

Standard Errors and Confidence Intervals in Nonlinear Regression: Comparison of Monte Carlo and Parametric Statistics

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A Monte Carlo method is employed to characterize distributions of parameter values calculated in nonlinear regression problems. Accurate estimates of confidence intervals are easily obtained. Two illustrative numerical examples are provided to compare the Monte Carlo uncertainty estimates with those derived by use of standard methods of parametric statistics. The customary assumptions that (1) the effects of covariances between pairs of the parameters can be ignored and (2) that the distributions of the parameters are normal are shown to lead to significant errors, up to 2- and 3-fold in the calculated uncertainties. The Monte Carlo method is free from these assumptions and their associated errors.

Introduction

Methods for the calculation of adjustable parameters in both linear and nonlinear regression problems have been extensively discussed.¹⁻⁸ Less attention has been paid to the calculation of the uncertainties in the optimized values of these parameters. Difficulties arising from nonnormal distributions of adjustable parameters calculated in nonlinear regressions and from the existence of errors in both dependent and independent experimentally determined quantities as well as errors in fixed quantities are often ignored. Finally, the interdependencies among the calculated parameters are generally not considered. As a consequence, standard error estimates and the confidence intervals obtained by conventional nonlinear regression methods are sometimes incorrect.

These difficulties can all be overcome by using a Monte Carlo simulation method.⁹ As will be shown below, the Monte Carlo method is extremely simple to implement. Because of its simplicity and because the method is essentially a realization of the definition of random errors in terms of many hypothetical repetitions of the entire experiment, the Monte Carlo method is highly intuitive. As such it provides a useful and accurate means of estimating statistical uncertainties in nonlinear regression problems.

The General Regression Problem

In a general regression problem ideal data, subject to neither systematic nor random error, are presumed to satisfy exactly an equation of the form

$$F(q_1, \dots, q_n; \alpha_1, \dots, \alpha_r; \beta_1, \dots, \beta_s) = 0 \quad (1)$$

F is a function of the n different measured properties q_i , the r parameters α_i whose values are initially unknown, and the s parameters β_i whose values are assumed to be known. The sought for α_i parameters are adjusted until (1) is satisfied exactly. The values of the r parameters α_i represent solutions to the regression problem.

Essentially the same procedure is employed to evaluate real experimental data where each of the measured properties q_i and

"known" parameters β_i is subject to random error. We will assume throughout this work that systematic errors are not present. Measured q_i values are substituted into (1), and the values of the α_i parameters are adjusted to obtain a "best fit" of the equation to the data. Because random errors are present in the q_i and β_i , the equation is now only approximately satisfied. Adjustment of the values of the α_i to obtain the best fit is accomplished by a least-squares procedure. First, it is assumed that one of the measured properties, here denoted by q_1 , can be expressed as an explicit function of the other measured properties and the parameters α_i and β_i . Second, it is assumed that the values of the remaining q_i and of the α_i and β_i parameters are taken to be error free so that only q_1 suffers an error. We have

$$q_1 + \epsilon_1 = Q_1 = f(q_2, \dots, q_n; \alpha_1, \dots, \alpha_r; \beta_1, \dots, \beta_s) \quad (2)$$

where Q_1 is the value of property q_1 calculated from the explicit function f . Its value differs from the observed q_1 by a random error ϵ_1 , whose expectation value $\langle \epsilon_1 \rangle$ is 0 and whose variance is $[\sigma(q_1)]^2$. It is also necessary to assume that when the experiment is repeated using different sets of values of the independent variables, the values of ϵ_1 for each q_1 are independent of each other. It is not necessary to assume that ϵ_1 is a normally distributed variable, but only that its variance is finite. The assumption of normality is required only for the construction of confidence intervals.

The least-squares criterion for the best fit is realized by minimizing χ^2 (chi-square), where

$$\chi^2 = \sum_{j=1}^N \left[\frac{q_{1j} - f(q_{2j}, \dots, q_{nj}; \alpha_1, \dots, \alpha_r; \beta_1, \dots, \beta_s)}{\sigma(q_{1j})} \right]^2 \quad (3a)$$

$$= \sum_{j=1}^N \left[\frac{q_{1j} - Q_{1j}}{\sigma(q_{1j})} \right]^2 \quad (3b)$$

In these equations, the sum is over N sets of experimental data indexed by j . Each set consists of n measurements of the properties q_i . Thus, q_{ij} represents the value of q_i observed during the j th experiment and $[\sigma(q_{1j})]^2$ is the variance of q_{1j} .

