 0.05$ as respectively 0.2041, 0.1633, 0.1225. This example shows the importance of using the covariance terms when the variables are correlated.

NONLINEAR REACTOR MODELS

Equation (1) gives a general nonlinear model for a chemical reactor. As discussed in the first section on expressions for reaction rates, the functional form of the reactor model depends upon the rate expressions r_i developed after model discrimination. Several functional forms used in kinetic studies are discussed in the six papers cited in that section. In this section, as an example, all reaction rates r_i are represented by generalized polynomials.

$$r_i = k_i \prod_{l=1}^{N} c_l^{\gamma_{il}} \tag{32}$$

In particular, Equations (1) and (32) define a model for an isothermal, constant-volume batch reactor (Aris, 1965). Detailed theoretical considerations of the mathematical properties of these models are provided by Gavalas (1968).

The reaction rate constant k_i may be given more generally by

$$k_i = k_{0i}\left(\frac{1}{T}\right)^{b_i} \exp\,(-E_i/T) \tag{33}$$

where E_i is the energy of activation of reaction i. Thus, the parameter k_i is in turn a function of the parameters, T, b_i, k_{0i}, E_i. $\sigma(k_i)$ can be calculated via the expressions for the variance (4) to (6). Since these parameters are often correlated, care should be exercised in the treatment of the covariances. Further details of the application of statistical sensitivity analysis are given in Appendix C.

In particular if all rates follow the law of mass action, then

$$\gamma_{ij} = \begin{cases} |\alpha_{ij}| & \text{if } \alpha_{ij} < 0 \\ 0 & \text{otherwise} \end{cases} \tag{34}$$

If there is no uncertainty in $\boldsymbol{\gamma}$, the parameters (for this model) are the R rate coefficients and N initial conditions. The parameters γ_{ij} will have uncertainty if they are determined empirically. Although treating uncertainty in $\boldsymbol{\gamma}$ increases the size of the problem, no essential difficulties are introduced.

To perform a sensitivity analysis of this nonlinear model, Equation (13) must be constructed for each class of parameter. The appropriate terms are given in Appendix C. The solution of these equations is presented in the next section.

COMPUTATION OF SENSITIVITY FUNCTIONS

In the two examples mentioned previously, it was shown that when a formal solution is known, the sensitivity functions may be found by direct differentiation. In the second example, however, it was easier to solve the sensitivity equations directly.

For large sets of reactions, especially those that are nonlinear, the model output variables must be solved numerically. One method of solution is to represent $\partial c_i/\partial p_j$ as a finite difference and compute values of the state for small changes in the parameter vector. A better method is to solve the differential equations for the sensitivity functions numerically. The first method is less accurate and requires at least as many integrations as a direct computation (Atherton et al., 1974).

It is well known that the differential equations for chemical kinetics are often stiff (Gelinas, 1972) in the numerical sense. Consequently, these equations must be solved using an appropriate numerical method, such as that of Gear (1969). The linear example in the previous section was chosen to reflect as much as possible the problems of real chemical systems, particularly stiffness. Numerical studies of that example have been performed using the method of Gear. It was anticipated that the sensitivity equations would be stiff as well. In practice this proved to be the case.

It is possible to structure the calculation so that a simultaneous solution of both the state and sensitivities is obtained. Large systems, however, require that the state be calculated first, stored, and then used to calculate subsets of sensitivities in subsequent runs. The above numerical methods were used in a study of the nonlinear kinetics of a set of 40 reactions representing stratospheric photochemistry (Atherton et al., 1974a).

SENSITIVITY AT EQUILIBRIUM

The solution of differential equations given by Equation (1), if it is a model for a chemical reactor, has equilibrium points (Gavalas, 1968). At equilibrium the equations for sensitivity are algebraic, and it is of interest to determine whether the sensitivities at equilibrium are the limit in time of the dynamic sensitivities.

Theorem 1

Let the following be true:

The solution for Equation (1) has an equilibrium point and $\lim_{t\to\infty} \mathbf{c}(t) = \mathbf{c}^{(e)}$ uniformly in $\mathbf{p}$.

