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SUMMARY

A quantal response model used in the analysis of an experiment described by Petersen, Cornell and Puleo (Space Life Sciences, 1969) is presented. The purpose of the experiment was to relate the probability of exposing one or more viable microorganisms, as the result of fracturing plastic rods, to the concentration of microorganisms within the plastic.

In the initial analysis a maximum likelihood estimate of the only parameter involved was computed for each of four fracture areas studied using observed proportions of fractured plastic discs showing growth of bacterial spores and corresponding experimentally determined concentrations. The concentrations were assumed to be measured without error. When the model was evaluated using the calculated parameter estimates it was found that it did not describe the data adequately.

In this paper an estimation procedure is developed for the concentrations which utilizes the observed proportions as well as the observed concentrations. Subsequent calculations like those carried out initially are illustrated and lead to practically the same estimates of the model parameter and its standard error, but dramatically reduce the chi-square statistic used to test the appropriateness of the model to a value somewhat less than its expectation.

1. INTRODUCTION

This paper is concerned with the evaluation of a quantal response model used in the analysis of an experiment described by Petersen, Cornell and Puleo [1969]. The immediate purpose of the experiment was to relate the probability of exposing one or more viable microorganisms, as the result of fracturing a contaminated solid, to the concentration of microorganisms within the solid and to the fractured surface area exposed. This experiment was a part of a long range program to obtain information on the possibility of viable microorganisms being released on planets by the impact of a space vehicle.

The experiment involved several rods of solid methyl methacrylate plastic inoculated during preparation with a wide range of concentrations of Bicillus subtilis var. niger spores. A batch of smaller discs was cut from each of these rods. Two discs from each batch were selected for assay. They were dissolved and incubated separately to obtain two spore counts and subsequent concentration extimates for each batch. We shall denote these observed concentrations by x_{i1} and x_{i2} for the i^{th} of k batches. We shall use θ_i to denote the corresponding true contentration. Two more discs from each batch were incubated for thirty days and observed for bacterial growth as a control on the surface sterilization and handling techniques. None of these controls exhibited growth.

The remaining discs from each batch were aseptically fractured exposing approximately 30.6 mm^2 of fractured surface on each half or quarter disc. As each disc was fractured one to four pieces were placed in a tube of sterile trypticase soy broth for incubation. Approximately 30.6, 61.2,

91.8 or 122.4 mm^2 of fractured surface were exposed depending on the number of pieces placed in the tube. The same fractured surface area was exposed in each of the tubes from each batch. The tubes from each batch were divided into either one or two sets of twenty. Any tube showing evidence of bacterial growth during thirty days of observation was recorded as positive. The proportion of positive tubes among the twenty tested was recorded for each set from each batch. We shall denote these proportions by y_{i1} and y_{i2} for sets one and two respectively, i=1,2,...,k.

In the analysis of the data from this experiment, Petersen et al. assumed that the bacterial spores were distributed independently throughout the plastic in accord with the Poisson distribution with the mean number of microorganisms on surfaces exposed by fracture proportional to the product of the area exposed and the spore concentration. The proportionality constant was called λ and was interpreted as the depth to which viable spores located near the fractured surface were exposed to liquid nutrient. The expected value of an observed proportion for the j^{th} set of tubes from batch i, denoted by P_j, was therefore given by

$$P_i \equiv E(y_{ij}) = 1 - \exp.\ (-\lambda\ \theta_i\ A)\ , \qquad (1)$$

where A is the area exposed by fracture and the number of positive tubes in such sets, represented by $20\ y_{ij}$, were taken to be binomially distributed.

Graphically for each of the four A values used, a plot of $[-\ln(1-y_{ij})]$ against the observed mean concentrations $\bar{x}_i = (x_{i1}+x_{i2})/2$ depicted a linear relationship through the origin with variability increasing as $\bar{x}_i$ increases, as would be anticipated with the model presented. Therefore, for each of these areas maximum likelihood estimates of λ, using $\bar{x}_i$ instead of θ_i for each i, were computed. We will denote such an estimate by $\hat{\lambda}_1$. The computational formulas were presented by Peto [1953], who also developed this model for a similar experimental situation. The estimates of λ for the four areas were close together and an overall estimate was computed. A goodness-of-fit statistic X^2 was also computed for each area, where

$$X^2 = 20 \sum_{i=1}^{k} \sum_{j=1}^{n_i} \frac{(y_{ij}-\hat{P}_i)^2}{\hat{P}_i(1-\hat{P}_i)} \qquad (2)$$