Minimization of χ^2 may be accomplished analytically when f is a linear function of the adjustable parameters. An example is the well-known weighted least-squares linear regression. Dependent y values are taken to suffer errors that may vary from one measurement to the next, while independent x values (q_{2j}) are taken to be exact. Best values of slope and intercept (α_1 and α_2) are analytical functions of the q_{1j} and q_{2j} . Variances of the slope and intercept are readily derived in closed form.

If the functional form of (2) is nonlinear in the adjustable parameters and if, once again, there are errors only in the dependent variables q_{1j} , then the Levenberg-Marquardt method provides an efficient iterative algorithm for determining best fit values of the adjustable parameters and their variances.^{9,10} In

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either case, if the functional form of (1) and (2) accurately represents the interrelationship of the data and the adjustable and fixed parameters, and if $[\sigma(q_{ij})]^2$ has a fixed (j -independent) value, then the value of χ^2 can be approximated by $N - r$, the number of degrees of freedom. Moreover, the best fit values of α_i represent the maximum likelihood values of these parameters. We defer the discussion of variance estimates and confidence intervals for the optimized values of α_i to a later section.

If the simplifying assumptions mentioned above are not satisfied, the problem becomes much more difficult. Nevertheless, methods for evaluating the optimized values of the parameters are by now well established and can be implemented by suitable modifications in the Levenberg-Marquardt procedure.

Extension of the Levenberg-Marquardt Method

The extension of the Levenberg-Marquardt method involves three steps.

1. If the model function is defined implicitly, it can be converted to an explicit form using numerical methods. One of the variables, say q_1 , is arbitrarily chosen to be dependent. Given the values of all the other q 's and the fixed and adjustable parameters, (1) can be solved numerically for q_1 . The derivatives of q_1 with respect to each adjustable parameter α_i and with respect to the other q 's can be evaluated by use of standard techniques of calculus for implicit differentiation.

2. Because there are errors in each of the independent variables and in each of the fixed parameters, $\sigma(q_{ij})$ must be replaced by

$$\sigma_j^2 = \sigma(q_{ij})^2 + \sum_{i=2}^N \left(\frac{\partial F}{\partial q_{ij}} \right)^2 \sigma(q_{ij})^2 + \sum_{i=1}^S \left(\frac{\partial F}{\partial \beta_i} \right)^2 \sigma(\beta_i)^2 \quad (4)$$

3. Finally, as Jefferys points out, all the derivatives used in the procedure should be evaluated by using the best estimates of the data points as well as the best estimates of the parameters rather than simply at the observation points.¹¹ Assuming two measured properties only, x an independent variable and y the dependent one, the correction δx to the observed value of x is given by

$$\delta x = \frac{\sigma_x^2(y - Y) \left(\frac{\partial Y}{\partial X} \right) + \sigma_y^2(x - X)}{\sigma_x^2 \left(\frac{\partial Y}{\partial X} \right)^2 + \sigma_y^2} \quad (5)$$

where x and y are the measured points, X is the present best guess of the corrected value of x , and Y is the value of the model function calculated at the best present values of X and of the parameters. Note that if there is no error in x , the correction is zero.

Examples of the implementation of points 1 and 2 are given by Wentworth;^{3,4} implementation of point 3 for linear regression problems is given by Lybanon.¹²

Standard Errors of the Parameters

The customary method for obtaining the uncertainties in each of the optimized values of the adjustable parameters involves inverting the matrix A whose k th element is given by

$$A_{kl} = \sum_{j=1}^N \left(\frac{\partial q_1(\bar{q}_j; \bar{\alpha})}{\partial \alpha_k} \right) \left(\frac{\partial q_1(\bar{q}_j; \bar{\alpha})}{\partial \alpha_l} \right) / \sigma_j^2 \quad (6)$$

where \bar{q}_j denotes the j th measurement of the $n - 1$ q 's chosen to be the independent variables and $\bar{\alpha}$ denotes the set of the r adjustable parameters. The diagonal element C_{ii} of the inverse matrix A^{-1} , called the covariance matrix, is the variance, i.e., the second central moment, of the parameter α_i . In most treatments of this subject it is maintained that the square root of C_{ii} , $\sigma(\alpha_i)$, is the standard error of α_i with the implication that there is a 68.3%

probability that the "true" value of α_i lies in a (confidence) interval of width $2\sigma(\alpha_i)$. However, the square root of the variance is the standard error only if each adjustable parameter α_i can be considered to be drawn from a Gaussian distribution. In other words, if the experiment were repeated many times, each repetition would yield a value of α_i , and the set of these α_i would be distributed normally.

