

# ***Sensitivity Analysis***

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# Local Methods

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## 5.1 INTRODUCTION

Mathematical models are widely used in various disciplines, and most of these models are based on systems of algebraic and differential equations. A growth in the number of variables and parameters of mathematical models has been observed over recent years. The basic reason for this is that, in the course of refinement of physical insight, models become more sophisticated. In addition, since the capacity of computers has grown, models that are more complex can be handled more easily. A common problem is that, in large models, the role of various parameters is not obvious. Usually it is not clear which are the important parameters, what is the effect of changing parameters, what is the uncertainty of the model results, originating from the uncertainty of parameters, and so on.

Local sensitivities provide the slope of the calculated model output in the parameter space at a given set of values. In many applications, this is exactly the information needed. In other areas, such as uncertainty analysis, local sensitivity analysis is a computationally efficient technique that allows a rapid preliminary exploration of the model.

There have been a number of reviews of local methods: A comprehensive review of sensitivity analysis was given by Rabitz *et al.* (1983). This review dealt mainly with local methods, and concentrated on distributed-parameter systems. Applications, mainly in chemical kinetics and molecular dynamics, were presented there. The review of Turányi (1990a) described both global and local methods, and provided an almost complete list of applications in chemical kinetics up to 1989. The review by Radhakrishnan (1990) dealt with the numerical aspects of local sensitivity methods, with an emphasis on combustion chemical modeling. The review by Tomlin *et al.* (1997) discussed the applications of several mathematical methods, including sensitivity analysis, to combustion kinetics.

Finally, we discuss some case studies that use SB. The ecological case study mentioned at the beginning of this section took 154 simulation runs to identify and estimate the 15 most important factors among the original 281 factors. Some of these 15 factors surprised the ecological experts, so SB may be a powerful statistical (black box) technique. Notice that on hindsight it turned out that there are no important interactions between factors, so only  $154/2 = 77$  runs would have sufficed (no foldover).

Another case study is the building thermal deterministic simulation in De Wit (1997). In his simulation, SB gave the 16 most important inputs among the 82 factors, after only 50 runs. He checked these results by applying Morris' screening technique described in Section 4.4; the latter technique took 328 runs.

## 4.8 CONCLUSIONS

In the initial phase of a simulation, it is often necessary to find out which factors amongst the multitude of potential factors are really important. The goal is then to reduce the number of factors to be further explored in the next phase.

Some designs (called supersaturated designs) require fewer runs than factors! In this chapter, we have surveyed several types of design: one-at-a-time (OAT) designs (including Morris's design), the systematic fractional replicate design proposed by Cotter, the iterated fractional factorial design (IFFD), and Bettonvil's sequential bifurcation (SB). Each type has its own advantages and disadvantages.

OAT designs have as a major limitation the neglect of factor interactions. The advantage is that OAT does not make simplifying assumptions such as that only a few factors have important effects or that the input/output (I/O) function is monotonic. Moreover, the computational cost of OAT designs is linear in the number of factors. However, OAT methods provide unbiased estimators of the effects of each individual factor, provided that these effects are the same at different settings of the other factors; that is, the factors act additively over the range of interest. Such an assumption, although advantageous to simplify the problem, can be rarely accepted. In fact, interactions are usually relevant, and need to be estimated by varying factors simultaneously. On the other hand, when the model is expensive to run, and there are many factors, Morris' method is both efficient and easy to implement. The Morris' method is available in the software package PREP-SPOP (SIMLAB) (see the software Appendix).

The systematic fractional replicate design of Cotter (1979) is computationally efficient and does not require any prior assumption about interactions or few important factors. However, the design lacks precision and cannot detect factors having effects that cancel each other out.

IFFD estimates the main effects, quadratic effects, and two-factor interactions of the most influential factors, with a number of runs that is small compared with the total number of factors. However, for good results, the model output should be determined by only a few highly influential factors. Andres' IFFD is available in the package SAMPLE2 (see the software Appendix).

