LETTERS TO THE EDITOR

[Brief letters to the Editor that make specific scientific reference to papers published previously in the BIOPHYSICAL JOURNAL *are invited. Receipt of such letters will not be acknowledged but those containing pertinent scientific comments and scientific criticisms will be published.]*

Dear Sir:

The computer method for fitting kinetic data presented by Berman, Shahn, and Weiss in the *Biophysical Journal* of May, 1962, raises the question of estimating the uncertainty, or standard error, of coefficients and of other variables in a solution computed on the basis of a postulated model.

Except in the trivial case where the equations of condition are orthogonal, the diagonal elements of the variance-covariance matrix referred to on pages 279-80 do not lead to a true indication of the standard error of the solution.

As we have pointed out (1), the true standard error must be obtained through an orthogonalizing transformation, such as that of Schmidt (2), on the matrix of the equations of condition (notation as in Berman, et al):

$$\sum_{j=1}^{r} \sigma_j f_{jk} = Q_k \qquad (k = 1, 2 \cdots m;\ m > r)$$

or, in matrix form, and with weighting factors,

$$\sigma w f = wQ$$

The normalized Schmidt transformation S transforms wf into a matrix g whose rows are orthonormal:

$$Swf = g$$

The elements of S are computationally easy to determine, involving at worst the inversion of a triangular matrix.

The coefficients γ obtained from

$$\gamma g = wQ; \qquad \gamma g g^T = \gamma = wQg^T$$

are in a statistical sense independent, and hence have a standard error μ_γ equal to the standard error of the data $w_{kk}Q_k$ (which is independent of k), multiplied by the square root of $m/(m-r)$.

Then, since $\gamma S = \sigma$, the standard error of a coefficient σ_j is given by

$$\mu_j = \mu_\gamma \left[\left(\frac{m}{m-r} \right) \left(\frac{\sum_k S_{kj}^2}{r - j + 1} \right) \right]^{1/2}$$

A similar, but more restricted, development is possible for variables upon which the solution has implicit dependence. It is assumed that errors are non-systematic; systematic error may also be treated.

The computational program used in our laboratory for the resolution of relaxation times from dielectric dispersion data yields the statistical information derived above. In practice, it is found that the true standard error can exceed by many orders of magnitude the value derived from the root diagonal elements of the variance-covariance matrix. The method given here provides a quantitative criterion for the validity of a fit.

REFERENCES

1. W. SCHEIDER, Numerical Evaluation of Distribution Functions, Abstract, 5th Annual Meeting Biophysical Society, St. Louis, 1961.
2. For a concise definition, see H. Margenau and G. Murphy, "The Mathematics of Physics and Chemistry," New York, Van Nostrand Publishing Co., 1943, 298.

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Respectfully,

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