and each $\hat{P}_i$ was computed from (1) after setting $\theta_i = \bar{x}_i$ for each i and replacing λ by its maximum likelihood estimate $\hat{\lambda}_1$. The symbol n_i is the number of sets of tubes tested for batch i and was either one or two for all batches. For the three smaller areas, X^2 was much larger than the appropriate 95^{th} percentile of chi-square, indicating an inadequate model. However, an examination of individual terms in (2) revealed many terms of 0.3 or less and many terms of 3 or larger with relatively few terms near one as would be expected. This is the pattern that would result if the computation of the $\hat{P}_i$ in (2) were in error, particularly for small $\hat{P}_i$, that is, for the smaller areas and concentrations. Since the largest contri-

butions to X^2 did occur for small A and $\bar{x}_i$ products and since the poorest fit of the model as described by X^2 was obtained for the smallest exposure area studied, it was surmised by Petersen et al. that the apparent inappropriateness of the model as measured by X^2 was due to the fact that the observed concentrations $\bar{x}_i$ were highly variable and did not approximate the true concentrations θ_i well enough instead of to inadequacy of the model as represented by (1).

In Section 2 of this paper, an alternative estimator of θ_i is developed which, for each batch, utilizes the observed proportions positive, y_{ij}, as well as the corresponding observed concentrations, x_{i1} and x_{i2}. These new concentration estimates, denoted by $\hat{\theta}_i$, are then used as were the $\bar{x}_i$ before to replace the θ_i in (1) in order to compute maximum likelihood estimates of λ and goodness-of-fit statistics. It has been found that the new concentration estimates lead to goodness-of-fit statistics very close to their expected values, thus verifying the conjecture made after the initial analysis. The computations are illustrated in Section 3 and compared with the corresponding results of Petersen et al. for the smallest exposure area studied of approximately 30.6 mm^2. This is the area for which poorest fit was obtained initially.

2. CONCENTRATION ESTIMATION

In this section we develop a procedure for estimating θ_i for the i^{th} batch which uses both the x_{ij} and y_{ij} observations. As indicated in the introduction, the range of the subscript i is from 1 to k throughout. The range of j when it is used as a subscript of x is from 1 to 2, while for y the subscript j equals one only for some i and equals either 1 or 2 for the others. The exposure area A is assumed to be known and the same for each batch.

For each batch we could take $\bar{y}_i$ as an estimate of $E(y_{ij})$, where

$$\bar{y}_i = \left(\sum_{j=1}^{n_i} y_{ij}\right)/n_i \ , \ n_i=1 \text{ or } 2 \ .$$

In accord with (1) we would then compute an estimate $\hat{\gamma}_i$ of $\gamma_i = \lambda\theta_i$ as

$$\hat{\gamma}_i = -\ (1/A)\ln(1-\bar{y}_i) \ . \tag{3}$$

From γ_i we could compute an estimate

$$v_i = \hat{\gamma}_i/\hat{\lambda}_1 \tag{4}$$

of θ_i, where $\hat{\lambda}_1$ is the maximum likelihood estimate of λ with θ_i replaced by $\bar{x}_i$ for each i. Since $\hat{\gamma}_i$ is a monotonic increasing function of $\bar{y}_i$, the v_i have the same order as the $\bar{y}_i$ and involve the x_{ij} only in the computation of the scale factor $1/\hat{\lambda}_1$.

The v_i concentration estiamtes computed from (4) along with the estimate $\hat{\lambda}_1$ appearing in the denominator of each v_i could be substituted into equation (2) for the goodness-of-fit statistic X^2. The evaluation of

each $\hat{P}_i$ would involve $\hat{\lambda}_1$ only in the product $\hat{\lambda}_1 \cdot v_i$, which equals $\hat{\gamma}_i$ and is a function of $\bar{y}_i$ but not of the x_{ij}. Therefore, X^2 computed using the v_i and $\hat{\lambda}_1$ is a function of only the y_{ij}. It involves the substitution of $\bar{y}_i$ for $\hat{P}_i$ in (2) and would not give a measure of the adequacy of (1) or of the appropriateness of the estimate $\hat{\lambda}_1$. Instead it would give a test of the assumption of binomial variation of the y_{ij} within each batch when it is compared with the chosen percentage point of the chi-square distribution with $\sum_{i=1}^{k} (n_i-1)$ degrees of freedom. It is used for this purpose in the next section.

