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ESTIMATING EXTREME QUANTILES OF QUANTAL RESPONSE FUNCTIONS IN LOGIT ANALYSIS

by

© Donald H. Tosh

A THESIS

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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled 'ESTIMATING EXTREME QUANTILES OF QUANTAL RESPONSE FUNCTIONS IN LOGIT ANALYSIS" submitted by Donald H. Tosh in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

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ABSTRACT

This thesis discusses estimating procedures in Logit analysis. The classical methods are outlined and their advantages and weaknesses discussed. A new sampling procedure, the First Zero sampling procedure, is then presented. Its main advantage is that it concentrates observations in the extreme quantile area of the response function, so it applies to analyses where these values are the quantities of interest. The First Zero distribution and its two limiting distributions are derived. One limit result holds in the general case, while the other holds under more restrictive limit conditions. How fast this convergence takes place is described graphically. Estimates of location and scale parameters of the response function are derived for each of these distributions. The performance of these esimates is compared under various sampling situations, and conditions are determined when each of the estimates offers advantages over the others. The estimates are also compared to classical estimates and it is found that in some cases First Zero estimates offer improved efficiency and/or simplicity over the classical ones.

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CHAPTER I

The Classical Methods

1.1 Introduction. The problem under investigation originates in pharmacology, although it may be applied to a number of other situations. The concern is to establish the relation between a stimulus and a response. A common example is in examining the potency of a certain drug. We are concerned with quantal responses. A quantal response is a zero-one response (or life-death, cured-not cured, etc.). In short, any response that can be classified in such a way that a specific condition can be observed as either occurring or not occurring is a quantal response experiment. In the example mentioned above, ie. that of examining the potency of a certain drug, the proportion of the population that will respond with a 1 to the dose z is a function of z. As z increases, the proportion of 1 responses increases to 1, and as z decreases the proportion of 1 responses decreases to 0. In fact, the dose itself is not usually the quantity of interest, but the logarithm of the dose. If we write x=ln[z] (either natural or common logs may be used since they are just linear transforms of each other), then we shall by an abuse of the language call x the dose. For a given dose x, the proportion of 1

responses at that dose is a function of x we will denote by F(x). F(x) is called the response function. It can be easily seen that F is a distribution function. Many functions have been proposed for F, but only two have gained any widespread acceptance. If F has the form of a normal distribution function, the analysis is called a Probit analysis. (Originally, when computations were performed by hand, the term probit described a normal variate shifted to the right by five standard deviations. This transformation avoided the use of negative numbers. Although this is still done today, any situation using the normal response function is termed probit even though the actual "probit" units are not used.) When F is given the form of the Logistic distribution, the analysis is termed Logit.

At present, probit analysis is more commonly used. This is mainly due to Finney. In his books, "Statistical Method in Biological Assay" and "Probit Analysis" he recommends the use of the normal distribution as the "natural" one We quote from the former: "When the reason for unlike behaviour of similarly treated subjects is primarily their intrinsic differences in susceptibility, the specification in terms of a frequency distribution of individual tolerances is natural, and ... the assumption of a normal distribution of log tolerances seems the most

reasonable procedure in the absence of evidence for any alternative." In the latter he does admit: "These two are very similar indeed in all respects except for very small or very large P, and extremely large experiments would be needed to show one as a better fit than the other. No one should believe that either formula for P represents perfect truth, and therefore perhaps nothing other than personal inclination can decide which is to be used." However, Finney uses probit analysis exclusively and since his books have become the authorities in the area of bioassay, most researchers follow suit and use the normal as well. Berkson [2], however, claims: "In view of the wide use of the normal curve to represent the distribution of biological traits and also because of direct experimental evidence of the normal distribution of susceptibility, it is to be conceded that the integral of the normal curve recommends itself. However, the logistic function is very near to the integrated normal curve, it applies to a wide range of physicochemical phenomena and therefore may have a better theoretic basis than the integrated normal curve. Moreover, there are reasons for believing it to be easier to handle statistically." We concur with Berkson and in the methods we propose, we assume we are dealing with a logit analysis. For completeness we include a brief description of the standard method of probit analysis. We then conclude the

chapter with a summary of the Robbins-Monro procedure, which is the most commonly used form of sequential approximation in this field.