Sequential bifurcation is simple, efficient, and effective (as several case studies have illustrated). Its major limitations are that the signs of main effects must be known, and that metamodels with only main effects and two-factor interactions must be adequate I/O approximations.

The screening designs described in this chapter are only a small subset of the total number available in the literature. We have presented only those designs that focus on the problem of the identification of the few important factors in a model.

## 5.2 FEATURES OF LOCAL SENSITIVITIES

Time-independent (stationary) systems can be characterized by the following system of algebraic equations:

$$0 = \mathbf{f}(\mathbf{y}, \mathbf{k}) \quad (5.1)$$

where  $\mathbf{y}$  is the  $n$ -vector of variables and  $\mathbf{k}$  is the  $m$ -vector of parameters. The solution of the implicit algebraic Equation (5.1) is denoted by  $\mathbf{y}^s$ . The solution changes when the values of parameters  $\mathbf{k}$  are changed, and the new solution can be obtained from the following equation:

$$\mathbf{y}^s(\mathbf{k} + \Delta\mathbf{k}) = \mathbf{y}^s(\mathbf{k}) + \sum_{j=1}^m \frac{\partial y_i}{\partial k_j} \Delta k_j + \frac{1}{2} \sum_{j=1}^m \sum_{i=1}^m \frac{\partial^2 y_i}{\partial k_i \partial k_j} \Delta k_i \Delta k_j + \dots \quad (5.2)$$

A chemical example of such a system is the concentration in a well-stirred (i.e. spatially homogeneous) stationary reactor.

Non-stationary systems can be described by differential or differential-algebraic systems of equations. Consider the following initial-value problem:

$$\frac{d\mathbf{y}}{dt} = \mathbf{f}(\mathbf{y}, \mathbf{k}), \quad \mathbf{y}(0) = \mathbf{y}^0. \quad (5.3)$$

Here again,  $\mathbf{y}$  is the  $n$ -vector of variables and  $\mathbf{k}$  is the  $m$ -vector of system parameters, and  $\mathbf{y}^0$  is the array of initial values. Solution of the initial-value problem (5.1) provides the time evolution of the system variables.

The effect of parameter change on the solution can be expressed through a Taylor series expansion:

$$\mathbf{y}^s(t, \mathbf{k} + \Delta\mathbf{k}) = \mathbf{y}^s(t, \mathbf{k}) + \sum_{j=1}^m \frac{\partial y_i}{\partial k_j} \Delta k_j + \frac{1}{2} \sum_{i=1}^m \sum_{j=1}^m \frac{\partial^2 y_i}{\partial k_i \partial k_j} \Delta k_i \Delta k_j + \dots \quad (5.4)$$

In both the time-dependent and time-independent cases, the partial derivatives  $\partial y_i / \partial k_j$  are called first-order local sensitivities.  $\partial^2 y_i / \partial k_i \partial k_j$  are called second-order local sensitivities, and so on. The first-order local sensitivities form the sensitivity matrix  $\mathbf{S} = \{s_{ij}\} = \{\partial y_i / \partial k_j\}$ .

Global sensitivity coefficients depend on the assumed probability density function of the parameters, and usually also on the method of calculation chosen. In contrast, local sensitivity coefficients are defined exactly by Equations (5.2) and (5.4). There are several numerical methods for the calculation of local sensitivities, but the calculated values should be identical within the numerical accuracy of the method used. Also, calculation of local sensitivities is much faster than that of global sensitivities. However, local sensitivities have some special limiting features that have to be kept in mind.

For all models of real systems, the values of the parameters are subject to some uncertainty. In most cases, such uncertainties can be very high, and sometimes when the parameters are changed within the range of uncertainty, a qualitatively different model is obtained. Unlike global sensitivities, local sensitivities are totally incapable of providing information on the effect of significant parameter changes. Local sensitivities are really local, and the information provided is related to a single point in the space of parameters. The point investigated is usually the point of best parametric estimate, also called the nominal value of parameters. Small variations in parameter values usually do not change

the local sensitivities dramatically, but a significantly different parameter set may result in a completely different sensitivity pattern.

