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FITTING LINEAR COMBINATIONS OF EXPONENTIALS TO HUMAN URANIUM-EXCRETION DATA

S. R. Bernard
B. R. Fish
J. R. Muir
B. L. Harless

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HEALTH PHYSICS DIVISION

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FITTING LINEAR COMBINATIONS OF EXPONENTIALS TO HUMAN URANIUM-EXCRETION DATA

INTRODUCTION

During the past several years the authors, with the advice and generous assistance of the Mathematics Panel, have investigated several methods for fitting linear combinations of exponentials to excretion data. These curve-fitting techniques are of interest as a possible method for determining the parameters of uranium distribution and excretion in humans.

A typical excretion curve is shown in Fig. 1. The measured counts per minute in urine excreted per hour are plotted vs time of measurement following an injection. These data are reported more fully elsewhere (*1,2*).

Parameters of distribution and excretion may be determined by applying a model of the distribution and excretion of uranium based on principles of linear kinetics. This is illustrated by letting S_i be the amount of uranium present in the ith compartment or body tissue. From a consideration of the kinetics of linear systems,

$$(1)\quad \dot{S}_i = \sum_{j=1}^{n} k_{ij} S_j \ , \qquad i = 1, 2, \ldots, n,$$

where S_n is the amount excreted in urine and $k_{nj} = 0$ for all $j \neq n - 1$ and, also, $k_{nj} = 0$ for every j because there is no interconnection between urine and any other compartment. The solution of Eq. 1 is of the form

$$(2)\quad S_i = \sum_{j=1}^{n} a_{ij} \epsilon^{-\lambda_j t} \ , \qquad i = 1, 2, \ldots, n,$$

where the λ_j's are the roots of the matrix K, and $A = (a_{ij})$ is a matrix with $AKA^{-1} = \Lambda = \text{diag}\ (\lambda_1, \lambda_2, \ldots, \lambda_n)$. Hearon (*3*) has shown that $\lambda_i \leqq 0$ for all i and at least one $\lambda_i = 0$. With measurements

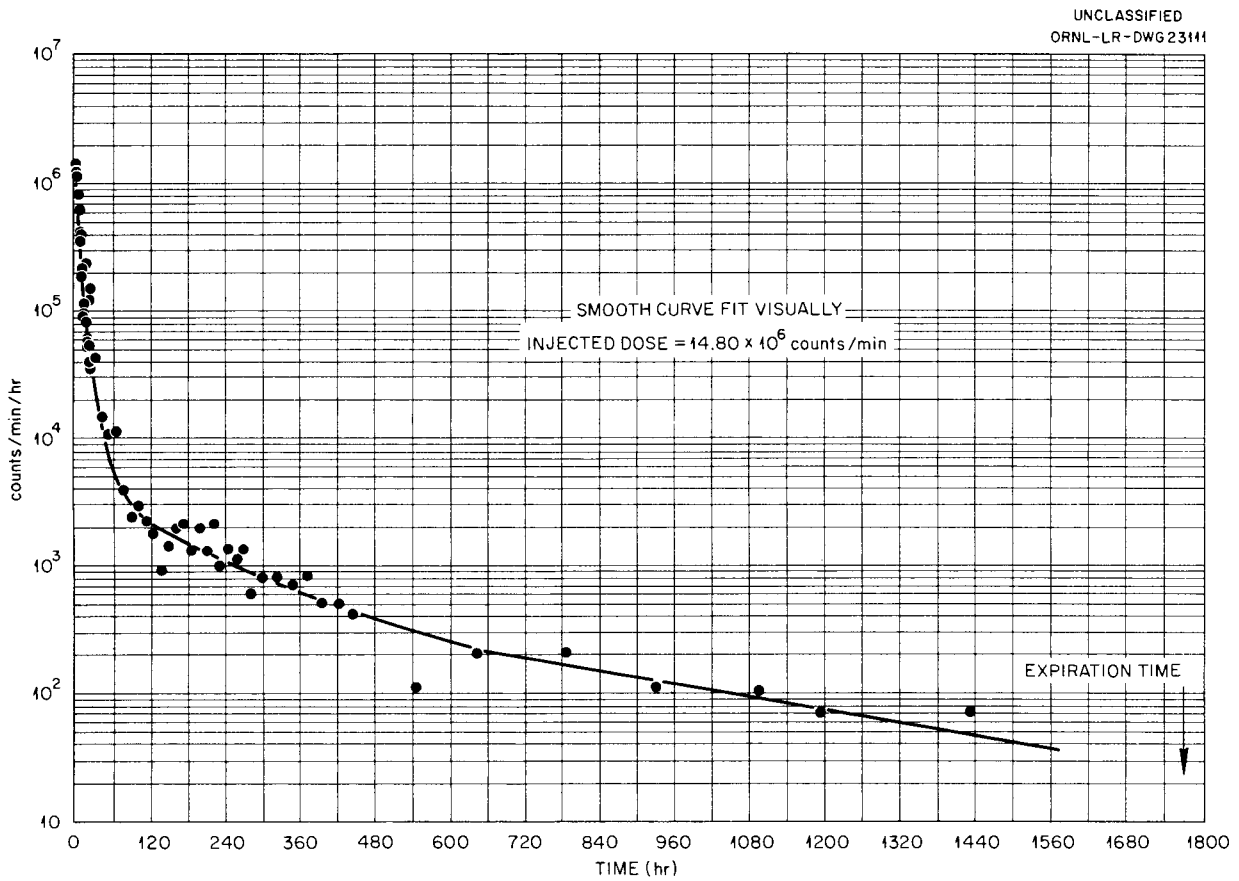

Fig. 1. Patient II Urinary-Excretion-Rate Curve.

of the S_n compartment, the data, when fitted with Eq. 2, will determine the a_{nj} and λ_i. With these values, the relation $K = A^{-1}\Lambda A$, and the characteristic equation, the k_{ij} may be determined. [Unique solutions for the parameters are not always obtained. Some k_{ij} may take on several values, a few of which may not be physically realizable. The procedure for determining these k_{ij} and their ranges of variation is discussed in the paper by Berman and Schoenfeld (*4*).] When the values of the k_{ij} are determined the $S_i(t)$, where $i < n$, can be computed and checked against the measurements of $S_i(t)$, $i < n$, that is, the amounts of uranium found in tissue samples taken at autopsy.

In application, the usual procedure is to select a value for n, the number of compartments in the system, and then employ the graphical curve-fitting method to estimate the parameters. Although this is a practical choice, it is inadequate because it introduces a bias of the investigator and does not yield estimates of the variances associated with the parameters.

There are analytical methods for estimating n and the parameters and their variances. Prony's method, cited by Whittaker and Robinson (*5*) as modified by Householder (*6,7*) offers some possibilities. It was coded for the high-speed digital computer, Oracle, and applied to excretion measurements and synthetic data, that is, values of the function $S_n(t)$ computed from Eq. 2 with specified values for the a_{nj} and λ_j having appended errors, Poisson-distributed at three different levels of variance.

This report describes the results obtained from the application of this method to the measured excretion data and the synthetic data. In addition, the results of similar tests of the method of Garwood (*8*) and an alternate least-squares method are described.

In general, it appears that these methods for fitting linear combinations of exponentials can be used for data which have small appended errors. For measurements such as those shown in Fig. 1 some additional modification is indicated. One possible modification was tested on a limited scale and shows promise of successful application to excretion measurements.