1.2 Classical Probit Analysis. Most of what is given in this section is a very brief summary of the techniques outlined in Finney's book "Probit Analysis". The same method could very easily be adapted to use the logistic distribution. At this point, however, it is the method that is of interest and not the model. We will describe the procedure used for estimating drug toxicity. The most commonly sought value is LD50, or Lethal Dose 50. This is the dose that would kill 50 percent of the population under consideration. (Similarly, LD90 is the dose that would kill 90 percent of the population.) A dual quantity which is equivalent statistically is the ED50, the Effective Dose 50. This term would be used to describe a drug's medicinal potency and refers to the dose that would cure 50 percent of the population. We assume that all trials are independent, meaning that no subject receives more than one dose.

If a subject receives an administration of dose X, the probability that it dies (ie. has a response of 1) is

$$(1.2.1)\quad F(X) = \int_{-\infty}^{X} (2\pi\sigma^2)^{-\frac{1}{2}} \exp\{-(x-\mu)^2/2\sigma^2)\}dx.$$

In this case, the parameters of interest are μ and σ (μ is the LD50). Commonly, the transformation $Y=\alpha+\beta X$ is made making the parameters α and β the parameters of interest

where $\alpha = -\mu/\sigma$ and $\beta = 1/\sigma$. The method of estimation is maximum likelihood. A typical experiment would take k samples (k would normally range from 2 to 5) of n subjects each (n may range from 5 to 500. It is not necessary to have the same number in each sample but it does simplify calculations) and administer each subject in the ith sample with dose X_i. For example, if k=3, typical values for X_1, X_2, and X_3 would be chosen hopefully near LD20, LD50, and LD80 respectively. The number r_i of 1 responses in the ith sample is observed. r_i has a binomial(n, P_i) distribution where $P_i = F(X_i)$. The joint density of the r_i's is

$$L = \prod_{i=1}^{k} \binom{n}{r_i} P_i^{r_i} (1-P_i)^{n-r_i}$$

leading to a log likelihood equation of

$$\ln L = \sum_{i=1}^{k} \{r_i \ln[P_i] + (n-r_i)\ln[1-P_i]\}.$$

(Note that the n's in the above will be subscripted by i if the sample size varies from sample to sample.)

To maximize lnL we take the partial derivative of lnL with respect to α and β, set these equal to 0, and solve. Ie.

$$\frac{\partial \ln L}{\partial \alpha} = 0 = \sum_{i=1}^{k} \{r_i / P_i - (n-r_i)/(1-P_i)\} \frac{\partial P_i}{\partial \alpha}$$

(1.2.2)

$$\frac{\partial \ln L}{\partial \beta} = 0 = \sum_{i=1}^{k} \{r_i / P_i - (n-r_i)/(1-P_i)\} \frac{\partial P_i}{\partial \beta}.$$

These cannot be solved explicitly, but a two parameter iteration procedure can be used to estimate α and β. Suppose that α_1 and β_1 are approximations of α and β. Second approximations to α and β will be of the form $\alpha_1 + \Delta\alpha$ and $\beta_1 + \Delta\beta$. Using the Taylor-Maclaurin expansion of lnL, these second approximations must satisfy both of

$$\frac{\partial \ln L}{\partial \alpha} + \Delta\alpha \frac{\partial^2 \ln L}{\partial \alpha^2} + \Delta\beta \frac{\partial^2 \ln L}{\partial \alpha \partial \beta} = 0$$

(1.2.3)

$$\frac{\partial \ln L}{\partial \beta} + \Delta\beta \frac{\partial^2 \ln L}{\partial \beta^2} + \Delta\alpha \frac{\partial^2 \ln L}{\partial \alpha \partial \beta} = 0.$$

These two linear equations can be solved for $\Delta\alpha$ and $\Delta\beta$. Finney recommends simplifying the second order partial derivatives in (1.2.3) by substituting $P_i = r_i/n$ in these derivatives after differentiation, giving expected values rather than empirical. The next step should now be clear. In general, it is best to have the iteration continue until convergence occurs. The covariance matrix of $\hat{\alpha}$ and $\hat{\beta}$ is asymptotic to

$$V = \begin{pmatrix} -E\,\frac{\partial^2 \ln L}{\partial \alpha^2} & -E\,\frac{\partial^2 \ln L}{\partial \alpha \partial \beta} \\ -E\,\frac{\partial^2 \ln L}{\partial \alpha \partial \beta} & -E\,\frac{\partial^2 \ln L}{\partial \beta^2} \end{pmatrix}^{-1}$$