Sensitivity analysis of time-dependent systems has another characteristic feature. In most cases, sensitivity analysis can be considered as probing the model using another set of parameters. However, sensitivity analysis can also be used for the analysis of a model via perturbation of the parameters. In the former case, the parameters are changed at simulation time zero, and therefore the initial time of sensitivity calculation is equal to the initial time of simulation. In the general case, however, the initial times of the model and of the sensitivities are different. Let the simulation be started at time 0, let the parameters be perturbed at time  $t_1$ , and let the effect of the perturbation be studied at time  $t_2$ . The perturbed solution  $\mathbf{y}'$  can be approximated from the original solution  $\mathbf{y}$  and sensitivity matrix  $\mathbf{S}$ :

$$\mathbf{y}'(t_2) \approx \mathbf{y}(t_1) + \mathbf{S}(t_2, t_1)\Delta\mathbf{k}_{t_1}. \quad (5.5)$$

This means that the sensitivity matrix  $\mathbf{S}$  has double time dependence in the general case, and the time limits  $t_1$  and  $t_2$  provide a degree of freedom in the analysis of models.

## 5.3 NUMERICAL METHODS FOR THE CALCULATION OF LOCAL SENSITIVITIES

### 5.3.1 Finite-Difference Approximation

The simplest way to calculate local sensitivities is based on slightly changing one parameter at a time and rerunning the model. Using the *finite-difference approximation*, elements of the sensitivity matrix can be approximated by

$$\frac{\partial \mathbf{y}}{\partial k_j} \approx \frac{\mathbf{y}(k_j + \Delta k_j) - \mathbf{y}(k_j)}{\Delta k_j}, \quad j = 1, \dots, m. \quad (5.6)$$

This procedure is also called the *brute force method* or the *indirect method*. The main advantage of this method is that no modification to the original model or extensive extra coding is needed. However, the brute force method is slower and less accurate than more sophisticated methods.

Calculation of local sensitivities in this way requires  $m + 1$  simulations of the original model. If central differences are used,  $2m$  simulations are required. The accuracies of the sensitivities calculated depend on the parameter change  $\Delta k_j$ . In the case of nonlinear models, parameter changes that are too large (e.g.  $> 5\%$ ) would damage the assumption of local linearity. If the parameter change is too small, the difference between the original and perturbed solutions is too small and the round-off error is too high. In most cases, a 1% perturbation is a good practical choice, but finding the best (or acceptable) value is a trial-and-error process.

### 5.3.2 Direct Method

Differentiation of Equation (5.3) with respect to  $k_j$  gives the following system of *sensitivity differential equations*:

$$\frac{d}{dt} \frac{\partial \mathbf{y}}{\partial k_j} = \mathbf{J} \frac{\partial \mathbf{y}}{\partial k_j} + \frac{\partial \mathbf{f}}{\partial k_j}, \quad (5.7)$$

or, in matrix form,

$$\dot{\mathbf{S}} = \mathbf{J}\mathbf{S} + \mathbf{F}. \quad (5.8)$$

Here  $\mathbf{J} = \{\partial f_i / \partial y_j\}$  is the derivative of the right-hand side of the differential equation with respect to the system variables (called the Jacobian matrix) and  $\mathbf{F} = \{\partial f_i / \partial k_j\}$  is the derivative with respect to the parameters, sometimes called the parametric Jacobian. The initial condition of the differential equation (5.7) is a zero vector.

*Direct methods* are based on the solution of the ODE (5.7). Numerical solution of Equation (5.7) requires knowledge of the values of the matrices  $\mathbf{J}$  and  $\mathbf{F}$  at each step of the ODE solver. To evaluate these matrices, the actual values of the system variables have to be known, and therefore a simultaneous or preceding solution of the ODE (5.3) is needed. In the first realizations of the direct method, Equations (5.3) and (5.7) were solved independently but simultaneously, and the solution of Equation (5.3) was used for setting up Equation (5.7). All variants of this algorithm were relatively slow.