METHODS AND RESULTS

Terminology

The lower-case letter y corresponds to an expected or true value of an ordinate, while Y designates the observed or measured value.

Synthetic Data

The equation

$$(3) \quad y_i = 1{,}420{,}608\, \epsilon^{-0.11550 t_i} + 7800\, \epsilon^{-0.01443 t_i} + 1300\, \epsilon^{-0.00161 t_i},$$

which approximates the measurements shown in Fig. 1, was computed for $t = 0, 50, 100, \ldots, 400$. Poisson-distributed errors were appended to these ordinates as follows: An aliquot, P, of v cubic centimeters of urine excreted in h hours, when analyzed for uranium, gave a count of γ total counts for T minutes. Consequently, the plotted ordinate, y, is given by

$$y_i = \left(\frac{\gamma_i}{T}\right)\left(\frac{1}{P}\right)\left(\frac{1}{k}\right).$$

Assuming that the variance in y is due to counting, then

$$V(y_i) = \left(\frac{1}{T \cdot P \cdot k}\right)^2 V(\gamma_i) = \left(\frac{y_i^2}{\gamma}\right),$$

by virtue of the properties of the Poisson distribution. Now let x_i be a sample from (*NID*) having zero mean and unit variance, or

$$x_i = \frac{Y_i - \mu}{\sigma} = \frac{Y_i - y_i}{\sigma}.$$

Solving for Y_i and substituting gives

$$Y_i = y_i\left(\frac{1 + x_i}{\sqrt{\gamma}}\right).$$

The x_i's are from a table of random deviates, and the y_i's, the true ordinates, are obtained from Eq. 3. The value of γ is set equal to 1500 counts which corresponds to ~3% counting error. In order to change the variance level, the x_i's are multiplied by 1, 3, and 10. The y_i's, x_i's, and the ordinates having 1, 3, and 10 levels of error appended to them are shown in Table 1. These ordinates are plotted vs time as shown in Fig. 2.

Householder's Modified Prony Method

Prony's method requires that the observations $Y_0, Y_1, \ldots, Y_N$ be made at times $t = 0, T, 2T, \ldots, NT$. Since the expected ordinate $y(t)$ is

$$(4) \qquad y(t) = \sum_{r=1}^{r=n} A_i \epsilon^{-a_i t},$$

then, by letting $u_i = \epsilon^{-a_i T}$,

$$(5) \qquad y_r = y(rT) = \sum_{r=1}^{r=n} A_i u_i^r ,$$

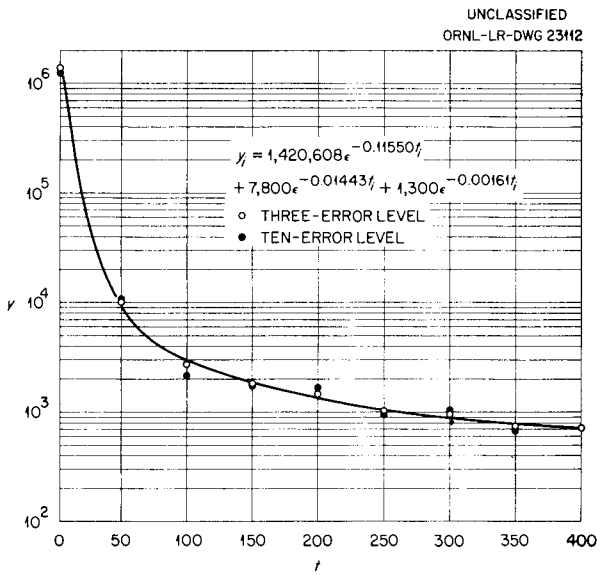

Fig. 2. Plot of the Synthetic Data.

where $r = 0, 1, \ldots, N$, and the y_r's must satisfy

$$(6) \qquad P_p = y_p s_n + y_{p+1} s_{n-1} + \cdots + y_{p+n-1} s_1 + y_{p+n} = 0$$

(where $p = 0, 1, \ldots, N - n$), an nth order difference equation. The coefficients, s_i's, are the elementary symmetric functions of an nth order polynomial, the roots of which are the required exponentials, the u_i.

Two modifications were made by Householder. First, he adapted an orthogonalization procedure for the computation of the s_i's which not only facilitated the computation but also permitted the estimation of n, the number of exponentials. Second, he converted the method to an iterative method, more suitable for high-speed computation. In addition, valid least-squares estimates of the elementary symmetric functions are provided as a result of the second modifications (9). Failure of the Prony method to provide statistically valid estimates has been one of the objections to the method (6,7,9).

The orthogonalization procedure prescribes the matrix Z_r having column vectors $z_0, z_1, \ldots, z_r$, where the components of the z_0 are $Y_0, Y_1, \ldots, Y_{N-r}$, while those of the z_r are $Y_r, Y_{r+1}, \ldots, Y_N$, to be orthogonalized. Thus, V_r is the matrix whose

Table 1. Synthetic Data

t	x_i	True Ordinate Values, y_i	One-Error Level	Three-Error Level	Ten-Error Level
0	−0.036	1429708.000	1416418.578	1389839.735	1296813.782
50	+0.59	9400.007232	9543.205062	9829.600723	10831.985534
100	−1.11	2963.389980	2878.361497	2708.504530	2114.005145
150	−0.37	1916.577000	1898.267173	1861.647520	1133.478733
200	+0.81	1377.327900	1406.133611	1463.856597	1665.385012
250	−0.49	1080.753700	1067.080220	1039.733261	944.018903
300	+0.55	904.796100	917.645109	943.343128	1033.286194
350	− 0.48	789.917700	780.127776	760.547928	692.018460
400	+0.02	706.997200	707.362293	708.092480	710.648134

$$Y_i = 1420608\, \epsilon^{-0.11550 t_i} + 7800\, \epsilon^{-0.01443 t_i} + 1300\, \epsilon^{-0.00161 t_i}$$

column vectors $v_0, v_1, \ldots, v_r$ are orthogonal to the columns of the Z_r matrix and

$$Z_r = V_r U_r \tag{7}$$

where U_r is a unit upper triangular matrix,

$$U = \begin{bmatrix} 1 & u_{10} & u_{20} & \cdots & u_{r0} \\ 0 & 1 & u_{21} & \cdots & u_{r1} \\ 0 & 0 & 1 & \cdots & u_{r2} \\ \cdot & \cdot & \cdot & \cdot & \cdot \\ 0 & 0 & 0 & \cdots & 1 \end{bmatrix} . \tag{8}$$

In the application, a maximal guess is made for r, that is, $r > n$, and the Z matrix is formed subsequent to the orthogonalization. The vectors v and the elements of the U matrix are computed sequentially. Householder proved that if the theoretically correct values, that is, the y's, are elements of the Z matrix, then the v_{n+1} column vector would vanish. Since the observed values, Y's, are used instead of the true values, then v_{n+1} can be expected to be small relative to the other column vectors. Having established v_n, the matrix U is then inverted and the nth column of U^{-1} contains the s_i's in reverse order. Thus n, the number of exponentials, and the s_i's are determined. When these are substituted into the nth order polynomial and its roots, ξ, are evaluated, then the α's are given by $(1/T)\ \ln(\xi)$.