Then

$$\lim_{t\to\infty} \frac{\partial c_i}{\partial p_j} = \frac{\partial c_i^{(e)}}{\partial p_j} \tag{35}$$

Proof: The theorem follows immediately after interchange of the limiting processes for time and differentiation. For a scalar parameter b

$$\lim_{t\to\infty} \lim_{\Delta p\to 0} \left[\frac{c_i(t, p + \Delta p) - c_i(t, 0)}{\Delta p} \right]$$

$$= \lim_{\Delta p\to 0} \frac{1}{\Delta p} \lim_{t\to\infty} [c_i(t, p + \Delta p) - c_i(t, p)].$$

A theorem due to Moore (Jeffries and Jeffries, 1972) then states that the limits are equal. Note that in the derivation of Equation (13) it has been assumed that $\mathbf{c}(t)$, $\partial \mathbf{c}/\partial t$, and $\partial \mathbf{c}/\partial \mathbf{p}$ are all continuous functions.

With regard to the variances as defined in Equations (5) or (6), we have the following corollary:

Corollary: Let Theorem 1 be true, and the variance defined by Equations (5) or (6), then the limit as $t \to \infty$ of the variance, is the variance of the equilibrium state.

$$\lim_{t\to\infty} \text{var}\,(c_j) = \text{var}\,(c_j^{(e)}) \tag{37}$$

The simple example in Appendix A and the example of linear kinetics both provide examples of these results.

LOGNORMAL ERROR DISTRIBUTIONS

Since the expression for the variance is based upon a Taylor series approximation, the question arises as to how to treat problems in which the errors are given in terms of a multiple of the nominal value. The answer is simply to treat parameters with this type of error distribution in terms of their logarithms: $\ln(p_j) \pm \sigma(\ln(p_j))$. Thus, we use the logarithmic transformation,

$$\tilde{p}_j = \ln p_j$$

Its inverse

$$p_j = \exp \tilde{p}_j \tag{38}$$

is substituted into the defining equations, and a new model is defined.

The sensitivity equations are then derived for the transformed model (see Appendix D). The only formal difference occurs when initial conditions for the model are transformed. In that case, the initial conditions for the sensitivity equation for the state initial condition will be changed.

$$\frac{\partial c_i}{\partial p_j} = \begin{cases} \delta_{ij} \exp \tilde{c}_j(0) \text{ (no sum) if } p_j \text{ is an initial condition} \\ 0 \text{ otherwise} \end{cases} \tag{39}$$

The errors for rate constants are often given in terms of a multiplicative factor (Garvin and Hampson, 1974). If that is the case, the lognormal distribution (Atchison and Brown, 1963) is the natural representation for rate constants and their error distribution. Indeed, that the errors are multiplicative in nature is a necessary condition for the error distribution to be lognormal. The lognormal distribution is given by

$$d\Lambda(x) = \frac{1}{x\sigma\sqrt{2\pi}} \exp\left\{ -\frac{1}{2\sigma^2} (\ln x - \langle \ln x \rangle)^2 \right\} dx \tag{40}$$

$$\Lambda(x) = \int_0^x d\Lambda(x') \tag{41}$$

As an example let $k = 2.2 \times 10^4$ with an error of a factor of 2. This fact is more easily represented by

$$\ln k = 10. \pm .69 \qquad (42)$$

if it is assumed that k is represented by a lognormal distribution.

To interpret further what this observation means, it is of interest to calculate the value of k with the highest probability, the mode; the expected value of k, the mean; and the value of k at which there is a 50% chance the true value of k is higher or lower. These are, respectively,

$$k_{\max} = \exp\left(<\tilde{k}> - \sigma^2(\tilde{k})\right) = 1.4 \times 10^4 \qquad (43)$$

$$<k> = \exp\left(<\tilde{k}> + 1/2\,\sigma^2(\tilde{k})\right) = 2.8 \times 10^4 \qquad (44)$$

$$k_{50} = \exp\left(<\tilde{k}>\right) = 2.2 \times 10^4 \qquad (45)$$

The relative position of these quantities is illustrated on the typical lognormal distribution shown in Figure 2.

