A Method for Parameter Sensitivity Analysis in Differential Equation Models[1]

Robert C. Kohberger
Division of Computer Science
Albany Medical College
Albany, New York

Donald Scavia
National Oceanic and Atmospheric Administration
Great Lakes Environmental Research Laboratory
Ann Arbor, Michigan

John W. Wilkinson
School of Management
Rensselaer Polytechnic Institute
Troy, New York

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Summary

A numeric method for analyzing global parameter sensitivity about a fixed point in parameter space for differential equation models is presented. The method is suitable for large scale, multiresponse systems which may not be in steady state. Using a quadratic model, the relationship between several global response characteristics and parameter perturbations is examined. Sensitivity relationships are defined with both backward elimination regression model selection procedures, and eigenvalue-eigenvector analyses. An example of the method is given using an ecosystem model consisting of 14 coupled differential equations.

I. Introduction

Differential equation models are useful tools in describing a variety of complex systems, having applications in such fields as economics, medicine (Jacquez, 1972), biology (McNaught and Scavia, 1976), and ecology (Park et al., 1974; Scavia et al., 1976; Thomann et al., 1975). At present, the primary use of such models is that of prediction. Input (or driving) variables are perturbed and resulting system behavior observed. Model validity is usually defined in terms of predictive capability (Aigner, 1972). Because many of the mathematical relationships used in defining the differential equation system are based on extant scientific principles, knowledge of the system may also be gained by examining the system under internal change, i.e. changes of the parameter values of the mathematical constructs.

Tomovic (1963) defines several sensitivity coefficients based on the sensitivity equation, a differential equation relating the change in response with a change in the parameters. For non-steady state systems, the sensitivity coefficient is a continuous function of time. The usefulness of the method depends on the ability to reformulate the system in analog terms or provide some analytical results for the solution to the sensitivity equation. For many large scale models this is not feasible. Steinhorst and Gustafson (1975) determine sensitivity by parameter perturbation and an analysis of variance. Such an approach assumes additive normal error and obscures the continuous relationship between the parameters and the objective criteria. Banning (1974) and Kleijnen (1975) discuss a sensitivity method applied to the driving variables of a stochastic simulation model.

This paper will present a method to quantify overall parameter sensitivity relationships with numeric techniques. It will describe an application of empirical model building in a linear regression framework and eigenvalue - eigenvector canonical analysis to evaluate parameter changes and system response. The method is not dependent on either an analytic solution to the differential equations or a formulation to an analog model. It is specifically designed for multiresponse systems.

2. Method

The method is, basically, to determine some objective criteria for all responses integrated over the primary variable, usually time. Parameters are perturbed from a given parameter set (driving variables being held constant), and new objective criteria determined. The objective criteria are defined as distance measures of the resulting perturbed response from that response obtained from the given parameter set. The relationship between the parameters and the objective criteria is then evaluated using a quadratic model.

The differential equation model may be formulated as:

$$\dot{y}_i = f_i(\underline{\theta}, \underline{x}(t), \underline{y}, t) \qquad i = 1,2, \ldots ,c \tag{1}$$

where c = number of responses (compartments)

$\dot{y}_i = dy_i/dt$

$\underline{\theta}$ = vector of parameter values

$\underline{y}$ = vector of response variables

$\underline{x}(t)$ = vector of driving variables

t = time

The integrated form of the response will be given as:

$$y_i = g_i(\underline{\theta}, \underline{x}(t), \underline{y}, t) \qquad i = 1,2, \ldots ,c \tag{2}$$

and the response at the given parameter set as:

$$y_i^* = g_i(\underline{\theta}^*, \underline{x}(t), \underline{y}, t) \qquad i = 1,2, \ldots, c \qquad (3)$$

In most cases, the analytical solution, $g_i(\cdot)$, is not known and Equations (2) and (3) must be represented by sets of discrete points over time. The spacing of these discrete points should be such that an adequate representation of the behavior of the responses over time is made. The grid should be the same for all responses or a bias will be introduced into the objective criteria. Usually the grid is easily made because Equation (3) is extensively studied before any sensitivity analysis is done.

The parameters ($\underline{\theta}$) are systematically perturbed from their given values ($\underline{\theta}^*$) and Equation (1) is integrated over a given time frame. Three values are used for each parameter: the given value, and $\pm$10% change from the given value. This results in 3^p perturbations, where p is the number of parameters to be examined. The actual percentage perturbation used in the analysis is dependent on the quantity of interest, i.e. the sensitivity of the system to parameter changes. Too large or too small a change may miss important features of the response surface; therefore, each system must be dealt with individually. A 10% change has proven to be successful for the ecosystem model used in the example.