Dunker (1981, 1984) was the first to show that a special relation between Equation (5.3) and Equation (5.7) allows a numerical shortcut, and called this algorithm the *decoupled direct method* or *DDM*. Equations (5.3) and (5.7) have the same Jacobian, and therefore a stiff ODE solver selects the same step size and order of approximation for the solution of both equations. In Dunker's method, the ODE solver decomposes the Jacobian only once, and then takes a timestep solving Equation (5.3) and then solving Equation (5.7) with all parameters one after the other. Since the triangularization of the Jacobian is the most time-consuming part of a stiff ODE solution, using the decoupled direct method, sensitivities can be calculated with relatively little extra cost.

Several implementations of the DDM exist, and the DDM has proved to be the best general method for the numerical calculation of local sensitivities.

In the case of stationary systems, if the stationary point is asymptotically stable, the stationary sensitivity coefficients are limits in time of the dynamic ones, and their time derivatives tend to zero. Therefore, Equation (5.8) can be transformed to

$$\mathbf{S}^s = -\mathbf{J}^{-1}\mathbf{F}. \quad (5.9)$$

The matrix  $\mathbf{S}^s$  is the *stationary sensitivity matrix* and the matrices  $\mathbf{J}$  and  $\mathbf{F}$  are evaluated at the variable values of the stationary point. Equation (5.9) can also be applied when the original model is defined as a system of algebraic equations (5.1).

### 5.3.3 The Green Function Method

Differentiating Equation (5.3) with respect to the initial values  $\mathbf{y}^0$ , the following equation is obtained:

$$\frac{d}{dt}\mathbf{K}(t, t_1) = \mathbf{J}(t)\mathbf{K}(t, t_1), \quad (5.10)$$

where  $t_1$  and  $t$  are the time of perturbation and the time of observation, respectively, and  $\mathbf{K}$  is the initial value sensitivity matrix, that is

$$\mathbf{K}(t, t_1) = \left\{ \frac{\partial c_i(t)}{\partial c_j^0(t_1)} \right\}, \quad \mathbf{K}(t_1, t_1) = \mathbf{I}, \quad t \geq t_1.$$

Equation (5.7) is a linear inhomogeneous system of differential equations, and therefore it can be solved by first determining the homogeneous part (5.10) and then calculating the particular solution:

$$\mathbf{S}(t_1, t_2) = \int_{t_1}^{t_2} \mathbf{K}(t_2, s) \mathbf{F}(s) ds. \quad (5.11)$$

In this equation,  $\mathbf{K}$  is known as the *Green function* or *kernel*, and the numerical method based on the solution of Equation (5.11) is called the *Green function method*.

The Green function method also has several variants. The most developed of these is called the analytically integrated Magnus version of the Green function method (GFM/AIM) (Kramer *et al.*, 1981). In this version, the matrix  $\mathbf{K}$  is approximated by a matrix exponential:

$$\mathbf{K}(t + \Delta t, t) = \exp \left[ \int_t^{t+\Delta t} \mathbf{J}(s) ds \right]. \quad (5.12)$$

The GFM/AIM method is several times faster than other versions of the Green function method.

Applying the direct method, the numerical effort increases linearly with the number of parameters. In the case of Green function methods, the numerical effort is proportional to the number of variables. In practice, however, the GFM is faster than the DDM only at a very high ratio of the number of parameters to the number of variables, and the numerical error is less easily controllable than in the case of the much simpler DDM algorithm.

### 5.3.4 Other Methods

Other methods have also been described in the literature, but they are much less widespread. It is frequently useful (Miller and Frenklach, 1983) to approximate the integrated solution of the original model by an array of simpler empirical equations as a function of parameters in a parameter region. Preparation of such an empirical model is very time-consuming, and cannot be justified by only the sensitivity calculations. However, if such an empirical function is available, differentiating it provides an estimate of the local sensitivities as a by-product.

According to the polynomial approximation method (Hwang, 1983), the solution of the sensitivity differential equations (5.7) is approximated by Lagrange interpolation polynomials. Although high computational speed and good numerical stability were demonstrated, this method was never applied to real problems.