A result that may be surprising is that the expected value for k, treated as having a lognormal distribution, is greater than the nominal value or the median. The difference increases with the variance. From a statistical viewpoint the expected value of k best characterizes the value of the reaction rate. Unfortunately the median, the reported nominal value, is often used in modeling instead.

CONCLUSION

This paper has shown how the effects of uncertainty in the state of information of the parameters of a kinetic model can be quantitatively assessed. Only the expressions for the variance and mean value contain approximations. Indeed, the development is valid for any set of ordinary differential equations. The sensitivity matrix is obtained for the entire time interval of interest; thus, the variance is available as a function of time. Analysis reveals that the sensitivity matrix and the variance have the proper behavior at equilibrium and that linear kinetics have an exact analytic representation.

The results of this paper provide valuable tools in the study of industrial reactors where there is large uncertainty in the rate constants and even in the rate law exponents. Not only does the variance indicate the effect of those errors on the model output, but the contributions to the variance indicate the value of improved knowledge of particular parameters and aid in the choice of new experiments.

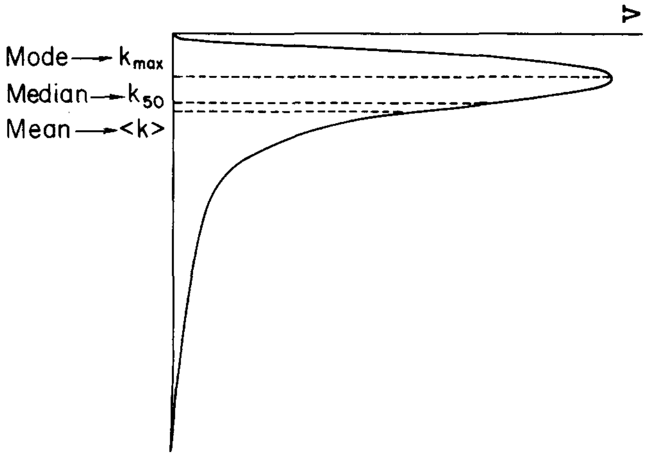


Fig. 2. The lognormal distribution.

ACKNOWLEDGMENT

This work was partially supported by a contract under the Climatic Impact Assessment Program, Office of the Secretary, Department of Transportation. We gratefully thank Dr. Alan Grobecker, Manager, C.I.A.P. for his interest in this work.

NOTATION

A = linear kinetic operator
b = exponent, see (33)
C = compound
$\mathbf{c}$ = concentration
E = energy of activation
$\mathbf{f}$ = function of state variables, see (10)
k = rate constant
k_0 = pre-exponential term
$k_{\max}$ = mode, see (43)
k_{50} = median, see (45)
N = number of compounds
$\mathbf{p}$ = parameter
R = number of reactions
r = rate of reaction
t = time
T = temperature
X = output variable

Greek Letters

α = stoichiometric coefficients
γ = rate law exponents
φ = sensitivity matrix
ν = variance contributions
δ_{ij} = Kronecker delta
Λ = lognormal distribution
μ_3 = third central moment

Operators

$<c>$ = expected value
var (c) = variance of c
$\sigma(c)$ = one standard deviation of c
Δc = increment
$\tilde{c}$ = $\ln c$

Superscripts

$C^{(e)}$ = equilibrium

LITERATURE CITED

Aitchison, J., and J. A. C. Brown, *The Lognormal Distribution*, Cambridge Univ. Press, England (1963).

Aris, Rutherford, *Introduction to the Analysis of Chemical Reactors*, pp. 7-114, Prentice Hall, Englewood Cliffs, N. J. (1965).

Atherton, R. W., "Sensitivity Analysis for Systems of Partial Differential Equations," submitted to *S.I.A.M. J. Appl. Math.* (1974).

Atherton, R. W., E. R. Ducot, and R. B. Schainker, "Statistical Sensitivity Analysis of Atmospheric Models," AMS/AIAA 2nd Intern. Conf. on the Environmental Impact of Aerospace Operations in the High Atmosphere, San Diego (1974a).

Atherton, R. W., R. B. Schainker, and E. R. Ducot, "A Comparison of Methods for the Sensitivity Analysis of Models for Chemical Kinetics," submitted to *J. Chem. Phys.* (1974b).