The formulation of objective criteria that compare the given and perturbed simulations is of prime importance. A simple sum of squares approach is not feasible because observed values of the model responses often differ by orders of magnitude. The following objective criteria were examined:

$$o_{1k} = \sum_{i=1}^{c} \sum_{j=1}^{n} \frac{|y^{*}_{ij} - y_{ijk}|}{y^{*}_{ij}} \quad (4)$$

$$o_{2k} = \sum_{i=1}^{c} \sum_{j=1}^{n} \left(\frac{y^{*}_{ij} - y_{ijk}}{y^{*}_{ij}} \right)^2 \quad (5)$$

k = perturbation $k=1,2,\ldots,3^p$

p = number of parameters examined

c = number of compartments

n = number of observations for each response

y^{*}_{ij} = j th observation for the i th response for the given parameter set

y_{ijk} = j th observation for the i th response for the k th perturbed parameter set

Objective criterion 1 (4) is an estimate of the integral absolute percentage difference and Objective criterion 2(5) is an estimate of the integral squared percentage difference. From the form of the objective criteria it is clear that sensitivity is being defined with respect to a given point in the parameter space.

Equation (1) is solved for the perturbed parameter points and the objective criteria calculated. The relationship between the objective criterion and the parameter values is then examined by a quadratic model given by:

$$o = \beta_0 + \underline{\beta}'\underline{\theta} + \underline{\theta}'\underline{A}\,\underline{\theta} \quad (6)$$

$$\underline{\beta}' = (\beta_1, \beta_2, \ldots, \beta_p)$$

$$\underline{\theta}' = (\theta_1, \theta_2, \ldots, \theta_p)$$

$$\underline{A} = \begin{bmatrix} \alpha_{11} & \alpha_{12}/2 & \cdots & \alpha_{1p}/2 \\ & \alpha_{22} & & \vdots \\ & \text{sym} & \ddots & \alpha_{pp} \end{bmatrix}$$

Such a model is equivalent to a second order Taylor series approximation to the functionality between the differential model (1) parameters and the objective criterion. The estimation of β_0, $\underline{\beta}$, and $\underline{A}$ of Equation (6) may be done by any standard least squares program.

The analysis of the fitted surface (6) proceeds along two different but complimentary paths. A canonical analysis is first used to examine the fitted Equation (6). By the usual differentiation techniques the stationary points of (6) are given as:

$$\underline{\theta}_0 = -\underline{A}^{-1}\underline{\beta}/2 \tag{7}$$

and the estimated response at this stationary point by:

$$\hat{\delta}_0 = \beta_0 + \underline{\theta}_0'\underline{\beta}/2 \tag{8}$$

Equation (6) in canonical form is

$$\hat{\delta} = \hat{\delta}_0 + \lambda_1 w_1^{\,2} + \lambda_2 w_2^{\,2} + \ldots \lambda_k w_k^{\,2} \tag{9}$$

where λ_i are the characteristic roots (eigenvalues) of A

$\underline{w} = \underline{M}\ (\underline{\theta}-\underline{\theta}_0)$

and M is the matrix whose rows are the normalized eigenvectors associated with the eigenvalues of A.

Since A is real and symmetric the eigenvalues λ_i are all real, and if A is of rank p then p eigenvalues exist.

The characterization of the stationary point (7) is accomplished by inspection of the eigenvalues of (9). Clearly if all eigenvalues are positive then a move away from $\underline{\theta}_0$ results in a higher value of the objective criterion and $\underline{\theta}_0$ then represents a minimum. Similarly if all eigenvalues are negative then $\underline{\theta}_0$ represents a maximum. Although the stationary points (7) should represent a minimum, in practice the eigenvalues will often be mixed in sign. Such a mixture is usually indicative of a saddle point. The first qualitative measure concerning the fit of (6) is that even though a saddle point may be obtained, the stationary point (7) should lie close to the given parameter set. If not, then the fitted equation is of little value in examining sensitivity.

If the eigenvalues are now ranked from largest to smallest the influence of the w_i's and, hence, $\underline{\theta}$ can clearly be seen. The largest eigenvalues have the greatest effect on the objective criteria, and the θ_i or combination of θ_i's having the greatest effect on the objective function can be determined by inspection of the associated eigenvectors.