and confidence bounds can be set for a and b (the estimates of α and β respectively). The above applies for any form that the P_i's may take. Specifically, in probit analysis, P_i has the form (1.2.1), and if we write $\phi(x)$ and $\Phi(x)$ as the standard normal density and distribution functions respectively, we have (recalling the transformation $Y_i = \alpha + \beta X_i$)

$$P_i = \Phi(Y_i), \quad \frac{\partial P_i}{\partial \alpha} = \phi(Y_i), \quad \text{and} \quad \frac{\partial P_i}{\partial \beta} = \phi(Y_i) X_i .$$

Thus, (1.2.3) in probit analysis becomes

$$\Delta a \sum_{i=1}^{k} n w_i + \Delta b \sum_{i=1}^{k} n w_i X_i = \sum_{i=1}^{k} (r_i/n - P_i)/\phi(a+bX_i)$$

(1.2.4)

$$\Delta a \sum_{i=1}^{k} n w_i X_i + \Delta b \sum_{i=1}^{k} n w_i X_i^2 = \sum_{i=1}^{k} n w_i X_i (r_i/n - P_i)/\phi(a+bX_i)$$

where $w_i = \phi^2(a+bX_i)/[P_i(1-P_i)]$.

If a and b are the present estimates, then by solving these

equations for Δa and Δb the next estimates a' and b' may be calculated by

$$a' = a + \Delta a \quad \text{and} \quad b' = b + \Delta b.$$

The procedure continues in this fashion until convergence occurs.

Usually a Chi-squared test is done to check the goodness of fit of the observed and estimated data. There is a reasonably high risk of having a small expected value in some of the extreme samples which could cause problems in the validity of the test.

The above analysis has proved itself over the several years since Finney first presented it in 1947 (in fact the method had been available as early as 1935. See [4], [5], and [6]). One advantage it has is that samples where the proportion of responses is either 0 or 1 do not affect the procedure. (It is possible to have unreliable results if a large number of the samples fall into this category, but this should not happen frequently in actual practice.) It is also not necessary to have equal sample sizes, and there are no theoretical problems arising from having a sample size of one. This is important to understand since the method has been erroneously criticized on both of these counts [8]. A possible problem which might be encountered

is the sensitivity of the convergence scheme to the choice of starting estimates for the parameters. Finney devotes a large section of his book to getting initial estimates graphically. This was practical when computations were done by hand and accurate initial values shortened the procedure. But now with the widespread availability of computers, it is cumbersome to have to rely on 'eyeball' procedures to get the initial values. The method does have other drawbacks in certain situations, which we will mention later when we compare this method to both the Robbins-Monro procedure and the method we propose.

We have presented here the classical probit analysis. The theory is the same for logit analysis except for two major differences. The first is the further simplification possible because of the form of the logistic distribution, which is

$$F(x) = 1/(1+e^{-x}).$$

Making the transformation $Y=\beta(X-\theta)$ gives

$$P_i=F(Y_i),\ \frac{\partial P_i}{\partial\theta}=-\beta P_i(1-P_i),\ \text{and}\ \frac{\partial P_i}{\partial\beta}=(X_i-\theta)P_i(1-P_i).$$

By defining $w_i=P_i(1-P_i)$ the corresponding form of (1.2.3) in logit analysis is

$$\Delta\theta \sum_{i=1}^{k} \beta w_i + \Delta\beta \sum_{i=1}^{k} (X_i - \theta) w_i = - \sum_{i=1}^{k} (r_i / n - P_i)$$

(1.2.6)

$$- \Delta\theta \sum_{i=1}^{k} (X_i - \theta) w_i + \Delta\beta \sum_{i=1}^{k} (X_i - \theta)^2 w_i = \sum_{i=1}^{k} (r_i / n - P_i)(X_i - \theta).$$

The second advantage is that from (1.2.6) it is apparent that

$$\sum_{i=1}^{k} r_i \quad \text{and} \quad \sum_{i=1}^{k} r_i X_i$$

are sufficient statistics for θ and β respectively. No sufficient statistics are forthcoming in probit analysis.