Our objective is to obtain an estimate of θ_i for each batch which combines information provided by both the x_{ij} and the y_{ij}. We have just seen that the v_i by themselves are not reasonable for this purpose since they do not utilize the form of the $E(y_{ij})$ as given by (1) and they only involve the x_{ij} in a scale factor. However, it is reasonable to consider for each i a weighted average of v_i, or a function of v_i, and an estimate of θ_i which is determined by the x_{ij}.

First let us propose an estimate of θ_i which depends only on the corresponding x_{ij}. The x_{ij} were determined from spore counts after diluting dissolved plastic discs so that each count was large enough to have two significant figures but small enough so that separate colonies could be distinguished. Therefore, for all batches, original counts were of the same order of magnitude, say μ, and since such counts can reasonably be assumed to exhibit Poisson variation, with common variance also approximately equal to μ. Each such count was then expanded by a known constant, say c_{ij}, depending on the dilution used to obtain a count of the desired order of magnitude, to yield the corresponding x_{ij} observed concentration. Hence x_{ij} has at

least approximately, mean $c_{ij}\mu$ and variance $c_{ij}^2\mu$. Since the variance of the logarithm of a random variable is approximately equal to the variance of that random variable divided by its mean squared, the variance of $\ln x_{ij}$ is approximately equal to $1/\mu$ for all i and j. As an estimate of any θ_i based on the corresponding x_{ij}, we therefore suggest, as an alternative to the sample mean $\bar{x}_i$ used in the original analysis, the geometric mean u_i defined by

$$\ln u_i = \left(\sum_{j=1}^{n_i} \ln x_{ij}\right)/n_i \ . \tag{5}$$

The $\ln u_i$ quantities are convenient to use in a weighted average to estimate the θ_i since they have approximately equal variances which can be estimated from all the x_{ij} data by

$$\hat{V}(\ln u_i) = \left[\sum_{i=1}^{k} (\ln x_{i1} - \ln x_{i2})^2\right]/2k. \tag{6}$$

Next let us construct the estimate $\hat{\theta}_i$ such that

$$\ln \hat{\theta}_i = W_{u_i} \ln u_i + W_{v_i} \ln v_i \tag{7}$$

with $W_{u_i} + W_{v_i} = 1$. This estimate achieves our objective of incorporating information from both the x_{ij} and y_{ij} samples since, from (5), u_i depends on the corresponding x_{ij} only and, as mentioned earlier, the v_i as defined by (4) are ordered like the $\bar{y}_i$ means. For k large as in the experiment under consideration, the value of $\hat{\lambda}_1$ would be unlikely to be altered appreciably if the x_{ij} values for any i were omitted from the calculations. That is, for practical purposes we can consider $\ln u_i$ and $\ln v_i$ to be independent. Hence it is reasonable to set W_{u_i} proportional to the inverse of

$\hat{V}(\ln u_i)$ as given by (6) for each i and W_{v_i} proportional to the inverse of the estimated variance of $\ln v_i$.

The variance of $\ln v_i$ from (4), with the subscript on $\hat{\lambda}_1$ suppressed, is given by

$$V(\ln v_i) = V(\ln \hat{\gamma}_i) + V(\ln \hat{\lambda}) - 2C(\ln \hat{\gamma}_i, \ln \hat{\lambda})$$

where the symbol V again denotes a variance and C denotes a covariance. Now $C(\ln \hat{\gamma}_i, \ln \hat{\lambda}) \doteq C(\hat{\gamma}_i, \hat{\lambda})/(\gamma_i \lambda)$. Using this approximation and similar ones for $V(\ln \hat{\gamma}_i)$ and $V(\ln \hat{\lambda})$ yields

$$V(\ln v_i) \doteq \frac{V(\hat{\gamma}_i)}{\gamma_i^2} + \frac{V(\ln \hat{\lambda})}{\lambda^2} - 2\frac{C(\hat{\gamma}_i, \hat{\lambda})}{\gamma_i \lambda} \quad . \tag{8}$$

Let us assume for the time being that $\bar{x}_i = \theta_i$ for each i; that is, that the $\bar{x}_i$ concentration estimates used in the calculation of the maximum likelihood estimate of λ, which in this instance we have denoted by $\hat{\lambda}$, are fixed and equal to the true concentrations. Next let us write the logarithm of our likelihood function, assuming binomial variation of the 20 y_{ij} about expected values given by (1), as

$$\begin{aligned} L &= \sum_{i=1}^{k} L_i \ , \\ L_i &= 20 \sum_{j=1}^{n_i} [y_{ij} \ln P_i + (1 - y_{ij}) \ln (1 - P_i)] + \text{constant} \ , \end{aligned} \tag{9}$$

where P_i is given by (1) and $\gamma_i = \lambda\theta_i$.