Box, G. E. P., and W. J. Hill, "Discrimination Among Mechanistic Models," *Technomet.*, 9, 57 (1967).

Cukier, R. I., C. M. Fortuin, K. E. Schuler, A. G. Petschek, and J. H. Schaibly, "Study of the Sensitivity of Coupled Reaction Systems to Uncertainties in Rate Coefficients, I. Theory," *J. Chem. Phys.*, 59, 3873 (1973).

DeRuso, Paul M., R. J. Roy, and C. M. Close. *State Variables for Engineers*, pp. 192-290, Wiley, New York (1967).

Froment, G. F., and R. Mezaki, "Sequential Discrimination and Estimation Procedures for Rate Modeling in Heterogeneous Catalysis," *Chem. Eng. Sci.*, 25, 293 (1970).

Gavalas, George R., *Nonlinear Differential Equations of Chem-*

ically Reacting Systems, Springer-Verlag, New York (1968).

Garvin, D., and R. F. Hampson, "Chemical Kinetics Data Survey, VII. Tables of Rate and Photochemical Data for Modeling of the Stratosphere (Revised)," NBSIR 74430, National Bureau of Standards, Washington, D. C. (1974).

Gear, C. W., "The Automatic Integration of Stiff Ordinary Differential Equations," *Information Processing 68,* A. J. Morrell (ed.), North Holland, Amsterdam (1969).

Gelinas, R. J., "Stiff Systems of Kinetic Equations—A Practitioner's View," *J. Comp. Phys.,* **9,** 222 (1972).

Hahn, G. J., and S. S. Shapiro, *Statistical Models in Engineering,* pp. 252-257, Wiley, New York (1967).

Himmelblau, David M., *Process Analysis by Statistical Methods,* Wiley, New York (1970).

Hill, W. J., W. G. Hunter, and D. W. Wichern, "A Joint Design Criterion for the Dual Problem of Model Discrimination and Parameter Estimation," *Technomet.,* **10,** 145 (1968).

Hille, Einar, *Lectures on Ordinary Differential Equations,* pp. 76-80, Addison-Wesley, Menlo Park, Calif. (1969).

Jeffreys, H., and B. S. Jeffreys, *Methods of Mathematical Physics,* p. 48, Cambridge University Press (1972).

Kittrell, J. R., "Mathematical Modeling of Chemical Reactions," *Adv. Chem. Eng.,* **8,** 97 (1970).

Mehra, R. K., "On the Identification of Variance and Adaptive Kalman Filtering," *IEEE Trans. Automatic Control,* **15,** 175 (1969).

Mezaki, R., and J. Happel, "Identification of Rate Models for Solid Catalyzed Gaseous Reactions," *Catalysis Reviews,* **3,** 241 (1969).

Papoulis, A., *Probability Random Variables and Stochastic Processes,* McGraw-Hill, New York (1965).

Schaibly, J. H., and K. E. Schuler, "A Study of the Sensitivity of Coupled Reaction Systems to Uncertainties in Rate Coefficients, II, Applications," *J. Chem. Phys.,* **59,** 3879 (1973).

Schainker, R. B., T. R. Ranweiler, and A. J. Tether, "Sensitivity Assessment of Parameter Uncertainties in Climatic Forecast Models," Proc. the Sixth Hawaii Intern. Conf. on Systems Sciences, Western Periodicals Co. (1973a).

Schainker, R. B., D. Stepner, and C. Wells, "Mathematical Modeling of Photo Chemical Smog—Phase I," Technical Report for Systems Applications, Inc., Systems Control, Inc., Palo Alto, Calif. (1973b).

Seinfeld, John H., T. A. Hecht, and P. M. Roth, "A Kinetic Mechanism for Atmospheric Photochemical Reactions," Appendix B of "Development of a Simulation Model for Estimating Ground Level Concentrations of Photochemical Pollutants," NTIS, Springfield, Va. (1971).

Stepner, D. E., and R. K. Mehra, "Maximum Likelihood Identification and Optimal Input Design for Identifying Aircraft Stability Derivatives," ASA Contract Report CR-2200 (1973).

Tumovic, R., and M. Vukobratovic, *General Sensitivity Theory,* Elsevier, New York (1972).