1.3 Sequential Approximation. This method of approximation gets its name from the type of procedure it requires. In the case of establishing drug potency, it would be necessary to make an administration at a certain level and then observe the response before the next administration is made. This is because the next dose is a function of the previous dose and the response. In general terms, we wish to estimate the root of a function $R(x)$ when the observations are subject to random error. Hence, what is observed is $R(x)+\varepsilon$ where ε is a random variable whose distribution may depend on x. In probit or logit analysis, $R(x)$ has the form $F(x)-0.5$ (in the case of estimating the LD50) where $F(x)$ is the normal or logistic distribution function respectively. Robbins and Monro [14] proposed a sequential method that would define X_1 arbitrarily and then define

$$(1.3.1)\quad X_{n+1} = X_n - a_n(R(X_n) + \varepsilon)$$

where a_n is a positive decreasing sequence of constants such that

$$\sum_{n=1}^{\infty} a_n \text{ diverges and } \sum_{n=1}^{\infty} a_n^2 \text{ converges.}$$

They showed that when R increases at most linearly and the

variance of the ε's is uniformly bounded, then X_n converges to the root of $R(x)$ in probability. Blum [7] later showed that in fact X_n converges to the root almost surely. Since then there have been numerous papers that have weakened the requirements on R and have dealt with various applications of the method to other situations, for example Kiefer and Wolfowitz [13] have altered the method to allow the maximum or minimum of a function to be approximated sequentially. Others have considered the problem of R having multiple roots. A considerable amount of effort has gone into finding the optimum values for the sequence $\{a_n\}$. For example, it has been shown that among all sequences of the form c/n^{α}, the optimal form is $a_n=c/n$.

This procedure when compared to classical analysis has advantages and disadvantages. Its primary disadvantage is its sequential nature. When testing the potency of insecticides it is highly undesirable to fumigate individual cockroaches with individual doses and then observe the life or death response before the next test is performed. Cockroaches are cheap and the cost of testing high so in this situation sequential analysis is not cost effective. Similarly, in testing the carcinogenic effect of a new drug on mice, it is again highly undesirable to wait the substantial period of time required for the effects to become noticeable before the next administration is made.

In this case the method is not time effective.

The method, however, does have several significant advantages. Chief of these, perhaps, is its simplicity. Finney when describing the use of probit analysis without a computer required several pages of explanation as well as some extensive examples. The sequential procedure, on the other hand, could be done by hand or small pocket calculator right in the laboratory by someone with a minimum of theoretical or computational skill. Also, there are many experimental situations involving expensive animals (for example Rhesus monkeys) and fast acting drugs that make the method very cost and time efficient. Another situation where this method is cost and time efficient is in the testing of plastic pipe for breaking strength. Here a given weight (the dose) is dropped from a fixed height on a sample piece of pipe, and the response of breaking or not breaking is recorded. The very nature of the testing procedure lends itself very nicely to sequential approximation. Another of this method's definite advantages is that it is nonparametric. The ability to estimate and predict various LD values in probit or logit analysis relies heavily on the underlying distribution that is chosen. In fact the estimates themselves depend upon the assumption of the model for their validity. The Robbins-Monro procedure, however, will converge to the LD50

regardless of the underlying distribution function. It also has the added advantage of placing most of the observations near the root of interest. This prevents the rather wasteful occurrence of taking a batch of observations nowhere near the root and then finding either 0 or 100 percent response in that group. As well, the experimenter has the choice of making the experiment consist of a fixed number of observations or letting it continue until the desired level of accuracy is achieved.

For the most part we have referred to the Robbins-Monro procedure as it is used to estimate the LD50. One reason for this is that this quantity is of great interest among researchers today and is used extensively for comparing drugs. Another reason, however, is that the method, although theoretically asymptotically unbiased, demonstrates considerable bias when used to approximate noncentral quantities (for example LD75 or LD95) in finite samples. Wetherill has considered this problem [16] and concludes that "Routine 1 (the Robbins-Monro procedure) is very efficient for estimation of L.5 (ie. LD50), both as a method of placing observations and as a method of estimation. It is very robust to errors in the starting value of the sequence and also to the value of the constant c (recall $a_n=c/n$). Actual small sample variances follow closely approximations given by asymptotic formulae based

on a simple model. However, Routine 1 is unsuitable for estimating even moderately extreme Lp, such as L.75, being subject to a heavy bias and yielding large variances." Finney's method must also be altered for the case when extreme quantiles are to be estimated, and he recommends using a sequential method (where practicable) proposed originally by Bartlett [1]. This involves sampling at a fixed dose until the desired number of responses is observed, thus yielding a negative binomial rather than binomial distribution for the number of zeros at each dose. Tsutakawa [15] has also proposed a method for determining what the optimal choices of dose would be. Wetherill [17] has suggested a Robbins - Monro - like procedure which would have smaller bias of extreme quantile estimates. His UDTR (Up and Down rule on a Transformed Response curve) is a variation of the up and down procedure first put forth by Dixon and Mood [9].