In general we have no reason for assuming that the parameters are distributed normally. A normal distribution of each of the adjustable parameters depends on the following conditions: (1) The errors in the data must be normally distributed. (2) The mathematical model must be expressed as a function linear in the adjustable parameters and linear in the data variables. If these conditions are satisfied, the optimized values of the adjustable parameters can be expressed as linear functions of the data points. Since linear functions of normally distributed variables are also normally distributed, the adjustable parameters are themselves normally distributed.

These conditions are satisfied for only the simplest textbook examples of linear and multiple linear regression. For these special cases, the square root of the diagonal matrix element C_{ii} is the standard error of α_i and confidence intervals can be calculated by using values of Student's t or the multivariate F statistic.¹³⁻¹⁵ Note that if the model equation has been transformed from a nonlinear to a linear form, then the errors of the transformed variables must be normally distributed, if the adjustable parameters are also to be normally distributed.

Even if the distribution of the adjustable parameters is normal, the standard error estimate derived from the diagonal matrix element C_{ii} of the covariance matrix does not necessarily reflect the uncertainty in α_i . The off-diagonal elements C_{ij} are the covariances of α_i and α_j , which are generally nonzero. The standard error estimate for a particular α_i obtained from the square root of the C_{ii} matrix element depends on the assumption that the other parameters are fixed at their optimized values.

Bard¹⁵ and more recently Schwartz¹⁴ have developed ad hoc methods for approximating joint confidence intervals for multi-parameter regression analysis. Their methods rely on the assumption that calculated α_i values are normally distributed, a condition that we have seen is generally not realized. Furthermore, the procedures suggested by these authors do not provide probabilistic interpretations of the approximate confidence intervals. We show below that the Monte Carlo method does provide such probabilistic interpretations.

Monte Carlo Calculation of Confidence Intervals

The Monte Carlo method of calculating the errors in the adjustable parameters overcomes all of the difficulties discussed in the previous section. An implementation of the procedure consists of the following steps:

1. Compute the optimized values of α_i using the extended Levenberg-Marquardt method.

2a. Simulate a repetition of the experiment by generating a new set of q_{ij} and β_i such that

$$q'_{ij} = q_{ij} + \epsilon_{ij} \quad (7a)$$

and

$$\beta'_i = \beta_i + e_i \quad (7b)$$

where ϵ_{ij} and e_i are random variables chosen to approximate uncertainties in q_{ij} and in β_i . We employ the Box-Muller method to provide random Gaussian-distributed values with mean zero and appropriate standard deviation for ϵ_{ij} and e_i .¹⁶ If x is the Gaussian-distributed variable with mean μ and variance σ^2 , then

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$$x = z\sigma + \mu \quad (8)$$

where

$$z = (-2 \ln(p_1))^{1/2} \cos 2\pi p_2 \quad (9)$$

In (9), z is a normally distributed variable (mean = 0; variance = 1), while p_1 and p_2 are uniformly distributed random numbers between 0 and 1.

It should be noted that other distributions, perhaps better suited to the data in question, could be used to generate the new set of q'_{ij} and β'_{ij} . However, alternative error distributions must be consistent with the least-squares best fit conditions which is inherent in regression analysis. That is, both ϵ_{ij} and e_i must have expectation values of zero and have finite variances.

2b. With the use of the new data set and fixed parameters, the extended Levenberg-Marquardt method is then used to calculate optimized values of the r adjustable parameters, which we call A_i .

3. Step 2 is now repeated many times. The set of calculated A_i values constitutes by definition the distribution function for each α_i .

At this point we note a most convenient property of the Monte Carlo method. It is frequently the case that a sought-for parameter is a function of two or more α_i parameters. A classic example is found in determining the pK for an indicator by spectrophotometric measurement. A plot of reciprocal absorbances versus $1/[H^+]$ provides slope and intercept values whose ratio is interpreted in terms of the indicator constant. The Monte Carlo method allows direct calculation of this ratio of the A_i values arising from the corresponding α_i parameters and thus provides the distribution of this ratio. This procedure automatically accounts for interdependencies (covariances) between α_i values.