## 5.4 DERIVED SENSITIVITIES

In the case of models defined by the differential equations (5.3), not only the actual values of variables are interesting but also their rates of change at a given time. The rates of change of variables are given by the left-hand side of Equation (5.3). Since

$$\frac{d}{dt} \left( \frac{\partial y_i}{\partial k_j} \right) = \frac{\partial (dy_i/dt)}{\partial k_j},$$

the sensitivities of the rates of change of variables can be calculated by Equation (5.7), knowing the local sensitivity coefficients.

The *rate sensitivity matrix*  $\hat{S}(t_1, t_2)$  also has double time dependence. If the two times coincide ( $t_1 = t_2$ ), the instantaneous effect of parameter change is obtained. It is clear from Equation (5.8) that the matrix  $F = \{\partial f_i / \partial k_j\}$  can be considered as an instantaneous rate sensitivity matrix. Knowing the values of variables at a given time,  $F$  can be calculated analytically and therefore the solution of the sensitivity ODE (5.8) is not needed. It has been shown (Turányi *et al.*, 1989) that  $F$  can provide valuable information on the structures of models.

Mathematical models may provide qualitative information. Such information can be whether a model oscillates, if a given variable reaches a threshold value during the time interval inspected, and so on. Sensitivity analysis cannot be used for the study of such information. On the other hand, frequently the information desired is quantitative, but may not be among the primary outputs of the model, although it can be deduced from the time histories of variables. Such information might be the maximum value of a variable, the time needed for a variable to reach a threshold value, or, in the case of periodic solutions, the period time. Such quantitative information can be called a *feature*, and its sensitivity is named *feature sensitivity*.

The brute force method offers a direct way to calculate feature sensitivities (Frenklach, 1984). A particular feature is evaluated from the original and perturbed solutions, and the feature sensitivity is calculated using finite differences.

In many cases, the feature sensitivities can also be calculated from the local sensitivities of variables. As an example, assume that variable  $i$  has a maximum (or minimum) at time  $t^*$ . This implies that the time derivative of the variable is zero:

$$\dot{y}_i(\mathbf{k}, t)|_{t=t^*} = 0. \quad (5.13)$$

Differentiating Equation (5.13) with respect to the parameter  $k_j$ , the following equation is obtained (Rabitz *et al.*, 1983) for the calculation of the sensitivity of the location of the maximum:

$$\frac{\partial t^*}{\partial k_j} = - \frac{\frac{\partial^2 y_i(t^*)}{\partial t \partial k_j}}{\frac{\partial^2 y_i(t^*)}{\partial t^2}}. \quad (5.14)$$

The numerator contains the appropriate rate sensitivity coefficient  $\dot{s}_{ij}(0, t^*)$ , while the denominator can be calculated from the Jacobian and the right-hand side of the original ODE:

$$\frac{\partial^2 \mathbf{y}}{\partial t^2} = \mathbf{JF}(\mathbf{y}). \quad (5.15)$$

Another frequently applied feature sensitivity is the sensitivity of the period time of periodic (oscillating) models. Period time sensitivities can also be calculated (Edelson and Thomas, 1981) approximately from the local variable sensitivities:

$$\frac{\partial \tau}{\partial k_j} = \frac{\frac{\partial y_i(t_2)}{\partial k_j(t_1)} - \frac{\partial y_i(t_2 + \tau)}{\partial k_j(t_1)}}{\frac{dy_i(t_2)}{dt}}. \quad (5.16)$$

## 5.5 INTERPRETATION OF SENSITIVITY INFORMATION

### 5.5.1 Effect of Changing One Parameter on a Single Variable

The sensitivity coefficient  $\partial y_i / \partial k_j$  is a linear estimate of the number of units change in the variable  $y_i$  as a result of a unit change in the parameter  $k_j$ . This also means that the sensitivity result depends on the physical units of variables and parameters, and is meaningful only when the units of the model are known. In the general case, the variables and the parameters each have different physical units, and therefore the sensitivity coefficients cannot be compared with each other.