The estimation procedure we propose originated from studying this particular problem. Our aim was to find a procedure which would efficiently estimate extreme quantiles such as LD75, LD95, or LD99. Such procedures are becoming important in areas such as environmental control and establishing safe levels for toxic drugs. We feel there is a need for a method that provides high accuracy with fewer 0 responses than the classical methods. In

particular, our methods will provide the same accuracy of estimates with fewer deaths in situations such as testing the polluting effects of certain chemicals on wildlife.

CHAPTER II

The First Zero Distribution

2.1 Introduction. We decided to call the distribution which we concentrated on the First Zero Distribution. We assumed we were dealing with the logistic model (or Logit) which has the distribution function

$$F(x)=1/(1+e^{-\beta(x-\theta)}).$$

β is the scale parameter (β is inversely proportional to the standard deviation) and θ is the location parameter (θ is the mean of the distribution). In the model, subjects are administered various doses of a drug. The subjects are observed for either of two possible reactions - response vs. non-response, death vs. survival, etc. - that are classified as either 0 or 1. We will denote doses by x and responses by Y. Hence, at any given dose x, the probability of having a response Y = 1 is F(x). We are interested in determining relatively large dosage levels, for example LD95. The test procedure goes as follows: Choose an arbitrary starting point X_1 (hopefully chosen near LD95) and an increment value Δ. The first subject is administered dose X_1 and the reaction observed. If the response Y_1 is 0

then N = 1 and we estimate LD95 accordingly. (N will be the random variable corresponding to the number of subjects treated before a 0 is observed.) If the response Y_1 is 1, then we set $X_2 = X_1 - \Delta$ and the next subject is administered dose X_2. If the response Y_2 is 0, then we set N = 2 and the estimate of LD95 is calculated. If the response Y_2 is 1, then we set $X_3 = X_2 - \Delta$ and repeat. The testing continues in this fashion until a 0 is observed (whence the name First Zero Distribution). Since we are stepping to the left, a 0 must occur with probability 1. The estimate is based on X_1, X_N, and Δ. Hence, N may be defined:

$$N = \inf \{j : Y_j = 0\}.$$

Equivalently, we may base the estimate on X_1, Δ, and D where D is the random variable defined by

$$D = X_1 - X_N = \Delta(N-1).$$

The resulting distribution can be explicitly written. Assuming the subjects' responses to be independent, the probability of a response of $Y_i = 1$ from the i'th administraion is

$$P(Y_i = 1) = F(X_i) = 1/(1 + e^{-\beta(X_i - \theta)})$$

where X_i is the dose administered to that subject. Hence, the probability that none of the first n responses are 0 is

$$P(X_N < X_n) = \prod_{i=1}^{n} 1/(1 + e^{-\beta(X_i - \theta)}).$$

Although we have the explicit First Zero Distribution, it does not lend itself to easy manipulations, especially in the area of parameter estimation. We had hoped to find simpler distributions which would approximate the First Zero Distribution and thereby facilitate the estimation procedure. In this we were successful: as X_1 goes to infinity and Δ goes to zero a function of D has a limiting Exponential distribution.

2.2 Weak Convergence of $e^{\beta D}-1$ to Exponential. To help simplify notation we introduce the quantity

(2.2.1) $m = e^{-\beta(X_1-\theta)}/(e^{\beta\Delta}-1)$.

Theorem 2.2.1: Let the constant $z>0$ be given. Then

$$P(m(e^{\beta D}-1) \leq z) \rightarrow 1-e^{-z}$$

as $X_1 \rightarrow \infty$ and $\Delta \rightarrow 0$.

Proof: Define d and n by

(2.2.2) $d = (\ln(1+z/m))/\beta$

and

(2.2.3) $n = 1 + [d/\Delta]$

$= 1 +$ greatest integer part of d/Δ.