The values of A_i and any other calculated parameters which are functions of the A_i are now sorted in numerical order. Standard error estimates are here defined as 68.3% confidence intervals. The number of Monte Carlo simulations is chosen to be sufficiently large so that the Student's t statistic is essentially 1.00 at the 68.3% confidence level. The confidence intervals are obtained from the ordered list by eliminating from the list those A_i values included in the upper and lower 15.8% $([100 - 68.3]/2)$ of values. In the same manner, 90% confidence intervals correspond to the range of parameter values that remain after the exclusion of the upper and lower 5% of the values. This procedure obviates the need for the frequently erroneous assumption that the values of α_i parameters are distributed normally and for the assumption that the experimental uncertainties ϵ_i be small compared with the measured quantities q_i .

Examples

We illustrate the Monte Carlo procedure using two examples. The first involves an analysis of kinetic data provided by Wentworth in an often quoted paper.⁴ The second calculates the equilibrium constant in a hypothetical dimerization reaction.

1. *Decomposition of Acetaldehyde.* Wentworth describes an experiment in which the rate constant and reaction order for the decomposition of acetaldehyde into methane and carbon monoxide is determined by measuring the total pressure of the gaseous mixture P in millimeters as a function of time t measured in seconds. The initial value of the pressure is P_0 at time zero. The reaction order is n and the model equation is

$$-(2P_0 - P_i)^{-n+1} + (n-1)kt_i + P_0^{-n+1} = 0 \quad (10)$$

In (10) P_0 , n , and k , the rate constant, are taken as adjustable parameters. The data are reproduced in Table I. We follow Wentworth in assuming normally distributed errors in P_i and t_i with $\sigma(P_i) = 1.0$ mm and $\sigma(t) = 1.0$ s.

Using the extended Levenberg-Marquardt method, we obtain the parameter values also shown in Table I. These values are close to those found by Wentworth. The two methods differ most in calculating the rate constant, k , which is estimated as 7.153×10^{-6} by Wentworth and here as 7.454×10^{-6} . We conclude that the Jefferys correction employed in the present calculation has

TABLE I: Decomposition of Acetaldehyde
 P versus t Data

P , mmHg	t , s
363.0	0.0
397.0	42.0
437.0	105.0
497.0	242.0
557.0	480.0
607.0	840.0
647.0	1440.0

Best Fit Parameter Values and Their Parametric Error Estimates

	Wentworth	Levenberg-Marquardt
P_0	364.08 ± 1.00	363.95 ± 0.997
n	1.983 ± 0.0259	1.976 ± 0.0252
$10^6 k$	7.153 ± 1.065	7.454 ± 1.090

Confidence Intervals

	Wentworth		Levenberg-Marquardt		Monte Carlo	
	68.3%	90%	68.3%	90%	68.3%	90%
P_0	1.13	2.13	1.13	2.12	1.02	1.53
n	0.029	0.055	0.028	0.054	0.025	0.036
$10^6 k$	1.20	2.27	1.24	2.31	1.08	1.56

only a minor effect. The χ^2 statistic, found to be 2.42, is in good agreement with the number of degrees of freedom ($N - r = 7 - 3$).

Wentworth obtains standard error estimates for each adjustable parameter by taking the square root of the appropriate diagonal element of the covariance matrix. He finds 1.00, 0.0259, and 1.065×10^{-6} for standard errors in P_0 , n , and k , respectively. The Levenberg-Marquardt algorithm also provides uncertainties based on the diagonal elements of the covariance matrix. The values obtained from this algorithm are similar to Wentworth's.

We employ these standard error estimates obtained from the covariance matrix to obtain the 68.3% and 90% confidence intervals for the three adjustable parameters. For each α_i , these intervals extend $t\sigma_i$ above and below the mean value α_i , where t is the Student's t statistic. For the present case of four degrees of freedom, t is equal to 1.13 and 2.13 for the 68.3% and 90% confidence intervals, respectively. We note that this procedure relies on the customary assumption of normally distributed α_i .