Now $\hat{\gamma}_i$ as given by (3) can be thought of as the maximum likelihood estimator of γ_i based on only the corresponding y_{ij} observations; that is, $\hat{\gamma}_i$ is the solution for γ_i of the equation $(\partial L_i/\partial \gamma_i) = 0$. From (2) we can approximate the variance of $\hat{\gamma}_i$ by

$$V(\hat{\gamma}_i) \doteq \frac{V(1-\bar{y}_i)}{A^2[E(1-\bar{y}_i)]^2} = \frac{V(y_{ij})}{A^2 n_i[E(1-\bar{y}_i)]^2} = \frac{P_i(1-P_i)}{20A^2 n_i(1-P_i)^2}$$

$$\doteq \frac{P_i}{20A^2 n_i(1-P_i)} \quad , \tag{10}$$

where we have again used the approximation for the variance of a logarithm as well as the mean and variance of the binomial distribution of $20y_{ij}$. The same approximation to $V(\hat{\gamma}_i)$ could have been obtained by using the asymptotic variance formula for maximum likelihood estimators, which in this case is

$$V(\hat{\gamma}_i) \doteq [-E(\frac{\partial^2}{\partial \gamma_i^2} L_i)]^{-1} \quad . \tag{11}$$

We will use (11) to derive an expression for $V(\hat{\lambda})$. In the meantime, we can estimate the variance of $\hat{\gamma}_i$ by substituting $\bar{y}_i$ for its expectation, P_i, in (10) to obtain

$$\hat{V}(\hat{\gamma}_i) = \bar{y}_i/[20A^2 n_i(1-\bar{y}_i)]. \tag{12}$$

It can be shown that (12) can also be written as

$$\hat{V}(\hat{\gamma}_i) = [-\partial^2 L_i/\partial \gamma_i^2]^{-1}_{\gamma=\hat{\gamma}_i} . \tag{13}$$

Next let us use the chain rule to write from (9) that

$$\frac{\partial L}{\partial \lambda} = \sum_{i=1}^{k} \frac{\partial L_i}{\partial \gamma_i} \frac{\partial \gamma_i}{\partial \gamma} = \sum_{i=1}^{k} \frac{\partial L_i}{\partial \gamma_i} \theta_i \quad , \tag{14}$$

where

$$[\frac{\partial L}{\partial \lambda}]_{\lambda=\hat{\lambda}} = 0 \quad . \tag{15}$$

An approximation to the variance of $\hat{\lambda}$ is given by

$$V(\hat{\lambda}) \doteq [-E(\frac{\partial^2 L}{\partial \lambda^2})]^{-1} . \tag{16}$$

Substitution of (14) into (16) and use of (11) gives

$$V(\hat{\lambda}) \doteq \{-E[\sum_{i=1}^{k} \frac{\partial}{\partial \lambda} (\frac{\partial L_i}{\partial \gamma_i} \theta_i)]\}^{-1} \tag{17}$$

$$\doteq \{\sum_{i=1}^{k} [-E(\frac{\partial^2 L_i}{\partial \gamma_i^2})]\theta_i^2\}^{-1}$$

$$\doteq \{\sum_{i=1}^{k} [V(\hat{\gamma}_i)]^{-1}\theta_i^2\}^{-1} . \tag{18}$$

The $V(\hat{\lambda})$ can then be estimated by replacing each $V(\hat{\gamma}_i)$ by the corresponding estimate as given by (12).

In order to estimate $C(\hat{\lambda},\hat{\gamma}_i)$, we first approximate $\partial L/\partial \lambda$ as given by (14) by replacing the $\partial L_i/\partial \gamma_i$ in that expression by the linear terms of their Taylor series expansions about the $\hat{\gamma}_i$. When we evaluate $\partial L_i/\partial \gamma_i$ for the maximum likelihood estimator $\hat{\lambda}$, this leads to

$$0 = [\frac{\partial L}{\partial \lambda}]_{\lambda=\hat{\lambda}} \doteq \sum_{i=1}^{k} [\frac{\partial L_i}{\partial \gamma_i}]_{\gamma_i=\hat{\gamma}_i} - \sum_{i=1}^{k} (\hat{\lambda}\theta_i - \hat{\gamma}_i)[-\frac{\partial^2 L_i}{\partial \gamma_i^2}]_{\gamma_i=\hat{\gamma}_i} . \tag{19}$$