The examination of the eigenvalues and eigenvectors of A give a qualitative indication of the sensitivities of the parameters $\underline{\theta}$. In the example to be discussed here the sensitivities of the parameters are clear because the eigenvalues differ by orders of magnitude. On other cases the determination is not so easy and a statistical approach must be used.

If we assume that deviations from the model (6) are independent and normally distributed with constant variance, then model fitting in a linear regression framework may be used to determine those parameters ($\underline{\theta}$) that contribute significantly to the fitting of the objective criterion and are, hence, the most sensitive in Equation (1). A backward elimination procedure is well suited for this purpose. In this procedure, variables (i.e. elements of $\underline{\beta}$ and $\underline{A}$) are successively removed from the model (5) according to some preselected probability level. The parameters ($\underline{\theta}$) remaining in the final reduced model are those that significantly explain variations in the objective criterion and may be judged as the most sensitive parameters.

3. Example

The method developed here was applied to a lake ecosystem model (Scavia et al., 1974; Park et al., 1974) describing the open water zone of Lake George, New York. This model consists of 14 coupled non-linear differential equations with over 150 parameters. To determine the utility of the method, two small parameter sets were analyzed independently. One set describes the temperature effect on primary production and the other the temperature effect on decomposition. In both sets the temperature parameters are the upper lethal temperature (TMAX), the optimal temperature (TOPT), and the slope of the suboptimal process rate curve (Q10). These parameters were chosen because of a detailed study of this temperature construct (Scavia and Park, 1976). Equations (1) were integrated over a one year period with a grid size of 5 days. The given parameter values about which sensitivity is measured were known to produce results consistent with ecological theory and available data (Scavia and Park, 1976).

The stationary points obtained from (7) all lie close to the given values (Tables 1 and 2). The associated eigenvalues are mixed in sign indicating that the stationary points are not unique minima. With the exception of Objective criterion 2 with decomposition parameters, the largest eigenvalue differs by several orders of magnitude from the others. (Tables 1 and 2). By examination of the eigenvector transformation to original coordinates, it is seen that the effect of TMAX is an order of magnitude smaller than TOPT or Q10. TOPT and Q10 are similar in the magnitude of their effects on the objective criteria. Also, the cross-product of Q10 and TOPT is seen to have a large effect.

Under the appropriate error assumptions the reduced model given by backward elimination confirm the results from the canonical analysis (Tables 3 and 4). The fit for Objective criterion 2 for decomposition is not statistically significant. The crossproduct of Q10 and TOPT, representing interactions, is significant. The effect of Q10 and TOPT is seen to be compensatory (Figures 1 and 2). This compensatory effect is supported by theoretical considerations (Scavia and Park, 1976). Examination of the residuals (Figures 3 and 4), reveals no serious departure from normality although Objective criterion 1 with decomposition may represent a uniform distribution. This uniform distribution will not greatly effect the F-tests for it is non-symmetric distributions which have the greatest effect on the stated probability level of the F-test.

4. Discussion

The proposed method obtains global parameter sensitivity results consistent with known relationships. It should prove useful in examining model constructs and parameters where theoretical conclusions are not available. For the parameters of the example, the objective criteria of normalized absolute deviation provides a better fit to a quadratic model than a normalized sum of squares. Both criteria should be calculated. The cost of these calculations is minimal compared to the amount of computer time necessary to integrate the differential equations, and the degree of consistency between results provides a check of the analysis.

In the example provided for demonstration purposes for $p=3$ only $3^3=27$ different parameter sets needed to be examined. In this instance, the computation was not excessive for examining all combinations. However, for $p>3$, the amount of computing would build up very rapidly. When this is the case it will be wise to look at only a subset of the possible 3^p combinations. One method would be to analyze in previously defined subsets as in the example. Although in some models it is easy to define subsets, such an approach precludes sensitivity comparisons between the subsets. Another procedure would be to take a balanced fraction, 3^{-q}, so that only 3^{p-q} combinations would need to be examined. Assistance in choosing such subsets for various values of p and q is provided by tables (National Bureau of Standards, 1959). Fairly substantial initial fractionalizing would be recommended, with sequential augmentation of subsequent blocks of additional fractions if more precision is needed.