The confidence interval half-widths $t\sigma_i$ are to be compared with those obtained from the Monte Carlo values, based on 200 hypothetical repetitions of the experiment, shown in Table I. These results indicate relatively minor differences in the 68.3% confidence intervals but predict significantly different 90% intervals. For example, the 68.3% half-interval for n based on the extended Levenberg-Marquardt solution and employing the standard error derived from the covariance matrix is 0.028. That is, the "true" value of n lies in the interval $1.948 \leq n \leq 2.004$ with 68.3% confidence. The corresponding Monte Carlo estimate of the half-width is 0.025, implying a 68.3% confidence interval of $1.951 \leq n \leq 2.001$. The 90% confidence half-width estimates are 0.054 and 0.036, based on the covariance matrix and on Monte Carlo calculations, respectively. Expressed as percent differences, the 68.3% and 90% confidence intervals for the parametric calculations differ by about 10% and 50% from the corresponding Monte Carlo calculations, respectively. These estimates, especially for the 90% confidence intervals, appear to be significantly different.

We note that the estimates based on the covariance matrix are too conservative compared with the Monte Carlo results. The joint parametric uncertainty estimates using the method suggested by Schwartz¹⁴ are even more conservative; they are about a factor of 3 larger than $t\sigma_i$.

The agreement for the 68.3% confidence interval is a result of two factors. First, the distributions of P_0 , n , and k are well approximated by a Gaussian distribution with a variance given by the diagonal elements of the covariance matrix in the central region (defined by the 68.3% confidence interval). This situation obtains in many problems, such as those discussed by Schwartz,¹⁴ where the experimental errors are sufficiently small so that the

TABLE II: Hypothetical Dimerization Reaction
A versus C Data

<i>A</i>	<i>C</i>	<i>A</i>	<i>C</i>	
0.0516	0.00297	0.1915	0.01537	
0.0733	0.00468	0.2777	0.02477	
0.0873	0.00511	0.3844	0.04004	
0.1053	0.00711	0.5048	0.06007	
0.1402	0.00989	0.7058	0.10011	
Best Fit Parameter Values and Their Parametric Error Estimates				
<i>K</i>		0.03052 ± 0.00531		
<i>a_M</i>		19.98 ± 0.88		
<i>a_D</i>		1.841 ± 0.491		
Confidence Interval Half-Widths				
	parametric		Monte Carlo	
	68.3%	90%	68.3%	90%
<i>K</i>	0.00563	0.01009	0.00226	0.00299
<i>a_M</i>	0.928	1.66	0.383	0.552
<i>a_D</i>	0.520	0.933	0.241	0.360

distribution in the central region is approximately Gaussian. Second, the agreement in this example depends on the fact that the covariances between pairs of the adjustable parameters are small and, moreover, have different signs and thus tend to cancel.

The lack of agreement between the Wentworth and Monte Carlo calculation for the 90% confidence interval indicates that the distribution of the parameters cannot be approximated by a Gaussian distribution if the "tails" of the distribution are important in the calculation of the interval. In the Wentworth example, the adjustable parameters have distributions that decay more steeply than does the Gaussian.

2. *Hypothetical Spectrophotometric Analysis of a Dimerization Equilibrium.* In the second example, we envision a series of 10 spectrophotometric measurements recording absorbances *A*, using a path length *b* cell with solutions of differing concentration *C*, of some substance which undergoes dimerization. Extinction coefficients for the monomer and dimer are *a_M* and *a_D*, respectively. The dimer dissociation constant is *K*. The model equation is

$$A = b(a_M - a_D/2)[M] + ba_D C/2 \quad (11)$$

where

$$[M] = [-K + (K^2 + 8CK)^{1/2}]/4 \quad (12)$$

Idealized *A* versus *C* data are obtained from (11) and (12) using $0.003 \leq C \leq 0.1$; $K = 0.03$, $a_M = 20.0$; $a_D = 2.00$; and $b = 1.00$. The measured quantities, *A* and *C*, are then subjected to experimental error by randomly perturbing their values using the Box-Muller method and arbitrarily taking σ_A and σ_C to be equal to 0.0005 and 0.0003, respectively. In this way we avoid the possibility of systematic errors in the following analysis. We assume that *b* is error-free. Randomly perturbed *A* and *C* data, shown in Table II, are now fit to the model equation by the extended Levenberg-Marquardt algorithm with results also given in Table II. The goodness-of-fit parameter, χ^2 , had a value of 4.9, reasonably close to the 7 degrees of freedom. The calculated *K*, *a_M*, and *a_D* values approximate their "true" values.