Since $\hat{\gamma}_i$ is the maximum likelihood estimator of γ_i based on just the y_{ij} proportions for the i^{th} batch, each $[\partial L_i/\partial \gamma_i]_{\gamma_i=\gamma_i} = 0$. Then using (15), we have from (19) that

$$\sum_{i=1}^{k} (\hat{\lambda}\theta_i - \hat{\gamma}_i)[\hat{V}(\hat{\gamma}_i)]^{-1} \doteq 0$$

which implies that

$$\hat{\lambda} \doteq \frac{\sum_{i=1}^{k} [\hat{V}(\hat{\gamma}_i)]^{-1} \hat{\gamma}_i}{\sum_{i=1}^{k} \theta_i [\hat{V}(\hat{\gamma}_i)]^{-1}} \quad . \tag{20}$$

Assuming that the variance estimates in (20) are approximately equal to their true variances, we can regard $\hat{\lambda}$ as approximately equal to a linear combination of the $\hat{\gamma}_i$ estimates with constant coefficients. This in turn leads to the covariance estimate between $\hat{\lambda}$ and any particular $\hat{\gamma}_i$ equal to the variance estimate of $\hat{\gamma}_i$ times its coefficient in the expansion for $\hat{\lambda}$ given by (20). Therefore, we write

$$\hat{C}(\hat{\lambda}, \hat{\gamma}_i) = \frac{1}{\sum_{i=1}^{k} \theta_i [\hat{V}(\hat{\gamma}_i)]^{-1}} \tag{21}$$

Substitution of $V(\hat{\lambda})$ and $\hat{C}(\hat{\lambda},\hat{\gamma}_i)$ as given by (18) and (21) in (8), and replacement of $V(\hat{\gamma}_i)$ by $\hat{V}(\hat{\gamma}_i)$, leads to

$$V(\ln v_i) \doteq \frac{\hat{V}(\hat{\gamma}_i)}{\gamma_i^2} + \frac{1}{\lambda^2 \sum_{i=1}^{k} [\hat{V}(\hat{\gamma})]^{-1} \theta_i^2} - \frac{2}{\lambda \gamma_i \sum_{i=1}^{k} [\hat{V}(\hat{\gamma}_i)]^{-1} \theta_i} \quad . \tag{22}$$

Writing $\lambda\theta_i$ as γ_i and replacing γ_i by its estimate $\hat{\gamma}_i$ enables us to write the estimate

$$\hat{V}(\ln v_i) = \frac{\hat{V}(\hat{\gamma}_i)}{\hat{\gamma}_i^2} - \frac{1}{\sum_{i=1}^{k} [\hat{V}(\hat{\gamma}_i)]^{-1} \hat{\gamma}_i^2} \quad . \tag{23}$$

For large k such as those in the experiment motivating this work the second term on the right of (23) will be small relative to the first, so we take as our estimate of the variance of $\ln v_i$ the first term only, namely,

$$\hat{V}(\ln v_i) = \hat{V}(\hat{\gamma}_i)/\hat{\gamma}_i^2 \ , \tag{24}$$

where $\hat{V}(\hat{\gamma}_i)$ is given by (13).

The estimate (23) is not the most efficient estimate of $V(\ln v_i)$. For instance, in estimating $\lambda\theta_i$ in the denominator of the second term of (23) a more efficient estimator than $\hat{\gamma}_i$ which would use all of the data would be $\hat{\lambda}\theta_i$. However, (23) is easily calculated for each batch i and does not involve the x_{ij}'s so that it is an appropriate estimator for any fixed $\bar{x}_i$'s regardless of whether or not they equal the corresponding θ_i concentration. That is, (23) gives an appropriate estimator of $\ln v_i$ with v_i defined with $\hat{\lambda}_1$ in the denominator, as in (4), even when the use of $\hat{\lambda}_1$ does not involve the assumption that $\bar{x}_i = \theta_i$ for each batch.