This method was coded for the Oracle, and both the excretion data and the synthetic data were processed. The elements of the Z, V, U, and U^{-1} matrices for the excretion data appear in Table 2, while the elements for the synthetic data, true ordinates,[1] and one-, three-, and ten-error levels[1] appear in Table 3. As can be noted in Table 2, the v_3 column vector has the smaller elements. Hence, the fourth column of U^{-1} contains the s_i's. Note that these symmetric functions correspond to an equation having no more than two real positive roots. This is precisely the case of interest; positive real roots are required because $\epsilon^{-\alpha T} > 0$ for positive real values of α. In Table 3 it is seen that negative roots do not exist for the true ordinate values, but they do exist for the one-, three-, and ten-error level data. Therefore, this method has a limited application because it yields untenable estimates for the α's.

The iterative version of Prony's method, when applied to the above data, overcomes some of the difficulty. This method evolves from considerations of the function

$$\phi = \sum_{r=0}^{N} w_r (Y_r - y_r)^2 + 2 \sum_{p=0}^{N-n} \lambda_p P_p \tag{9}$$

where w is a statistical weighting factor, λ is a Lagrange multiplier, while the Y_r and y_r are, as before, the observed and true values and P_p is given by Eq. 6. Equation 9 was minimized by setting

$$\frac{\partial \phi}{\partial y} = 0 , \qquad \frac{\partial \phi}{\partial s} = 0 .$$

These, in turn, were made linear by expanding in Taylor series about initial estimates Y_r and r_i for the y_r and s_i which are related in the following:

$$Y_r = y_r + \eta_r , \qquad r_i = s_i + \rho_i . \tag{10}$$

Thus, the η_r and ρ_i are correction factors (presumably small) to be calculated at the end of each iterative step and used to adjust the Y's and r's. The equations, in matrix notation, to be solved for these correction factors are

$$\begin{aligned} Y'Q^{-1}Y\rho &= Y'Q^{-1}\bar{P} , \\ \lambda &= Q^{-1}\bar{P} - Q^{-1}Y\rho , \\ \eta &= W^{-1}R\lambda . \end{aligned} \tag{11}$$

The matrix Y is

$$Y = \begin{bmatrix} Y_0 & Y_1 & \cdots & Y_{n-1} \\ \cdot & \cdot & \cdot & \cdot \\ Y_{N-n} & Y_{N-n+1} & \cdots & Y_N \end{bmatrix} , \tag{12}$$

while

$$Q = R'WR . \tag{13}$$

The value $\bar{P}$ is a column vector, its components calculated with Eq. 6 by inserting r's and Y's for the s and y. The matrix R has $N - n - 1$ columns.

[1]The data for the true ordinates and the one-, three-, and ten-error levels are biased because computation errors were introduced into the calculations of the true ordinates. Compare components of Z matrix in Table 3 with those data in Table 1. The calculations were not repeated because changes in the memory unit of the computer rendered the programs obsolete.

Components of the first column are the r's entered in reverse order followed by a 1 and $N - n$ zeros. The second column has a zero followed by the r's in reverse order, a 1, and $N - n + 1$ zeros, etc. The matrix $W = \text{diag}\,(w_0, w_1, \ldots, w_N)$, a diagonal matrix of the weights; ρ is a column vector; λ is a column vector; and η a column vector of η's, entered in reverse order.

The equations of Eq. 11 are solved sequentially. From the first of these a solution for the ρ's is obtained, and with the ρ's the second can be solved for the λ's and the last for the η's.

This method was coded for the Oracle and the solution was checked by a comparison with solutions obtained with desk calculators. The excretion data were then processed, unit weights were specified, and the initial estimates for the r's were obtained with the orthogonalization procedure. Convergence set in rapidly. These new r's were substituted into the polynomial and at east one negative root was found.

The processing of synthetic data (true ordinate values[1] and the 1-, 3-, and 10-error levels[1]) reveals that negative roots occur when data having high levels of variance are processed. In computations with the synthetic data, unit weights were assigned, but the true values for the r's were used for initial estimates. Figure 3 shows the plot of the r's computed at each iteration. Also plotted, for purposes of comparison, are those r's

Table 2. Application of Orthogonalization Procedure to Patient Excretion Data

z_0	z_1	z_2	z_3	z_4	z_5
1420608	10687	2871	1412	1291	1123
10687	2871	1412	1291	1123	797
2871	1412	1291	1123	797	723
1412	1291	1123	797	723	557
1291	1123	797	723	557	462
1123	797	723	557	462	270

v_0	v_1	v_2	v_3	v_4	v_5
1420608	−26.709145	1.8193559	−0.0594230	−11.104810	−9.2729431
10687	2790.402531	−415.0656693	−3.6305357	1159.634151	−980.3519978
2871	1390.347962	385.6309315	86.4600498	571.894343	−466.4129972
1412	1280.351209	291.7617557	−114.1674027	532.096176	−412.3131088
1291	1113.263747	74.1108537	50.0849149	475.910446	−389.9031366
1123	788.530742	210.5499037	−24.9372761	333.835010	−369.8452503

$$U = \begin{pmatrix} 1 & 0.007541637 & 0.002031849 & 0.001003641 & 0.000916908 & 0.000796541 \\ 0 & 1 & 0.646985974 & 0.559022956 & 0.046271333 & 0.350935487 \\ 0 & 0 & 1 & 0.664941650 & 0.423464332 & 0.446648177 \\ 0 & 0 & 0 & 1 & -0.059692129 & 0.522776159 \\ 0 & 0 & 0 & 0 & 1 & 0.842398162 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}$$

$$U^{-1} = \begin{pmatrix} 1 & -0.007541637 & 0.002847484 & 0.001318896 & -0.001695027 & 0.001316664 \\ 0 & 1 & -0.646985974 & -0.128815041 & 0.220014907 & -0.179959238 \\ 0 & 0 & 1 & -0.664941650 & -0.463156115 & 0.291129603 \\ 0 & 0 & 0 & 1 & 0.059692129 & -0.573060735 \\ 0 & 0 & 0 & 0 & 1 & -0.842398762 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}$$

Table 3. Application of Orthogonalization Procedure to Synthetic Data

True Ordinate Values*

z_0	z_1	z_2	z_3
1429708	9472.59	3095.51	1925.67
9472.59	3095.51	1925.67	1458.95
3095.51	1925.67	1458.95	1082.32
1925.67	1458.95	1082.32	905.723
1458.95	1082.32	905.723	790.413
1082.32	905.723	790.413	707.278

v_0	v_1	v_2	v_3
1429708	−27.939755	0.7664598	+0.02099546
9472.59	3032.563844	−211.7341596	15.91191562
3095.51	1905.100076	122.4216100	−94.97314580
1925.67	1446.153761	68.6905387	+38.68072495
1458.95	1072.625155	153.8381873	+36.65699531
1082.32	898.530893	160.8687278	+41.64731336

$$U = \begin{pmatrix} 1 & 0.006645084 & 0.002178239 & 0.001357019 \\ 0 & 1 & 0.698013530 & 0.546675516 \\ 0 & 0 & 1 & 1.075144436 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

$$U^{-1} = \begin{pmatrix} 1 & -0.006645084 & +0.002460119 & -0.000369298 \\ 0 & 1 & -0.698013530 & +0.203789847 \\ 0 & 0 & 1 & -1.075144436 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

$$X^3 - 1.07514\,X^2 + 0.20379\,X - 0.00369 = 0$$

$$\text{roots} = \begin{cases} +0.83020 \\ +0.24309 \\ +0.00185 \end{cases}$$

$$\alpha\text{'s} = \begin{cases} 0.00360 & (0.00161) \\ 0.02846 & (0.01443) \\ 0.12420 & (0.11550) \end{cases}$$