Note that

(2.2.4) $0 \leq n\Delta - d < \Delta$

and also that

$$(2.2.5)\quad z = m(e^{\beta d}-1).$$

Now $$P(D>d) = P(Y_1=1, Y_2=1, \ldots, Y_n=1)$$

$$= \prod_{i=1}^{n} 1/(1+e^{-\beta(X_i-\theta)})$$

and hence

$$(2.2.6)\quad -\ln P(D>d) = \sum_{i=1}^{n} \ln(1+e^{-\beta(X_i-\theta)}).$$

Using the inequality $a-a^2 \le \ln(1+a) \le a$ for all $a>0$ termwise on (2.2.6) gives

$$(2.2.7)\quad \sum_{i=1}^{n} e^{-\beta(X_i-\theta)} - \sum_{i=1}^{n} e^{-2\beta(X_i-\theta)}$$

$$\le -\ln P(D>d)$$

$$\le \sum_{i=1}^{n} e^{-\beta(X_i-\theta)}$$

which factors into

$$(2.2.8)\quad e^{-\beta(X_1-\theta)} \sum_{i=0}^{n-1} e^{\beta\Delta i} - e^{-2\beta(X_1-\theta)} \sum_{i=0}^{n-1} e^{2\beta\Delta i}$$

$$\leq -\ln P(D>d)$$

$$\leq e^{-\beta(X_1-\theta)} \sum_{i=0}^{n-1} e^{\beta\Delta i}.$$

Summing the geometric series gives

$$(2.2.9)\quad e^{-\beta(X_1-\theta)}(e^{\beta n\Delta}-1)/(e^{\beta\Delta}-1) - e^{-2\beta(X_1-\theta)}(e^{2\beta n\Delta}-1)/(e^{2\beta\Delta}-1)$$

$$\leq -\ln P(D>d)$$

$$\leq e^{-\beta(X_1-\theta)}(e^{\beta n\Delta}-1)/(e^{\beta\Delta}-1)$$

which is equivalent to

$$(2.2.10)\quad m(e^{\beta n\Delta}-1) - m^2(e^{2\beta n\Delta}-1)(e^{\beta\Delta}-1)/(e^{\beta\Delta}+1)$$

$$\leq -\ln P(D>d)$$

$$\leq m(e^{\beta n\Delta}-1).$$

We wish to show that the second term in the left hand side of (2.2.10) goes to zero as X_1 tends to infinity and Δ tends to 0; ie. we wish to show that

$$(2.2.11)\quad m^2(e^{2\beta n\Delta}-1)(e^{\beta\Delta}-1)/(e^{\beta\Delta}+1) \to 0.$$

To see this, note that

$$0 \le m^2(e^{2\beta n\Delta}-1)(e^{\beta\Delta}-1)/(e^{\beta\Delta}+1)$$

$$\le m^2(e^{2\beta n\Delta}-1)(e^{\beta\Delta}-1)$$

$$\le m^2(e^{2\beta(d+\Delta)}-1)(e^{\beta\Delta}-1) \quad \text{[from (2.2.4)]}$$

$$\le m^2(e^{2\beta\Delta(1+z/m)^2}-1)(e^{\beta\Delta}-1) \quad \text{[from (2.2.2)]}$$

$$\le m^2(e^{2\beta\Delta}-1 + 2ze^{2\beta\Delta}/m + z^2e^{2\beta\Delta}/m^2)(e^{\beta\Delta}-1)$$

$$\le (e^{\beta\Delta}+1)e^{-2\beta(x_1-\theta)}+2ze^{-\beta(x_1-\theta-2\Delta)}+z^2(e^{\beta\Delta}-1)e^{2\beta\Delta}$$

[from (2.2.1)]

The first two terms go to 0 as X_1 tends to infinity. The last term goes to 0 as Δ tends to 0.