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Table 1

Canonical Analysis for Primary Production Parameter Sensitivity Analysis

	Stationary Points		
	TOPT	TMAX	Q10
Objective 1	19.04	34.39	1.76
Objective 2	19.61	34.31	1.83
Given	20.0	35.0	1.9

		Eigenvector		
	Eigenvalue	(TOPT)	(TMAX)	(Q10)
Objective 1	1954.59	.1348	-.0096	.9908
	-15.35	.9895	-.0517	-.1352
	.62	-.0525	-.9986	-.0025
Objective 2	62606.99	.1392	-.0068	.9902
	-751.93	.9903	-.0028	-.1392
	15.68	.0018	-.9999	-.0071

Table 2

Canonical Analysis for Decomposition Parameter Sensitivity Analysis

	Stationary Points		
	TOPT	TMAX	Q10
Objective 1	22.50	56.47	1.69
Objective 2	22.27	48.56	1.61
Given	25.0	50.0	1.7

		Eigenvector		
	Eigenvalue	(TOPT)	(TMAX)	(Q10)
Objective 1	3398.08	.0651	-.0075	.9978
	-8.59	.9707	-.2311	-.0651
	.90	-.2311	-.9729	.0078
Objective 2	-2091.31	-.1355	.1961	.9712
	214.39	-.9846	.0825	-.1541
	103.71	-.1103	-.9771	.1819

Table 3

Estimated Models for Primary Production Parameter Sensitivity

	Parameter	Coefficient	Std. Error	F to Remove
Objective 1	TOPT	-1767.1	270.4	42.7
	Q10	-17399.9	2598.9	44.8
	$(TOPT)^2$	20.4	6.4	10.1
	(TOPT)(Q10)	525.9	45.3	134.8
	$(Q10)^2$	1924.4	640.7	9.0
Objective 2	TOPT	-29959.1	3360.6	79.5
	Q10	-550184.4	>10000.0	29.6
	(TOPT)(Q10)	17457.3	1762.2	98.1
	$(Q10)^2$	61568.1	24922.0	6.1

Estimated models for Eqn. (6) using the stepwise backward elimination technique. F to remove values used to test significance of the parameters in the model.

Table 4

Estimated Models for Decomposition Parameter Sensitivity

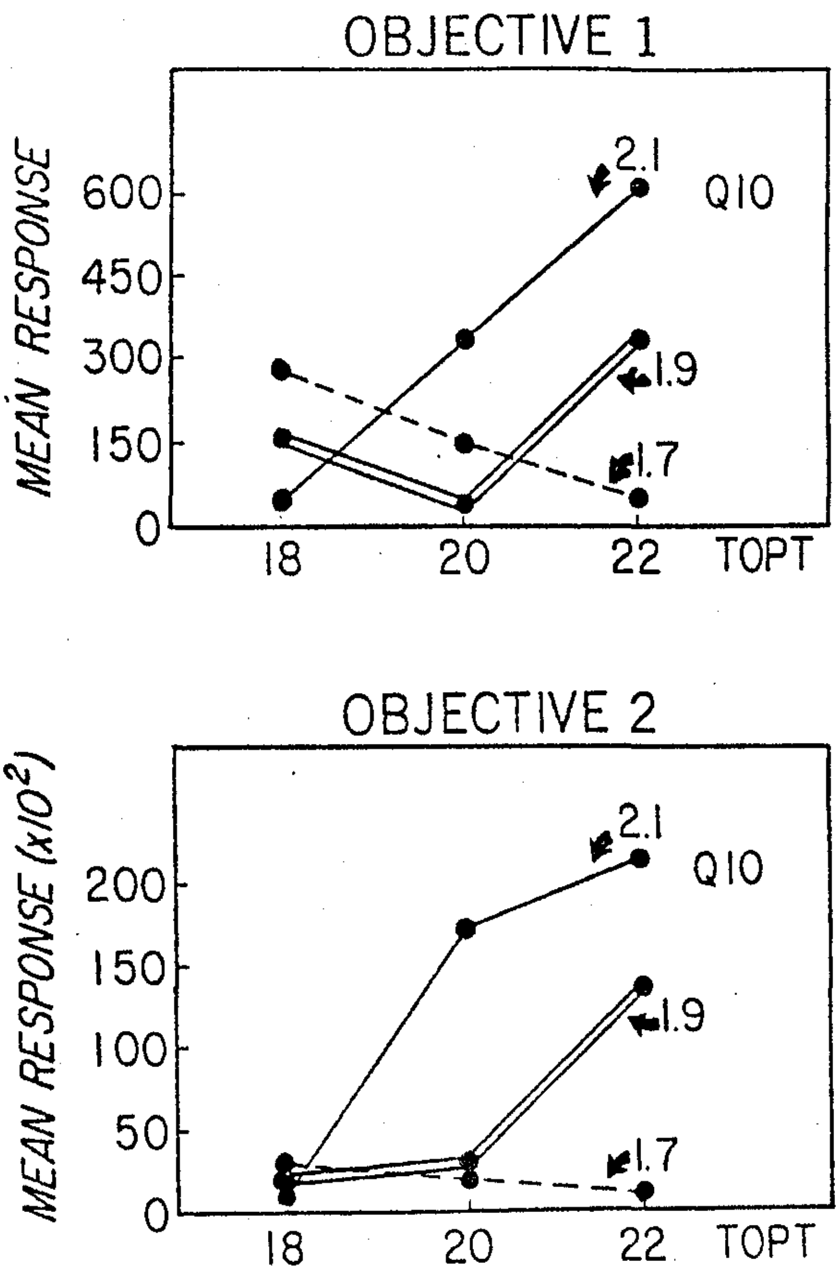
	Parameter	Coefficient	Std. Error	F to Remove
Objective 1	TOPT	-716.1	176.4	16.5
	Q10	-10670.3	2594.7	16.9
	(TOPT)(Q10)	442.6	103.4	18.3
Objective 2	No significant variables ($p>.05$)			