One-Error Level*

z_0	z_1	z_2	z_3
1416426	9617	3007	1907
9617	3007	1907	1489
3007	1907	1489	1069
1907	1489	1069	919
1489	1069	919	781
1069	919	781	708

v_0	v_1	v_2	v_3
1416426	−27.764746	0.764059	0.038804
9617	2941.515674	−200.991558	2.949331
3007	1886.524657	143.803882	−121.170140
1907	1476.014806	17.472145	72.541593
1489	1058.861062	164.398277	39.182146
1069	911.720937	131.713520	78.264595

$$U = \begin{pmatrix} 1 & 0.006809226 & 0.002136320 & 0.001356843 \\ 0 & 1 & 0.709649990 & 0.561244647 \\ 0 & 0 & 1 & 0.885151683 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

$$U^{-1} = \begin{pmatrix} 1 & -0.006809226 & +0.002695847 & +0.000078565 \\ 0 & 1 & -0.709649990 & +0.066903236 \\ 0 & 0 & 1 & -0.885151683 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

Table 3 (continued)

Three-Error Level*				Ten-Error-Level*			
z_0	z_1	z_2	z_3	z_0	z_1	z_2	z_3
1389848	9905	2829	1871	1296817	10916	2208	1742
9905	2829	1871	1550	10916	2208	1742	1764
2829	1871	1550	1041	2208	1742	1764	945
1871	1550	1041	944	1742	1764	945	1034
1550	1041	944	761	1764	945	1034	692
1041	944	761	708	945	1034	692	711
v_0	v_1	v_2	v_3	v_0	v_1	v_2	v_3
1389848	8911.765975	−889.6979732	−247.6315533	1296817	−25.107566	−0.4763517	−1.9047993
9905	2821.921540	781.6328955	346.1793110	10916	2115.902864	21.1759650	311.2186718
2829	1868.978298	829.2692347	70.9278861	2208	1723.371338	373.8995554	−307.4434277
1871	1548.662918	443.8888501	275.5270827	1742	1749.302930	−465.1593527	−77.0216785
1550	1039.892316	542.9931099	175.8847338	1764	930.117319	+282.7680713	−0.0292371
1041	943.256065	397.3331114	230.2509927	945	1026.027135	−134.975176	33.4055933

$$U = \begin{pmatrix} 1 & 0.000714635 & 0.000204939 & 0.000135749 \\ 0 & 1 & 0.385318007 & 0.272082760 \\ 0 & 0 & 1 & 0.556117708 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

$$U = \begin{pmatrix} 1 & 0.008436894 & 0.001718572 & 0.001358070 \\ 0 & 1 & 0.804415048 & 0.684009665 \\ 0 & 0 & 1 & 0.188933514 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

$$U^{-1} = \begin{pmatrix} 1 & -0.000714634 & 0.000070423 & +0.000019528 \\ 0 & 1 & -0.385318007 & -0.057800593 \\ 0 & 0 & 1 & -0.556117708 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

$$U^{-1} = \begin{pmatrix} 1 & -0.008436894 & +0.005068192 & +0.003455284 \\ 0 & 1 & -0.804415048 & -0.0532027395 \\ 0 & 0 & 1 & -0.188933514 \\ 0 & 0 & 0 & 1 \end{pmatrix}$$

*These data are biased because of the computation errors introduced into the calculations of the true ordinates. Compare components of Z matrix with those in Table 1.

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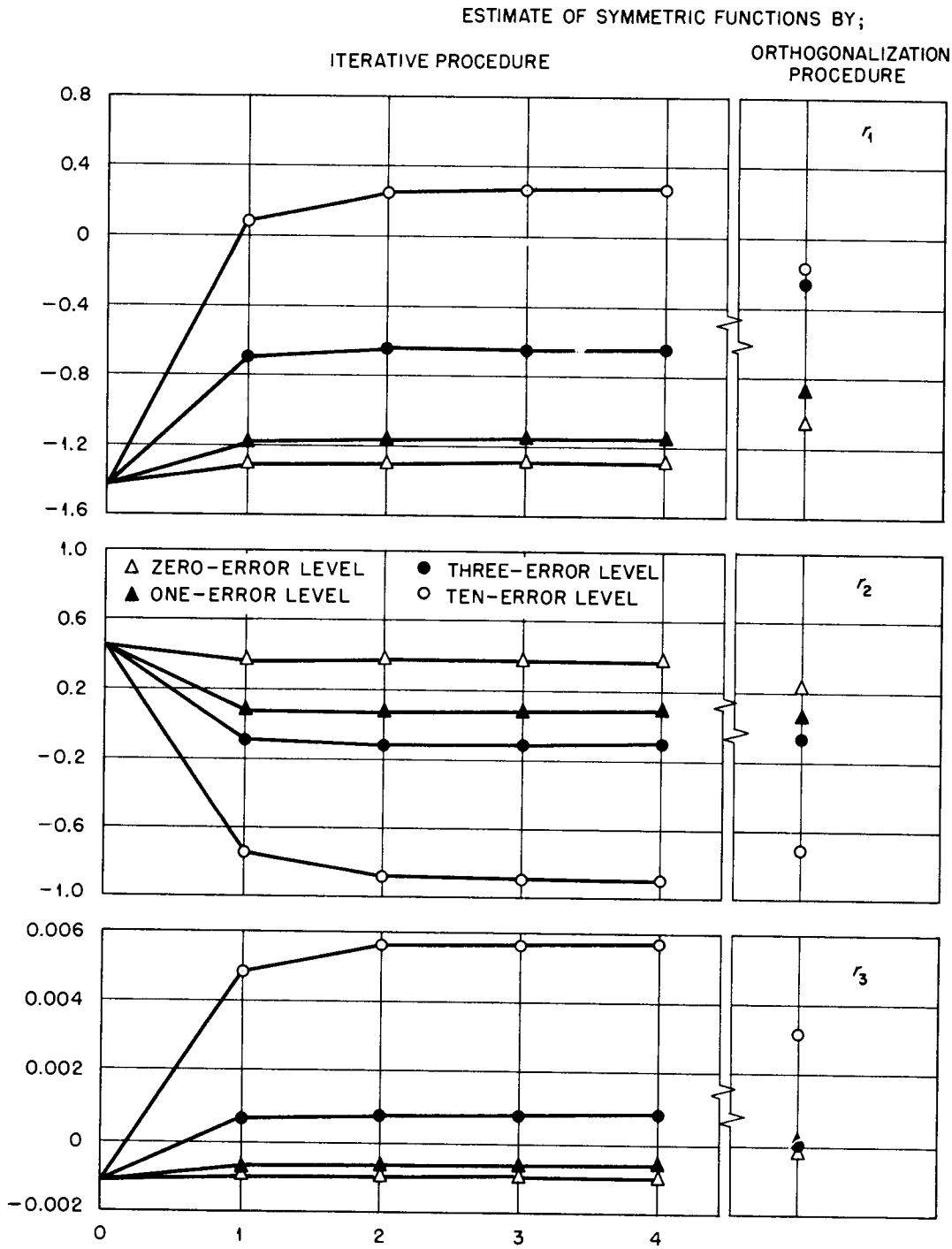

Fig. 3. Plot of Symmetric Functions Estimated by Householder's Modified Prony Method. The data for the true ordinates and the one-, three-, and ten-error levels are biased because computation errors were introduced into the calculations of the true ordinates.

computed by the orthogonalization procedure. As can be noted, convergence is rapid. Larger changes are experienced by the r's for the case of higher-variance-level data. A usable estimate can be obtained for the case of 1-error level data but not for the higher variance levels. The investigation of this procedure was terminated at this step in favor of the method next described.