To make the sensitivity results independent of the units of the model, usually normalized sensitivity coefficients are applied. The normalized local sensitivity matrix is denoted by  $\bar{\mathbf{S}}$  and is defined as

$$\bar{\mathbf{S}} = \left\{ \frac{k_j}{y_i} \frac{\partial y_i}{\partial k_j} \right\}. \quad (5.17)$$

These coefficients represent a linear estimate of the percentage change in the variable  $y_i$  caused by a one percent change in the parameter  $k_j$ . The normalized sensitivity coefficients are independent of the original units of the model, and are comparable with each other.

A practical difficulty in handling sensitivity matrices comes from their size. A reasonably sized model may consist of 50 variables and 100 parameters. This results in a sensitivity matrix of 5000 elements. In addition, if the sensitivities are studied at 20 time points then  $10^5$  numbers have to be compared and analyzed. It is inevitable that some methods have to be used for summarizing the sensitivity information.

### 5.5.2 Effect of Changing one Parameter on Several Variables

In model optimization, the improvement of the fit is expressed by the change in a single number. This is achieved by introducing an objective function, which converts the multivariate output of the model to a single value. As an example, such an objective function can be:

$$e(t_1, t_2) = \sum_{i=1}^n w_i \left[ \frac{y_i^*(t_1, t_2) - y_i(t_2)}{y_i(t_2)} \right]^2, \quad (5.18)$$

where  $y_i(t_2)$  is the solution of the model at time  $t_2$  at the nominal parameter set and  $y_i^*(t_1, t_2)$  is the solution of the model at time  $t_2$  using a parameter set perturbed at time  $t_1$ . The weights  $w_i$  allow the expression of the relative importance of the model variables according to the modeller. For some variables, this weight can be zero, showing that the variable has to be present in the model as an auxiliary variable, but its value is not interesting at all.

The sensitivity of the objective function above can be calculated from the local variable sensitivities:

$$\frac{\partial e}{\partial k_j}(t_1, t_2) = \sum_{i=1}^n w_i \left[ \frac{1}{y_i} \frac{\partial y_i}{\partial k_j}(t_2, t_1) \right]^2. \quad (5.19)$$

Investigation of the sensitivity of objective functions significantly decreases the number of sensitivities to be inspected. However, for a fixed time of perturbation  $t_1$ , the sensitivities still have to be studied at several time points  $t_2$  to get an impression of the change of sensitivities in time.

The next stage of information compression is the application of time-integrated sensitivities. The corresponding objective function is

$$e = \int_{t_1}^{t_2} \sum_{i=1}^n w_i \left[ \frac{y_i^*(t_1, t_2) - y_i(t_2)}{y_i(t_2)} \right]^2 dt \quad (5.20)$$

The sensitivity of this objective function can be approximately calculated by

$$\frac{\partial e}{\partial k_j} = \sum_{h=2}^l \sum_{i=1}^n w_i \left[ \frac{1}{y_i} \frac{\partial y_i}{\partial k_j}(t_h, t_1) \right]^2. \quad (5.21)$$

Sensitivities of objective functions, calculated from normalized sensitivities are called *overall sensitivities* (Vajda *et al.*, 1985). Selecting proper weights  $w_i$ , the overall sensitivities provide information on the importance of model parameters.

### 5.5.3 Effect of Simultaneously Changing Several Parameters on Several Variables

The overall sensitivities give information on the change of single parameters only. However, changing several parameters simultaneously can strengthen or weaken the effect of single parameter changes. First-order local sensitivities always correspond to 'changing one parameter at a time', and do not show the effect of simultaneous parameter changes. *Principal component analysis* (Vajda *et al.*, 1985; Vajda and Turányi, 1986) can, however, be used to estimate the effect of simultaneous parameter changes on several variables, based on local sensitivities only.