Estimated models for Eqn. (6) using the stepwise backward elimination technique. F to remove values used to test significance of the parameters in the model. The model fit by Objective 2 is not satisfactory with the full model having $F(9,17) = 1.58$.

Legend for Illustration

Figure 1

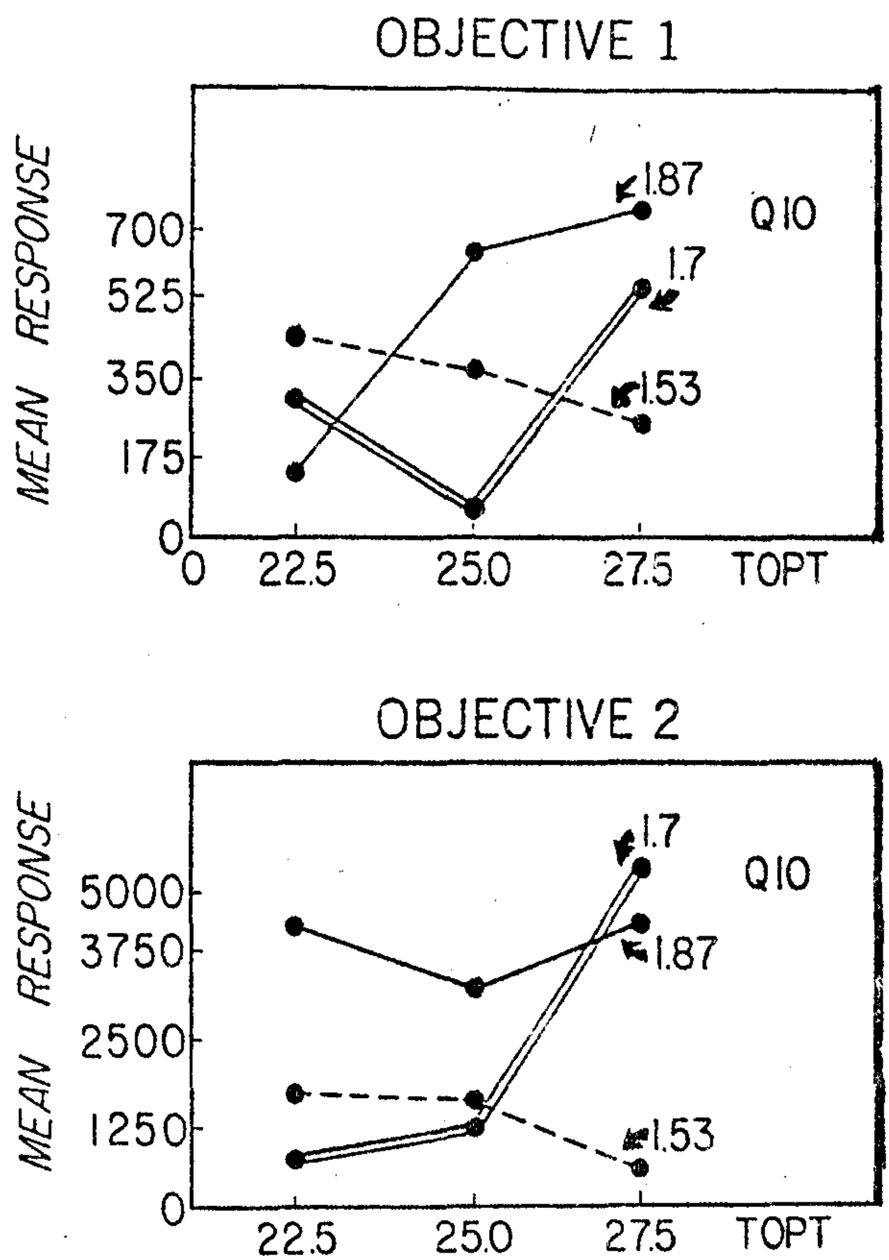
Interaction Plot - Primary Production Parameters