Alternate Least-Square Procedure (Brute-Force Method)

A procedure, suggested by the members of the Mathematics Panel, based on the least-squares principle allows direct manipulation of the parameters of the exponentials. This method begins by minimizing the function

$$(14) \quad \phi = \sum_{r=0}^{N} w_r \left(Y_r - \sum_{j=1}^{n} A_j \epsilon^{-\alpha_j t_r} \right)^2 ,$$

that is, setting

$$\frac{\partial \phi}{\partial A_j} = \phi_{A_j} = 0 , \qquad \frac{\partial \phi}{\partial \alpha_j} = \phi_{\alpha_j} = 0$$

to obtain

$$(15) \quad \begin{aligned} &\phi_{A_j};\ \sum_{r=0}^{N} w_r \left(Y_r - \sum_{j=1}^{n} A_j \epsilon^{-\alpha_j t_r} \right) \epsilon^{-\alpha_j t_r} = 0 , \\ &\phi_{\alpha_j};\ \sum_{r=0}^{N} w_r \left(Y_r - \sum_{j=1}^{n} A_j \epsilon^{-\alpha_j t_r} \right) t_r \epsilon^{-\alpha_j t_r} = 0 . \end{aligned}$$

Here, the w_r are the weights, the Y_r are the observations made at time t_r, and the A_j and α_j are the parameters whose values are to be determined. Suppose initial estimates for the α's are available. Inserting these values into the first of Eq. 15 and expanding yields n equations linear in the A_j's, which can be determined easily. To improve the α's, these A's and all the initial estimates for the α's except one can be inserted into the second equation of Eq. 15, and upon expansion a function will evolve, whose root $\epsilon^{-\alpha}(= X)$ can be determined with the Newton-Raphson root evaluation procedure. Thus, an improved α is obtained by taking the logarithm of X. This new α replaces the initial estimate and, together with $n - 2$ of the initial estimates for the α's, again may be substituted into the equation for the ϕ_{α_j}, and the function evolved after expansion is solved for its root, thus yielding an improved value for another α. This process is continued, n functions being solved for their roots to obtain improved values for the α's, it being understood that whenever a new value for an α is evolved it replaces the old value. When all the α's are determined they can be substituted into the first part of Eq. 15 and another set of A's can be determined and the process for adjustment of the α's can be repeated if necessary. In summary, this procedure calls for the following stepwise solution:

Step 1 – Insert the values for the Y's, t's, and w's together with initial estimates for the α's into the equation

$$(16) \quad \phi_{A_j};\ \sum_{r=0}^{n} w_r \left(Y_r - \sum_{j=1}^{n} A_j \epsilon^{-\alpha_j t_r} \right) \epsilon^{-\alpha_j t_r} = 0 , \qquad j = 1, 2, \ldots, n,$$

then expand and solve the linear set for the A's.

Step 2 – Insert these A's and the w's, Y's, and t's together with $n - 1$ of the α's into

$$(17) \quad \phi_{\alpha_j};\ \sum_{r=0}^{N} w_r \left(R_{rk} - A_k X_k^{t_r} \right) t_r X_k^{t_r} = 0 ,$$

where

$$(18) \qquad X_k = \epsilon^{-\alpha_k} ,$$

and

$$(19) \qquad R_{rk} = Y_r - \sum_j{}' A_j \epsilon^{-\alpha_j t_r} ,$$

where Σ' indicates $j \neq k$, and perform the indicated summation in Eq. 17, then determine the root X_k of the resulting function with the Newton-Raphson procedure. Calculate

$$(20) \qquad -\alpha_k = \ln X_k .$$

Whenever a new α_k is determined, use it in Eq. 19. When all α_k have been evaluated, return to step 1 if the values of the α's are different from the initial values.

This method was also programed for the Oracle, and the synthetic data, true ordinates, and the 1- and 3-error-level data were processed. Unit

weights and two iterations on each polynomial with the Newton-Raphson procedure were specified. The true values for the α's were used for initial estimates. Results of this series of computations are shown in Fig. 4. Here, the A's and α's are plotted for each iterative step. Note that the residual sums of squares decrease monotonically but that the parameters course peculiar paths throughout the course of the computation. This code was outdated by changes made in the arithmetic unit of the computer. Further investigation is needed. Attempts to accelerate convergence should be considered.

Garwood's Method

The Garwood method (*8*) is a well-known procedure for fitting nonlinear functions in general. It requires initial estimates for both the A's and α's. The function is defined as in Eq. 14 and is minimized with respect to the A's and α's as given by Eq. 15. Equation 15 is then made linear by expanding about the initial estimates for the