Ware, C. W., private communications (1974).

Wei, J., and C. D. Prater, "The Structure and Analysis of Complex Reaction Systems," *Adv. Cat.,* **13,** 302 (1962).

APPENDIX A. A SIMPLE EXAMPLE

To illustrate the simplicity and the utility of the ideas involved, a single first-order reaction, the simplest possible kinetics, will be treated.

$$C_1 \overset{k}{\rightarrow} C_2 \tag{A1}$$

The kinetics are given by

$$\frac{dc_1}{dt} = -kc_1 \tag{A2}$$

$$\frac{dc_2}{dt} = kc_1 \tag{A3}$$

The equations governing the sensitivities are as follows:

$$\frac{d}{dt}\left(\frac{\partial c_1}{\partial k}\right) = -k\left(\frac{\partial c_1}{\partial k}\right) - c_1; \quad \left(\frac{\partial c_1}{\partial k}\right)\Bigg|_{t=0} = 0 \tag{A4}$$

$$\frac{d}{dt}\left(\frac{\partial c_1}{\partial c_1(0)}\right) = -k\left(\frac{\partial c_1}{\partial c_1(0)}\right); \quad \left(\frac{\partial c_1}{\partial c_1(0)}\right)\Bigg|_{t=0} = 1 \tag{A5}$$

$$\frac{d}{dt}\left(\frac{\partial c_1}{\partial c_2(0)}\right) = -k\left(\frac{\partial c_1}{\partial c_2(0)}\right); \quad \left(\frac{\partial c_1}{\partial c_2(0)}\right)\Bigg|_{t=0} = 0 \tag{A6}$$

$$\frac{d}{dt}\left(\frac{\partial c_2}{\partial k}\right) = k\frac{\partial c_1}{\partial k} + c_1; \quad \left(\frac{\partial c_2}{\partial k}\right)\Bigg|_{t=0} = 0 \tag{A7}$$

$$\frac{d}{dt}\left(\frac{\partial c_2}{\partial c_1(0)}\right) = k\frac{\partial c_1}{\partial c_1(0)}; \quad \left(\frac{\partial c_2}{\partial c_1(0)}\right)\Bigg|_{t=0} = 0 \tag{A8}$$

$$\frac{d}{dt}\left(\frac{\partial c_2}{\partial c_2(0)}\right) = k\frac{\partial c_1}{\partial c_2(0)}; \quad \left(\frac{\partial c_2}{\partial c_2(0)}\right)\Bigg|_{t=0} = 1 \tag{A9}$$

The solutions to the state and the sensitivities are as follows:

$$c_1 = c_1(0)\ e^{-kt} \tag{A10}$$

$$c_2 = c_1(0)\ (1 - e^{-kt}) + c_2(0) \tag{A11}$$

$$\left(\frac{\partial c_1}{\partial k}\right) = -c_1(0)\ te^{-kt} \tag{A12}$$

$$\left(\frac{\partial c_1}{\partial c_1(0)}\right) = e^{-kt} \tag{A13}$$

$$\left(\frac{\partial c_1}{\partial c_2(0)}\right) = 0 \tag{A14}$$

$$\left(\frac{\partial c_2}{\partial k}\right) = c_1(0)\ te^{-kt} \tag{A15}$$

$$\left(\frac{\partial c_2}{\partial c_1(0)}\right) = 1 - e^{-kt} \tag{A16}$$

$$\left(\frac{\partial c_2}{\partial c_2(0)}\right) = 1 \tag{A17}$$

Obviously, with this simple system the easiest approach is to solve for c_1 and c_2 and then obtain the sensitivity matrix directly. It may be verified that solution of the differential equations gives the same result.