Standard error estimates from diagonal elements of the covariance matrix are listed along with confidence intervals based on $t = 1.06$ and 1.90 for 68.3% and 90% confidence levels, respectively. Monte Carlo confidence intervals, obtained from 200 simulations, for the three adjustable parameters are 2–3 times smaller than those obtained from the diagonal elements of the covariance matrix. That is, the Monte Carlo simulation indicates that the *A* versus *C* data determine the values of the adjustable parameters with a much higher precision than the usual methods of uncertainty estimation would indicate.

We attribute the differences between the error estimates obtained from the two methods, even at the 68.3% confidence level, principally to significant covariances between parameters rather than to deviations from parameter normal distributions. We have seen earlier that the effects of non-normal parameter distributions

TABLE III: Confidence Intervals as a Function of Number of Monte Carlo Simulations for the Dimerization Example

no. of Monte Carlo simulns	confidence interval half-width					
	<i>K</i>		<i>a_M</i>		<i>a_D</i>	
	68.3%	90%	68.3%	90%	68.3%	90%
60 (10, 3) ^a	0.0021	0.0028	0.38	0.52	0.28	0.39
100 (16, 5)	0.0022	0.0030	0.39	0.53	0.28	0.39
200 (32, 10)	0.0023	0.0030	0.38	0.55	0.24	0.36
400 (64, 20)	0.0023	0.0030	0.39	0.54	0.24	0.39

^a Parenthetic values indicate the number of upper (and lower) extreme values used to identify the 68.3% and 90% confidence intervals, respectively.

are minor at the 68.3% confidence level in problems such as these where the experimental errors are small. In the present example, standard error estimates from diagonal elements of the covariance matrix neglect the interdependencies between parameters and lead to erroneous results. We note that one cannot conclude that confidence intervals based on the covariance matrix will always be too conservative. In other problems the parameter covariances could be such that estimates based on the covariance matrix would be too optimistic.

Both the parametric and Monte Carlo error analyses rely on accurate estimates of the uncertainties in the measured quantities (concentrations and absorbances in this example). In many practical applications such estimates may not be available. In such cases the χ^2 statistic obtained in the fitting procedure provides some information. Suppose that the uncertainty in one of the measured quantities (perhaps in the concentration) is known. The error in the other quantity (absorbance) can then be estimated by choosing its value so that χ^2 becomes approximately equal to the number of degrees of freedom. In the two examples, the values of χ^2 differ from the number of degrees of freedom by approximately 40% and 30%, respectively. Using (3b) and assuming for simplicity that all the $\sigma(q_{ij})$ are equal, we find that the errors in the estimates of the $\sigma(q_{ij})$ are probably no greater than 20%. This procedure of course assumes that the mathematic model describing the experiment is correct. While this approach has often been employed in estimating experimental uncertainties, it seems inferior to the traditional "experimental" method of simply repeating a given measurement an appropriate number of times.

Practical Considerations

How many times should the Monte Carlo simulation be repeated? In an effort to answer this question we determined confidence intervals of the adjustable parameters derived in the dimerization equilibrium problem using 60, 100, 200, and 400 repetitions. The results of these calculations appear in Table III. They indicate that, at least for this example, essentially constant estimates of the confidence intervals are obtained after only 60 repetitions. These results are not unreasonable since each Monte Carlo simulation involves an average over 20 random variables (10 absorbances and 10 concentrations). The adjustable parameters are in a sense mean values derived from the data, so that the random fluctuations in the data points tend to cancel.

There do exist theoretical estimates, such as the Chebychev inequality and estimates based on the central limit theorem, of the number *L* of Monte Carlo simulations required for a particular problem.¹⁶ We believe that the most practical means of determining *L* in the problem of determining confidence intervals is to note that if the confidence intervals derived from *L* and from *2L* simulations are reasonably similar, these intervals are quite probably accurate estimates of the "true" confidence intervals. The number of simulations required to determine the 90% confidence interval is naturally larger than the number needed for the 68.3% since the 90% interval relies on the relatively few number of extreme *A_i* values. A prudent course involves choosing *L* large enough so that at least 5–10 extreme *A_i* values from each side of the distribution are discarded. This corresponds to $L > 30$ for the 68.3% interval and $L > 100$ for the 90% interval. A repetition of the calculation with *2L* simulations can then be

employed to confirm the results.