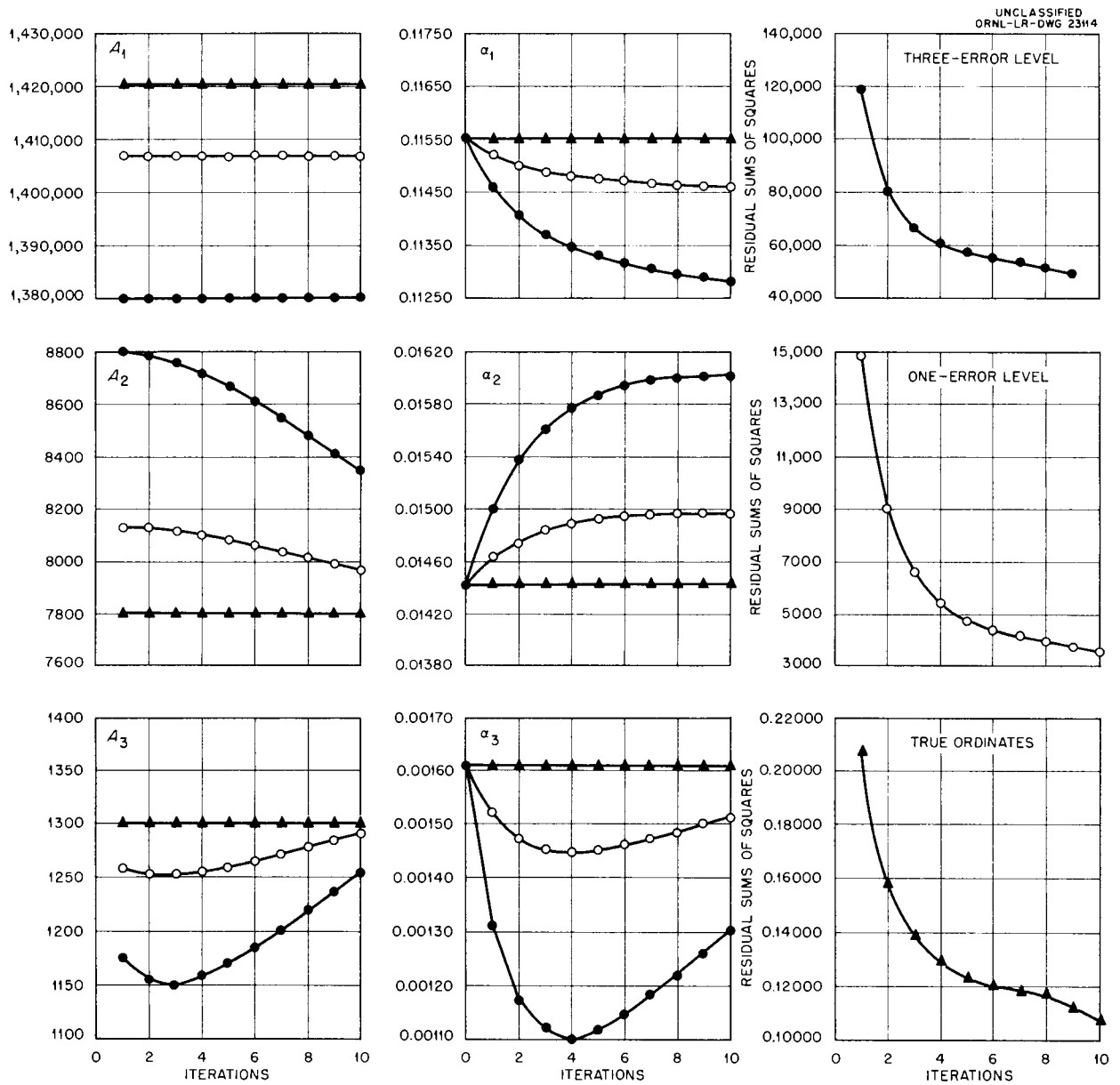

Fig. 4. Application of "Brute-Force Method" to Synthetic Data with Unit Weights.

A's and α's in Taylor series, retaining only linear terms in the expansion.

It is expedient to define the function whose parameters are sought as

$$f(A_1, A_2, \ldots, A_{2n})_r = y_r ,$$

where the odd-number subscripts correspond to the coefficients of the exponential terms, while the even numbers are to be associated with the α's. Thus, for example,

$$f(A_1, A_2)_r = A_1 \epsilon^{-\alpha_2 t_r} ,$$

etc. In addition, we define

$$(21) \qquad \begin{aligned} rd_j &= \frac{\partial y_r}{\partial A_j} , & j &= 1, 2, \ldots, 2n, \\ rd_{ij} &= \frac{\partial^2 y_r}{\partial A_i \partial A_j} , & i &= 1, 2, \ldots, 2n. \end{aligned}$$

Expanding Eq. 15 in Taylor's series and expressing in matrix notation yields

$$(22) \qquad D_i' \overline{W} D_i x - \Delta W D_{ii} x = D_i W V ,$$

where x is the column vector of iterates whose solution is required. The matrix D_i is a matrix of first partials whose column vectors are rd_1, rd_2, ..., rd_{2n} as defined in Eq. 21; W is a diagonal matrix of the weights and V is a column vector of residuals whose components are $Y_0 - y_0$, $Y_1 - y_1$, ..., $Y_n - y_n$; Δ is a matrix, the first column of which contains the vector V followed by $(2n - 1)(n + 1)$ zeros, and the second column has $(n + 1)$ zeros followed by vector V and $(2n - 2)(n + 1)$ zeros, etc; $\overline{W}$ is a diagonal, partitioned matrix of the w's, while D_{ii} is a matrix of second partials whose elements, rd_{ij}, are given by the second equation of Eq. 21. It is understood that the function and its partial derivatives are evaluated with the initial estimates of the A's and α's. Thus, substituting the appropriate values into Eq. 22 and solving yields the x's which are corrections (presumably small) to be appended to the A's and α's. These calculations are repeated with the adjusted A's and α's if the corrections are too large.

This procedure was programed for the Oracle by N. M. Dismuke for the general fitting case while B. R. Fish coded the necessary subroutines for processing exponential combinations. The code employs single-line, floating-point arithmetic and Jordan's matrix inversion procedure. The number of iterations to be performed is specified. At the completion of the last iteration the matrix $D'WD$ is formed. It is then inverted and the diagonal elements of the inverse, multiplied by $V'WV$ and divided by the degrees of freedom $(N - n)$, are the estimates of the asymptotic variances.

This method has been tested extensively with the synthetic data. The effect upon the convergence properties was investigated by varying the weights and the initial parameter estimates.

Table 4 presents the results of the application to the true ordinate data. Note that finite variances occur for the true ordinates; this result is probably due to round-off error in the computer. Note also the effect of weighting the residuals with $1/Y^2$; the estimated parameters are nearer the true parameter values. When unit weights are specified, one of the parameters, A_3, differs from the true value by as much as $\sim 10\%$.

This method is poorly behaved and extremely sensitive when the error level appended to the ordinates is increased. The results of application to the synthetic data, where unit weights and true initial parameter estimates were employed, are shown in Fig. 5. Convergence set in for the case of the one-error level data. The value of the parameters and the estimates of variance are shown in Table 4. In the case of the three-error level data, on the first iteration, the residual sum of squares increased from 10^{10} to 10^{14}, and three of the parameters (A_3, α_2, α_3) change sign. In succeeding iterations the residual sum of squares decreases and the α's move in the direction of the true values, but the A_2 and A_3 increase in magnitude. Obviously, the corrections calculated in the first iteration are too large. The reasons for this are not known.

Weighting the residuals with the inverse square ordinate had the effect of reducing the tendency to overcorrect a single parameter, but it did not improve the convergence properties. Nine iterations were performed on the synthetic data. Again, true values for initial estimates were used, but weights were set equal to $1/Y^2$. These results appear in Fig. 6. The paths followed by the parameters and weighted residual sum of squares are erratic and unpredictable. The parameters did

Table 4. Estimates of Parameters and Standard Errors Determined with Garwood's Method

	Error Level of 1, Weight Factor of 1		Error Level of 0, Weight Factor of $1/Y^2$		Error Level of 0, Weight Factor of 1		True Values
	Parameter Value	Standard Error of Parameter	Parameter Value	Standard Error of Parameter	Parameter Value	Standard Error of Parameter	
Parameter							
A_1	1,408,420	583.04	1,420,460	2,830.1	1,420,340	119.13	1,420,608
A_2	1,210.45	322.52	1,342.56	34.84	1,380.52	43.93	1,300
A_3	6,790.59	343.93	7,900.89	104.89	7,988.62	82.64	7,800
α_1	0.113188	0.000566	0.115624	0.000178	0.115751	0.000118	0.11550
α_2	0.00148098	0.000637	0.00168348	0.000062	0.00174982	0.0000080	0.00161
α_3	0.0131895	0.001472	0.0147243	0.000225	0.0149598	0.000038	0.01443
Number of iterations to converge	7		4		4		
Residual sum of squares	1,723.96		0.0000117		23.7345		

not converge for the one-error level data, which is unlike the case where unit weights were employed. Some negative variances were computed for the one-error-level weighted data since some of the diagonal elements in the $(D'WD)^{-1}$ were negative. These results may be the effect of ill-conditioned matrices since negative diagonal elements for this matrix are theoretically impossible.