It is also clear that only the equations for one state need be solved since the others may be obtained from considerations of conservation of mass. Conservation of mass implies that the following hold:

$$\left(\frac{\partial c_1}{\partial k}\right) + \left(\frac{\partial c_2}{\partial k}\right) = 0 \tag{A18}$$

$$\left(\frac{\partial c_1}{\partial c_1(0)}\right) + \left(\frac{\partial c_2}{\partial c_1(0)}\right) = 1 \tag{A19}$$

$$\left(\frac{\partial c_1}{\partial c_2(0)}\right) + \left(\frac{\partial c_2}{\partial c_2(0)}\right) = 1 \tag{A20}$$

In solving large, complex problems, usually numerically, it may be preferable to compute the sensitivities directly from the differential equations and retain the relations deduced from mass conservation above as consistency checks on the results. To apply the sensitivity analysis, we compute the variance:

$$\text{var}\ (c_1) = [c_1(0)\ t\ e^{-kt}]^2\ \text{var}\ (k) + e^{-2kt}\ \text{var}\ (c_1(0)) \tag{A21}$$

$$\text{var}\ (c_2) = [c_1(0)\ t\ e^{-kt}]^2\ \text{var}\ (k) + (1 - e^{-kt})^2\ \text{var}\ (c_1(0)) + \text{var}\ c_2(0) \tag{A22}$$

The final step in the analysis is to rank order the ν_{ij}, and to determine the parameter whose error is most significant.

Note that

$$\lim_{t\to\infty} \text{var}\ (c_1) = 0 \tag{A23}$$

$$\lim_{t\to\infty} \text{var}\,(c_2) = \text{var}\,(c_1(0)) + \text{var}\,(c_2(0)) \qquad \text{(A24)}$$

These limits must necessarily coincide with the equilibrium state. Physically the chemical reaction converts all mass to C_2. This implies that, regardless of the values of k $(k > 0)$ and the initial conditions, c_1 must approach zero for long times; hence, there is no uncertainty in the equilibrium value for c_1. Similarly, since all mass is converted to C_2, the uncertainty in c_2 is the sum of the uncertainties in the initial conditions.

APPENDIX B. SOLUTION FOR LINEAR EXAMPLE

State

$$c_1 = 1.5\,e^{-t} + .5\,e^{-1000t} \qquad \text{(B1)}$$

$$c_2 = 1.5\,e^{-t} - .5\,e^{-1000t} \qquad \text{(B2)}$$

$$c_3 = 3 - c_1 - c_2 \qquad \text{(B3)}$$

Rate Constants

$$\begin{bmatrix} \dfrac{\partial c_1}{\partial k_1} \\ \\ \dfrac{\partial c_2}{\partial k_1} \end{bmatrix} = -\frac{1}{4}t \begin{bmatrix} 3e^{-t} + e^{-1000t} \\ \\ 3e^{t} - e^{-1000t} \end{bmatrix} - \frac{1}{4(999)} \begin{bmatrix} 4e^{-t} - 4e^{-1000t} \\ \\ -2e^{-t} + 2e^{-1000t} \end{bmatrix} \qquad \text{(B4)}$$

$$\begin{bmatrix} \dfrac{\partial c_1}{\partial k_2} \\ \\ \dfrac{\partial c_2}{\partial k_2} \end{bmatrix} = \frac{t}{2} \begin{bmatrix} -e^{-1000t} \\ \\ e^{-1000t} \end{bmatrix} + \frac{1}{2(999)} \begin{bmatrix} 3e^{-t} - 3e^{-1000t} \\ \\ -3e^{-t} + 3e^{-1000t} \end{bmatrix} \qquad \text{(B5)}$$

$$\begin{bmatrix} \dfrac{\partial c_1}{\partial k_3} \\ \\ \dfrac{\partial c_2}{\partial k_3} \end{bmatrix} = \frac{t}{2} \begin{bmatrix} -e^{-1000t} \\ \\ e^{-1000t} \end{bmatrix} + \frac{1}{2(999)} \begin{bmatrix} -3e^{-t} + 3e^{-1000t} \\ \\ 3e^{-t} - 3e^{-1000t} \end{bmatrix} \qquad \text{(B6)}$$

$$\begin{bmatrix} \dfrac{\partial c_1}{\partial k_4} \\ \\ \dfrac{\partial c_2}{\partial k_4} \end{bmatrix} = -\frac{t}{4} \begin{bmatrix} 3e^{-t} + e^{-1000t} \\ \\ 3e^{-t} - e^{-1000t} \end{bmatrix} - \frac{1}{4(999)} \begin{bmatrix} -4e^{-t} + 4e^{-1000t} \\ \\ 2e^{-t} - 2e^{-1000t} \end{bmatrix} \qquad \text{(B7)}$$