Use the time-integrated objective function (5.20) to assess the effect of parameter changes and replace the integral by a summation:

$$e(\mathbf{x}) = \sum_{h=2}^l \sum_{i=1}^n \left[ \frac{y_i^*(t_h) - y_i(t_h)}{y_i(t_h)} \right]^2. \quad (5.22)$$

Assuming that all parameters are positive, normalized parameters,  $\alpha$ , defined as  $\alpha = \ln k$ , can be used. If some of the parameters are negative, a simple modification of the model can lead to all-positive parameters. For simplicity, let the weights now be either 1 or 0. Weight 0 deletes the corresponding row from the sensitivity matrix. The local change of the objective function above around the nominal values of parameters  $\alpha^0$  can be approximated by the local sensitivity matrix:

$$e(\mathbf{x}) \approx (\Delta \mathbf{x})^T \tilde{\mathbf{S}}^T \tilde{\mathbf{S}} (\Delta \mathbf{x}), \quad (5.23)$$

where  $\Delta \mathbf{x} = \mathbf{x} - \mathbf{x}^0$ , and the matrix  $\tilde{\mathbf{S}}$  has been composed from a series of local sensitivity matrices, belonging to times  $(t_1, t_2), \dots, (t_1, t_h)$ :

$$\tilde{\mathbf{S}} = \begin{bmatrix} \tilde{\mathbf{S}}_2 \\ \tilde{\mathbf{S}}_3 \\ \vdots \\ \tilde{\mathbf{S}}_h \\ \vdots \\ \tilde{\mathbf{S}}_1 \end{bmatrix}. \quad (5.24)$$

Equation (5.23) is a quadratic approximation to the real shape of the objective function. Any cross-section of this approximate objective function is a hyperellipsoid, defined by the matrix  $\tilde{\mathbf{S}}^T \tilde{\mathbf{S}}$ . The orientation of the ellipsoid with respect to the parameter axes is defined by the eigenvectors of the matrix  $\tilde{\mathbf{S}}^T \tilde{\mathbf{S}}$ , while the relative lengths of the axes of the ellipsoid are revealed by the eigenvalues of this matrix.

If the axes of the ellipsoid are parallel to the axes of the parameter space, there is no synergistic effect among the parameters, and the relative lengths of the axes define the relative importance of parameters. However, if, say, the direction of the longest axis of the ellipsoid is at  $45^\circ$  on the plane of two of the parameter axes, this means that the effect on all variables by changing one parameter can be well corrected by also changing another parameter.

A similar interpretation can be given using the term *principal component*. A principal component is a new parameter, obtained via a linear combination of the original parameters. Let matrix  $\mathbf{U}$  denote the matrix of normalized eigenvectors of  $\tilde{\mathbf{S}}^T \tilde{\mathbf{S}}$ . Principal components are defined as

$$\Psi = \mathbf{U}^T \alpha, \quad (5.25)$$

and, using principal components, the objective function (5.23) can be given in a simpler form:

$$e = \sum_{i=1}^n \lambda_i (\Delta \Psi_i)^2, \quad (5.26)$$

where  $\Delta \Psi = \mathbf{U}^T \Delta \alpha$  and  $\lambda$  is the vector of eigenvalues. Equation (5.26) provides another explanation of why the eigenvectors of matrix  $\tilde{\mathbf{S}}^T \tilde{\mathbf{S}}$  reveal the related parameters and why the corresponding eigenvalues show the relative weights of these parameter groups.

From a practical point of view, principal component analysis is an inexpensive post-processing technique that extracts otherwise-unavailable information from the local sensitivity matrices.

## 5.6 INITIAL SENSITIVITIES

The solution of the initial-value problem (5.3) depends on the values of the parameters, but also on the initial values of the variables. Calculation of the *initial-value sensitivity matrix* has been introduced as a first step in the calculation of local sensitivities, according to the Green function method. It has been shown in Section 5.3.3 that the initial-value sensitivity matrix  $\mathbf{K}(t, t_1) = \{\partial c_i(t) / \partial c_j^0(t_1)\}$  can be obtained as the solution of the following initial-value problem (Equation (5.10)):

$$\frac{d}{dt} \mathbf{K}(t, t_1) = \mathbf{J}(t) \mathbf{K}(t, t_1).$$

The initial value of  $\mathbf{K}$  is a unit matrix. The initial-value sensitivities can be considered as if a unit perturbation were applied to the initial values, one-by-one, and the fate of this perturbation were monitored.