The overcorrection phenomenon also occurred when the three-error-level data were processed with a set of initial estimates found with the graphical procedure. The values for the initial parameter estimates were

$$A_1 = 1{,}380{,}000 \quad (1{,}420{,}608) ,$$

$$A_2 = 8{,}785 \quad (7{,}800) ,$$

$$A_3 = 1{,}150 \quad (1{,}300) ,$$

$$\alpha_1 = 0.1145 \quad (0.11550) ,$$

$$\alpha_2 = 0.015 \quad (0.01443) ,$$

$$\alpha_3 = 0.0013 \quad (0.00161) ,$$

which are noted to be slightly different from the true values appearing in parentheses. Figure 7 presents the results corresponding to this set of parameters. Again, unit weights were used. When true ordinates were operated upon, these initial estimates were changed in the direction of the true values, and the residual sum of squares decreased from 10^9 to 10^2 after only four iterations. When the three-error-level data were processed an overcorrection occurred on the second iteration, the A_3, α_2, and α_3 changed their sign, while the sum of squares increased from 10^5 to 10^{15}. Twenty-six iterations were performed and on the 26th a zero entered into the denominator of a quotient and computations ceased at this point. The first nine iterations were repeated, and the same results were reproduced, thereby eliminating the possibility of machine error as being the cause of this overcorrection.

Another approach, which is used in iterative solutions of algebraic equations and which was suggested to us by H. L. Lucas, shows some promise for successful application of this method to data with higher levels of variance appended to

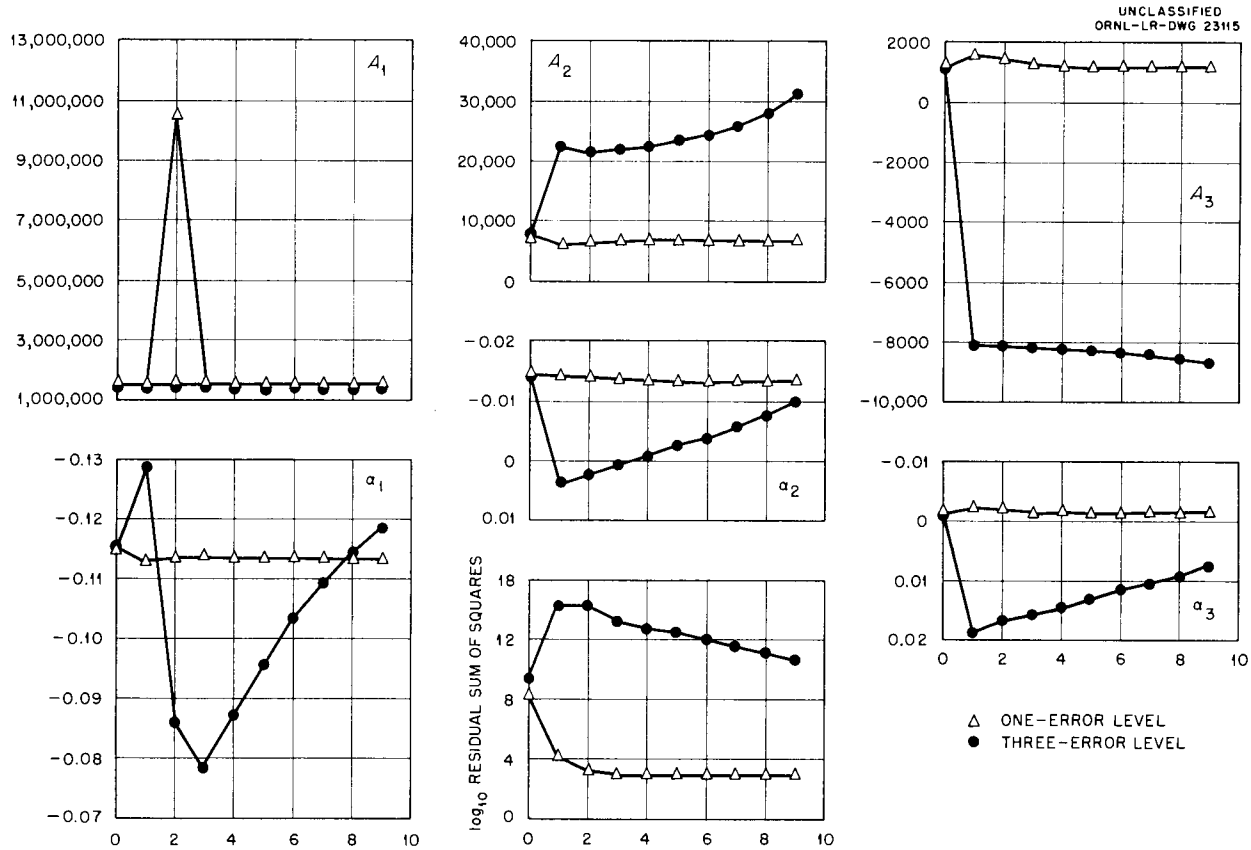

Fig. 5. Garwood Method Applied to Synthetic Data with Unit Weights and True Values for Initial Estimates.

them. Overcorrection can be suppressed by multiplying the solution vector x of iterates by a fraction and employing it to correct the estimates rather than the whole vector. This maneuver was applied to the solution vector obtained at the second iteration upon the three-error-level data. The vector was multiplied by $1/30$ and the resultant was used to adjust the parameters. The maximum change in the parameters was $\sim 10\%$. This new set of parameters was then supplied to the computer along with the three-error-level data and unit weights. The results of this maneuver are plotted in Fig. 7 also. The sum of squares increased from 10^5 to 10^6 and after nine iterations reduced to 10^4, thereby improving the parameters. This single test cannot be said to be adequate, but, in view of the improvement it offered, it certainly warrants additional investigation. There was insufficient time to code this additional step into Garwood's method before the scheduled shutdown of the Oracle.

SUMMARY AND CONCLUSIONS

Householder's modified Prony method, Garwood's method, and a modified least-squares approach for fitting linear combinations of exponentials were coded for the Oracle and applied to a set of synthetic data which approximately represents human uranium-excretion measurements. The synthetic data were determined with the function

$$y = 1{,}420{,}608\, \epsilon^{-0.11550t} + 7800\, \epsilon^{-0.01443t} + 1300\, \epsilon^{-0.00161t}$$

by appending errors (Poisson-distributed) of different level to the ordinates.

A brief description of the methods employed precedes the discussion of the results obtained, the emphasis being placed on the findings.

In general, the aforementioned methods recover the true values of the parameters when the data depart slightly from the correct ordinates, but when the higher levels of error are appended the

methods either do not converge or, if they do, they converge upon estimates which are not tenable. In the application of the modified Prony method convergence set in rapidly, regardless of the variance level, but the parameters converged upon for the high variance level were not tenable. An alternate least-squares method, on the other hand, was slow in converging; the residual sum of squares decreased slowly but monotonically; however, the parameters followed unusual paths as iterative improvement is applied. The Garwood method was found to be extremely sensitive, its behavior depending upon the error level appended to the data, the initial parameter estimates, and the weights employed. It converges for the case of data slightly different from the theoretically correct ordinates, recovers the parameter values, and yields estimates of the variance associated with these parameters, but when the error level is increased the method overcorrects the parameters. This overcorrection phenomenon could be suppressed by applying a fraction of the iterates rather than the whole.

ACKNOWLEDGMENTS

N. M. Dismuke of the Mathematics Panel deserves much of the credit for programing the "brute-force method" and the main routine for the Garwood method. We also express appreciation to A. S. Householder, J. Z. Hearon, and A. W. Kimball for their advice and consultation.