$$\frac{\partial c_3}{\partial k_1} = 3/2\;te^{-t} + \frac{1}{2(999)}\,(e^{-t} - e^{-1000t}) \qquad \text{(B8)}$$

$$\frac{\partial c_3}{\partial k_2} = 0 \qquad \text{(B9)}$$

$$\frac{\partial c_3}{\partial k_3} = 0 \qquad \text{(B10)}$$

$$\frac{\partial c_3}{\partial k_4} = 3/2\;te^{-t} + \frac{1}{2(999)}\,(-e^{-t} + e^{-1000t}) \qquad \text{(B11)}$$

Initial Conditions

$$\begin{bmatrix} \dfrac{\partial c_1}{\partial c_1(0)} \\ \dfrac{\partial c_2}{\partial c_1(0)} \\ \dfrac{\partial c_1}{\partial c_2(0)} \\ \dfrac{\partial c_2}{\partial c_2(0)} \end{bmatrix} = 0.5 \begin{bmatrix} e^{-t} + e^{-1000t} \\ \\ e^{-t} - e^{-1000t} \\ \\ e^{-t} - e^{-1000t} \\ \\ e^{-t} + e^{-1000t} \end{bmatrix} \qquad \text{(B12)}$$

$$\frac{\partial c_1}{\partial c_3(0)} = 0 \qquad \text{(B13)}$$

$$\frac{\partial c_2}{\partial c_3(0)} = 0 \qquad \text{(B14)}$$

$$\frac{\partial c_3}{\partial c_3(0)} = 1 \qquad \text{(B15)}$$

$$\frac{\partial c_3}{\partial c_1(0)} = 1 - e^{-t} \qquad \text{(B16)}$$

$$\frac{\partial c_3}{\partial c_2(0)} = 1 - e^{-t} \qquad \text{(B17)}$$

APPENDIX C. REACTOR SENSITIVITY—NORMAL ERRORS

$$f_j = \sum_{i=1}^{R} \alpha_{ij}\, k_i \prod_{m=1}^{N} c_m{}^{\gamma_{im}} \qquad \text{(C1)}$$

$$\frac{\partial f_j}{\partial c_l} = \sum_{i=1}^{R} \alpha_{ij}\, k_i\, \gamma_{il} \prod_{m=1}^{N} c_m{}^{\gamma_{im} - \delta_{ml}} \qquad \text{(C2)}$$

$$\frac{\partial f_j}{\partial k_l} = \alpha_{lj} \prod_{m=1}^{N} c_m{}^{\gamma_{lm}} \qquad \text{(C3)}$$

$$\frac{\partial f_j}{\partial \gamma_{il}} = \alpha_{ij}\, k_i \ln c_l \prod_{m=1}^{N} c_m{}^{\gamma_{im}} \quad (\text{no sum on } i) \qquad \text{(C4)}$$

APPENDIX D. REACTOR SENSITIVITY—LOGNORMAL ERRORS

$$f_j = \sum_{i=1}^{R} \alpha_{ij} \exp\,(\tilde{k}_i) \prod_{m=1}^{N} c_m{}^{\gamma_{im}} \qquad \text{(D1)}$$

$$\frac{\partial f_j}{\partial c_l} = \sum_{i=1}^{R} \alpha_{ij} \exp\,(\tilde{k}_i)\, \gamma_{il} \prod_{m=1}^{N} c_m{}^{\gamma_{im} - \delta_{ml}} \qquad \text{(D2)}$$

$$\frac{\partial f_j}{\partial \tilde{k}_l} = \alpha_{lj} \exp\,(\tilde{k}_l) \prod_{m=1}^{N} c_m{}^{\gamma_{lm}} \qquad \text{(D3)}$$

$$\frac{\partial f_j}{\partial \gamma_{il}} = \alpha_{ij} \exp\,(\tilde{k}_l) \ln c_l \prod_{m=1}^{N} c_m{}^{\gamma_{lm}} \qquad \text{(D4)}$$

Manuscript received July 1, 1974; revision received and accepted January 17, 1974.