After using (24) to calculate each $\hat{V}(\ln v_i)$ and (6) to calculate $\hat{V}(\ln u_i)$, we can compute for each i,

$$W_{u_i} = \frac{\hat{V}(\ln u_i)}{\hat{V}(\ln u_i)+\hat{V}(\ln v_i)} \ ; \tag{25}$$

$$W_{v_i} = 1 - W_{u_i} \ . \tag{26}$$

Then the desired estimates $\hat{\theta}_i$ of the θ_i concentrations can be computed using (7). Moreover, the variance of each such $\tilde{\theta}_i$ can be estimated by

$$\hat{V}(\hat{\theta}_i) = \hat{V}(\ln u_i) + \hat{V}(\ln v_i) \ .$$

These $\hat{\theta}_i$ estimates can be regarded as fixed and be used instead of the $\bar{x}_i$ to compute a new estimate of λ, say $\hat{\lambda}_2$, from (9) and (15). The variance of $\hat{\lambda}_2$ would be evaluated from (16) with $\hat{\lambda}_2$ substituted for λ and each θ_i replaced by $\hat{\theta}_i$.

3. ILLUSTRATION

In this section the application of the results of Section 2 to the experiment which motivated this research is discussed and illustrated with data for exposure areas of approximately 30.6 mm^2. Concentrations are expressed as spores per gram of plastic multiplied by 100 and estimates of λ are given in terms of microns. Fifty-four batches are included in the analysis with two sets of tubes, and consequently, two y_{ij} proportions, for each batch, so $n_i=2$, $i=1,2,\ldots,54$.

In the original analysis, based on concentrations estimated by the $\bar{x}_i$, it was found that $\hat{\lambda}_1=3.18$ with estimated standard error $\sqrt{\hat{V}(\hat{\lambda}_1)}=0.119$. The goodness-of-fit statistic X^2 with 107 degrees of freedom was 172.8, which is greater than even the 99^{th} percentile of the corresponding chi-square distribution. Using the u_i defined by (5) instead of the $\bar{x}_i$ leads to an even larger X^2 value of 178.9. Replacing the $\bar{x}_i$ by the v_i as computed from equation (4) yields a X^2 of 55.4 with 54 degrees of freedom which is very close to its expected value and indicates that the assumption of binomial variation within batch pairs of y_{ij} proportions is reasonable and that the initially calculated poor fit of the model to the data was due to a failure to adequately estimate the P_i as given by (1). When the $\hat{\theta}_i$, as given by (7) along with (4), (5), (6) and (24), are used as concentration estimates, X^2 with 107 degrees of freedom is 93.0, which is somewhat less than its expected value. Thus the conclusion is that the model proposed by Petersen et al. and presented in the introduction to this paper describes this illustrative data well when the $\hat{\theta}_i$ as developed in Section 2 of this paper are used as concentration estimates.

These X^2 goodness-of-fit measures resulting from using the $\bar{x}_i$, u_i and $\hat{\theta}_i$ as concentration estimates are given Table 1. In addition, that table lists the values of the maximum likelihood estimates of λ, denoted there by $\hat{\lambda}$, and their estimated standard errors calculated using (9), (15) and (16), assuming in each instance that the concentration estimates used are fixed. These estimates of λ for the $\bar{x}_i$ and the $\hat{\theta}_i$ have been previously called $\hat{\lambda}_1$ and $\hat{\lambda}_2$, respectively.

Note from Table 1 that the maximum likelihood estimates of λ and their estimated standard errors are almost the same regardless of the set of concentration estimates used. Therefore, using the $\hat{\theta}_i$'s as concentration estimates instead of the $\bar{x}_i$ does not effect the estimation of λ appreciably for this illustration, but unlike the initial analysis, it leads to the conclusion that the model used is adequate. Furthermore, although the estimation of concentrations was not of primary interest of itself in this study, the $\hat{\theta}_i$'s are more reasonable concentration estimates than the $\bar{x}_i$'s since the $\hat{\theta}_i$'s combine the information from both the y_{ij} and x_{ij} data.

TABLE 1

GOODNESS-OF-FIT AND ESTIMATION CALCULATIONS FOR THREE MEASURES OF CONCENTRATION

	Concentration Estimates		
	$\bar{x}_i$	u_i	$\hat{\theta}_i$
X^2(107 degrees of freedom)	172.8	178.9	93.0
$\hat{\lambda}$	3.18	3.24	3.23
$\sqrt{\hat{V}(\hat{\lambda})}$	0.119	0.122	0.121

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REFERENCES

Petersen, N. J., Cornell, R. G. and Puleo, J. R. [1969]. Release of microbial contamination from fractured solids. Space Life Sciences (in press).

Peto, S. [1953]. A dose-response equation for the invasion of micro-organisms. Biometrics 9, 320-335.