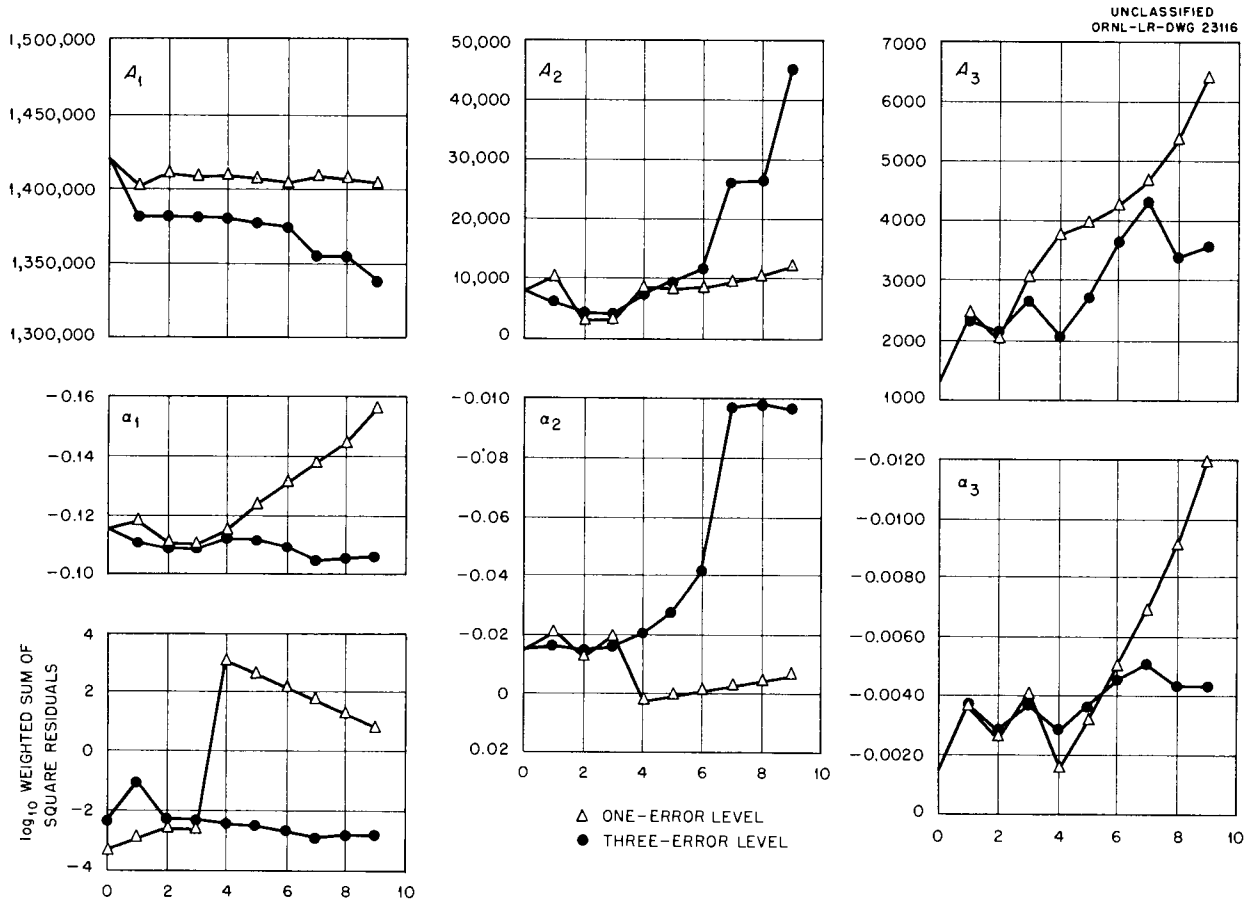

Fig. 6. Garwood Method Applied to Synthetic Data with Weights of $1/y^2$ and True Values for Initial Estimates.

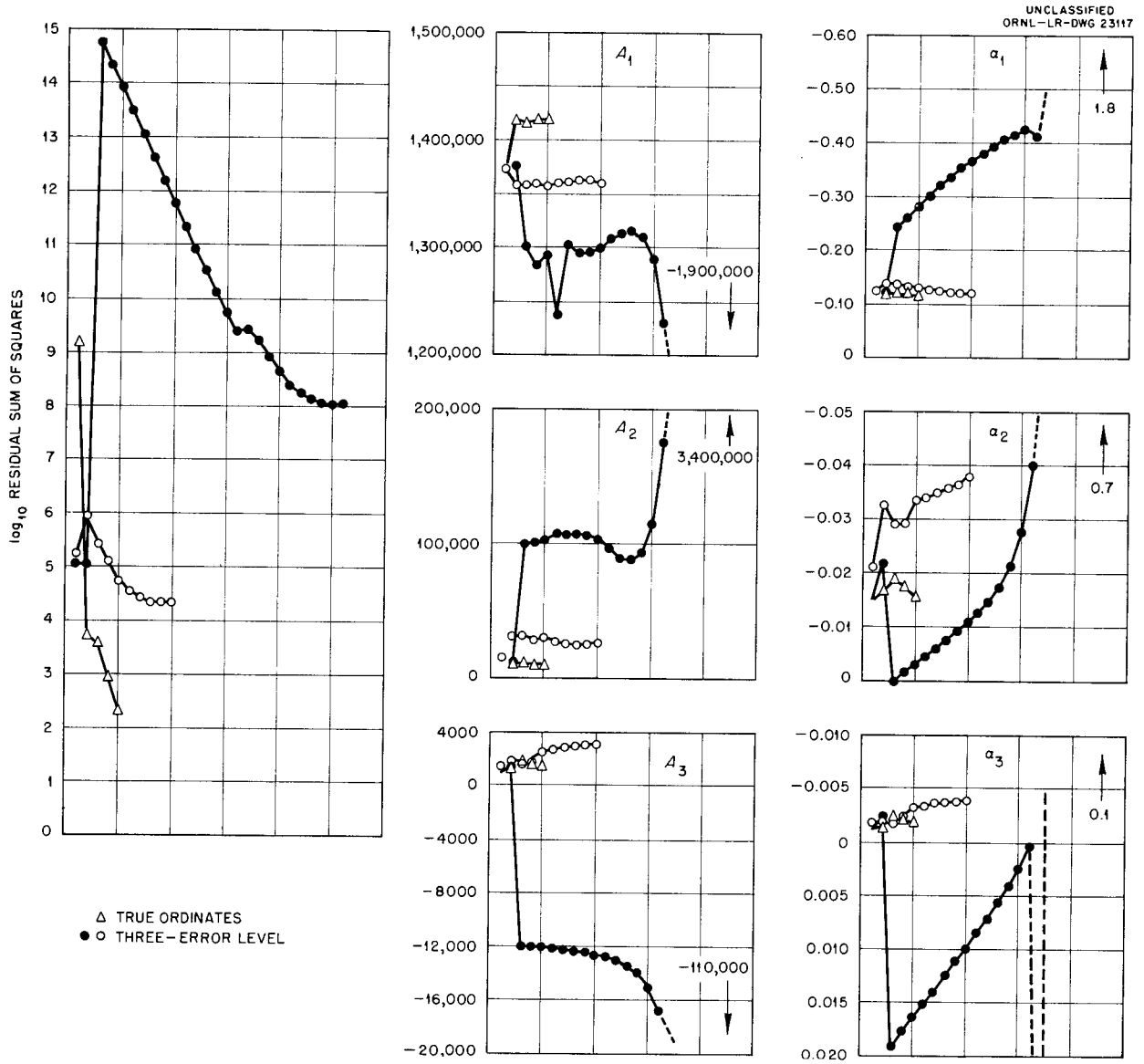

Fig. 7. Garwood Method Applied to Synthetic Data with Unit Weights and the Initial Estimates Obtained by Graphical Procedure.

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