Initial-value sensitivities are interesting because they are related to time scales of models. If the time scales are well separated, variables can be categorized as fast or slow. The slow variables respond very slowly to a perturbation, since the perturbation puts them on a trajectory almost parallel to their original one, and therefore the initial value sensitivity of

a slow variable (i.e. the diagonal element belonging to a slow variable) remains close to unity for a long time. Fast variables quickly return to their original trajectory after the perturbation, and therefore their initial-value sensitivities decay to zero quickly. If the initial-value sensitivity of a variable exceeds the unit value instead of remaining close to unity or decaying this indicates that a slight increase in the variable increases its production rate. Such behavior is called *autocatalysis* in chemical kinetics.

The point of the quasi-steady-state approximation (QSSA) is that the values of slow variables determine the values of fast variables (Turányi *et al.*, 1993). This means that it is enough to solve a system of differential equations for the slow variables, and the values of fast variables can be calculated from the values of the slow ones using algebraic equations. The critical step in the application of the quasi-steady-state approximation is appropriate division of variables into fast and slow ones. Initial-variable sensitivities can do the job, but there are other approximate techniques, which provide similar information in a computationally less expensive way.

During the solution of initial-value problem (5.10), the values of variables change, and therefore the elements of the matrix  $\mathbf{J}$  are continuously changing. On fixing the elements of  $\mathbf{J}$  at the starting time, Equation (5.10) becomes a homogeneous linear system of differential equations with constant parameters. The solution of such a system is

$$\mathbf{K}' = \exp[\mathbf{J}(t_1)t]. \quad (5.27)$$

It has been shown that the Jacobians of chemical kinetic differential equations can frequently be rearranged to approximately lower triangular form (Turányi *et al.*, 1993). It is possible that a similar observation holds for many models in other disciplines. Consequently, for most chemical kinetic systems, the eigenvalues of the Jacobian are close to the diagonal elements of the Jacobian,  $\lambda_i \approx j_{ii}$ , where  $j_{ii}$  is the  $i$ th diagonal element of the Jacobian. Since the lifetime can be defined as  $\tau_i = -1/j_{ii}$ , this relation supports the traditional observation that short-lifetime variables decay rapidly after perturbation and behave as fast variables. This also means that the time history of the diagonal of the initial-value sensitivity matrix can be approximated as

$$k_{ii}(t) \approx \exp(j_{ii}t). \quad (5.28)$$

A more sophisticated handling of timescales takes into account that eigenvectors of the Jacobian define variable groups. The time scale separation is better if variable groups, not single variables, are considered and therefore a more accurate quasi-steady-state approximation with fewer variables can be applied. The corresponding numerical techniques (Lam and Goussis, 1988; Maas and Pope, 1992) represent a further development of the classical QSSA.

So far, only the interpretation of the diagonal elements of the initial-value sensitivity matrix has been discussed. The off-diagonal elements of the matrix  $\mathbf{K}$  also contain important dynamic information, but their interpretation depends on the actual physical model. In general, the off-diagonal elements show the displacement of the trajectory of all other variables, in response to perturbing a given variable slightly. As an example, a large off-diagonal element indicates strong coupling between a fast and a slow variable, introducing large error into the QSSA calculation (Turányi *et al.*, 1993).

The whole initial-value sensitivity matrix can also be approximated based on an eigenvector-eigenvalue analysis of  $\mathbf{J}(t_1)$  (Maas and Pope, 1994). Let  $t_2$  be the time of observation of the initial-value sensitivity calculation and let  $\mathbf{V}$  and  $\tilde{\mathbf{V}}$  denote the matrices of right- and left-eigenvectors of  $\mathbf{J}(t_1)$ , respectively. The matrices  $\mathbf{V}_f$  and  $\tilde{\mathbf{V}}_f$  are truncated arrays, obtained