Legend for Illustration

Figure 2

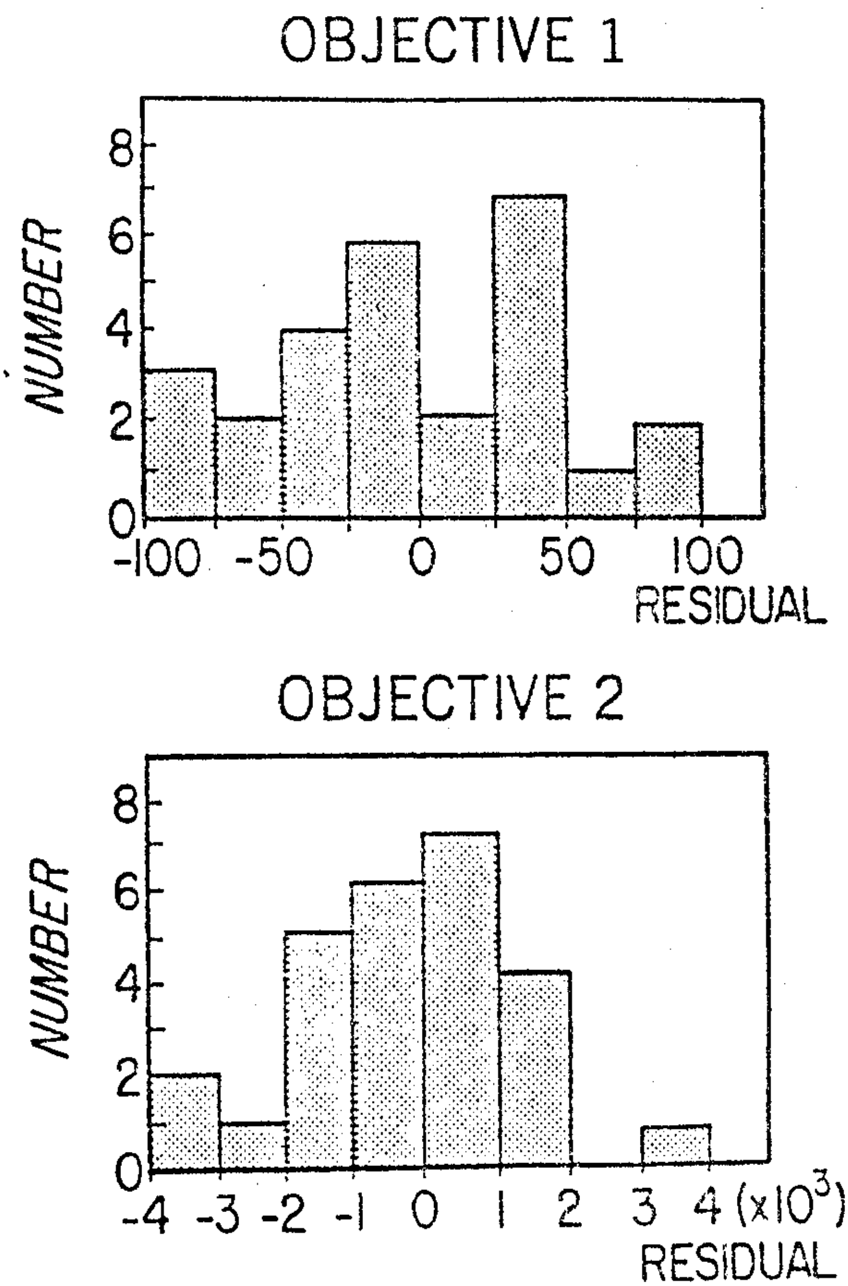
Interaction Plot - Decomposition Parameters



Legend for Illustration

Figure 3

Residual Histogram - Primary Production Parameters



Legend for Illustration

Figure 4

Residual Histogram - Decomposition Parameters