Summary

The present calculations indicate that Monte Carlo simulations are capable of providing useful estimates of confidence intervals for optimized values of parameters derived from nonlinear regression problems. Customary methods of variance analysis based on calculation using the covariance matrix may lead to incorrect

results in problems where parametric covariances are important. Even in cases where the covariances may be safely neglected, non-Gaussian distributions of calculated parameters preclude probabilistic interpretations of standard error estimates derived in the usual manner.

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Radiolytic Generation of Organic Radical Cations in Zeolite Na-Y

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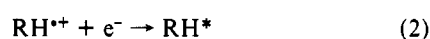
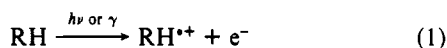
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Several examples of radiolytically generated organic radical cations in zeolite Na-Y are illustrated. EPR studies of organic radical cations can be carried out in a wide range of temperatures up to room temperature. In every case, monomeric radical cations were observed. Comparison to previous work in freon and xenon matrices is made, illustrating that in the zeolite Na-Y there is considerably weaker radical cation-host interaction. A mechanism of radiolytic generation of radical cations in zeolite Na-Y is proposed.

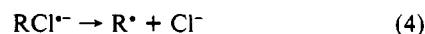
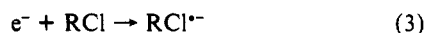
Introduction

The study of organic radical cations is closely tied to the methods that allow their preparation and stabilization. In the past decade, many organic radical cations have been examined by EPR and optical absorption spectroscopy using low-temperature halocarbon solvents.¹ With smaller organic cations, the more inert neon matrix was successfully utilized.² Recently, we have found that xenon matrices can be used to study organic radical cations by EPR over a considerable temperature range.³ A recent report has illustrated how superacidic membranes such as Nafion can be used to stabilize and study radical cations, even at room temperatures.⁴

In order to stabilize organic radical cations, two dominant processes must be prevented. First, we must prevent the reverse electron transfer when the electron, ejected from the neutral to give the radical cation (eq 1), returns to neutralize the radical cation (eq 2).



This is accomplished by scavenging the electron and preventing the possibility of back electron transfer as in halocarbons, where dissociative electron capture (eqs 3 and 4) takes care of the electron permanently.



The second reaction we must prevent is an ion-molecule reaction of the radical cation. Several dominant radical cation reactions

have been examined by the time-resolved fluorescence detected magnetic resonance (FDMR) technique.⁵ The main reaction that alkane radical cations undergo in hydrocarbons is proton transfer to the neighboring neutral molecules. This reaction can be prevented by segregating the radical cation from its parent neutrals as is done in halocarbons or inert gas matrices. In some cases, as in neon matrices, the rigidity of the matrix and the very low temperatures used, 4–10 K, effectively freeze any molecular motion.

However, restricted temperature range is a serious limitation of neon or any inert gas matrix for the study of radical cations since well-resolved EPR spectra of larger organic cations and other temperature-dependent effects cannot generally be observed. Halocarbon matrices have had the most widespread use due to a considerable temperature range available up to ~160 K. But, there is often a very strong cation-matrix interaction. The structure and chemistry exhibited by the radical cation can be a consequence of matrix interaction and may not reflect an intrinsic behavior of radical cations. The xenon matrix also has a wide temperature range, up to 110 K, but electron scavengers must be used, so there is still a possibility of interaction between the cation and anions produced, albeit far less than in the halocarbon matrix.

Here we describe yet another way of generating and stabilizing organic radical cations. As this preliminary report will illustrate, zeolite Na-Y satisfies two main criteria for stabilizing radical cations. A variety of organic radical cations can be radiolytically generated in zeolite Na-Y where no electron scavengers are used, and the tremendous flexibility and temperature range make zeolite Na-Y one of the most promising means of stabilizing and studying organic radical cations with minimal matrix and counterion complications. Radical cations of a few aromatic compounds were studied on γ -irradiated silica gel or the H-Y molecular sieve,⁶ but we are aware of only one previous report in which alkane radical cations were observed at 4 K in a synthetic zeolite (ZSM-5).⁷

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