Next we wish to show that

$$(2.2.12)\quad (e^{\beta n\Delta}-1)/(e^{\beta d}-1) \to 1$$

This follows from

$$1 \le (e^{\beta n\Delta}-1)/(e^{\beta d}-1) \quad \text{[from (2.2.4)]}$$

$$\leq (e^{\beta(d+\Delta)}-1)/(e^{\beta d}-1) \quad \text{[from (2.2.4)]}$$

$$= (e^{\beta\Delta}(1+z/m)-1)/(z/m) \quad \text{[from (2.2.2)]}$$

$$= m(e^{\beta\Delta}-1)/z + e^{\beta\Delta}$$

$$= e^{-\beta(X_1-\theta)}/z + e^{\beta\Delta}$$

The left term tends to 0 as X_1 tends to infinity and the right term tends to 1 as Δ tends to 0. Now noting that

$$P(D>d) = P(m(e^{\beta D}-1) > m(e^{\beta d}-1))$$

$$= P(m(e^{\beta D}-1) > z) \quad \text{[from (2.2.5)]}$$

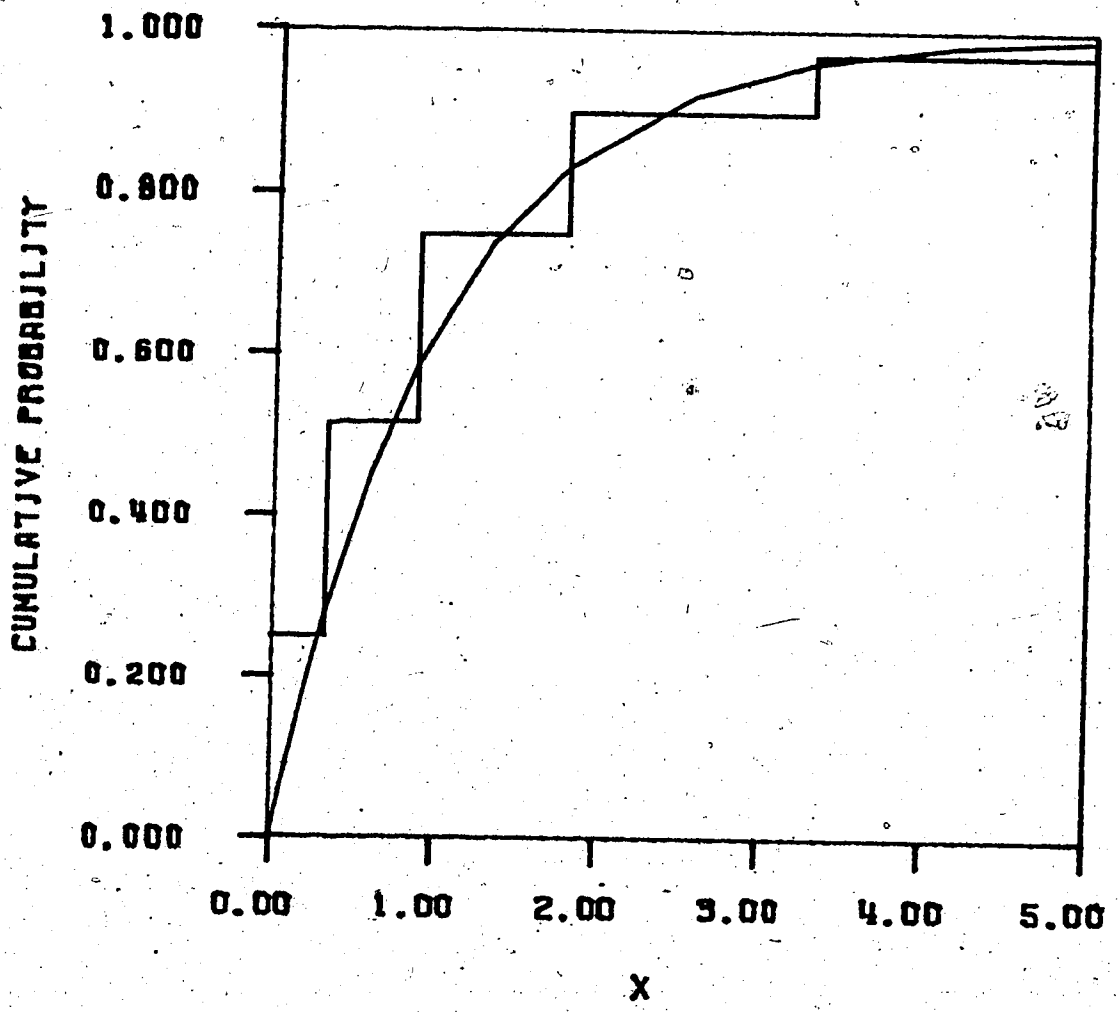
we have, by applying (2.2.11) and (2.2.12) to (2.2.10), that

$$-\ln P(m(e^{\beta D}-1) > z) \to z$$

which is the result we wanted.

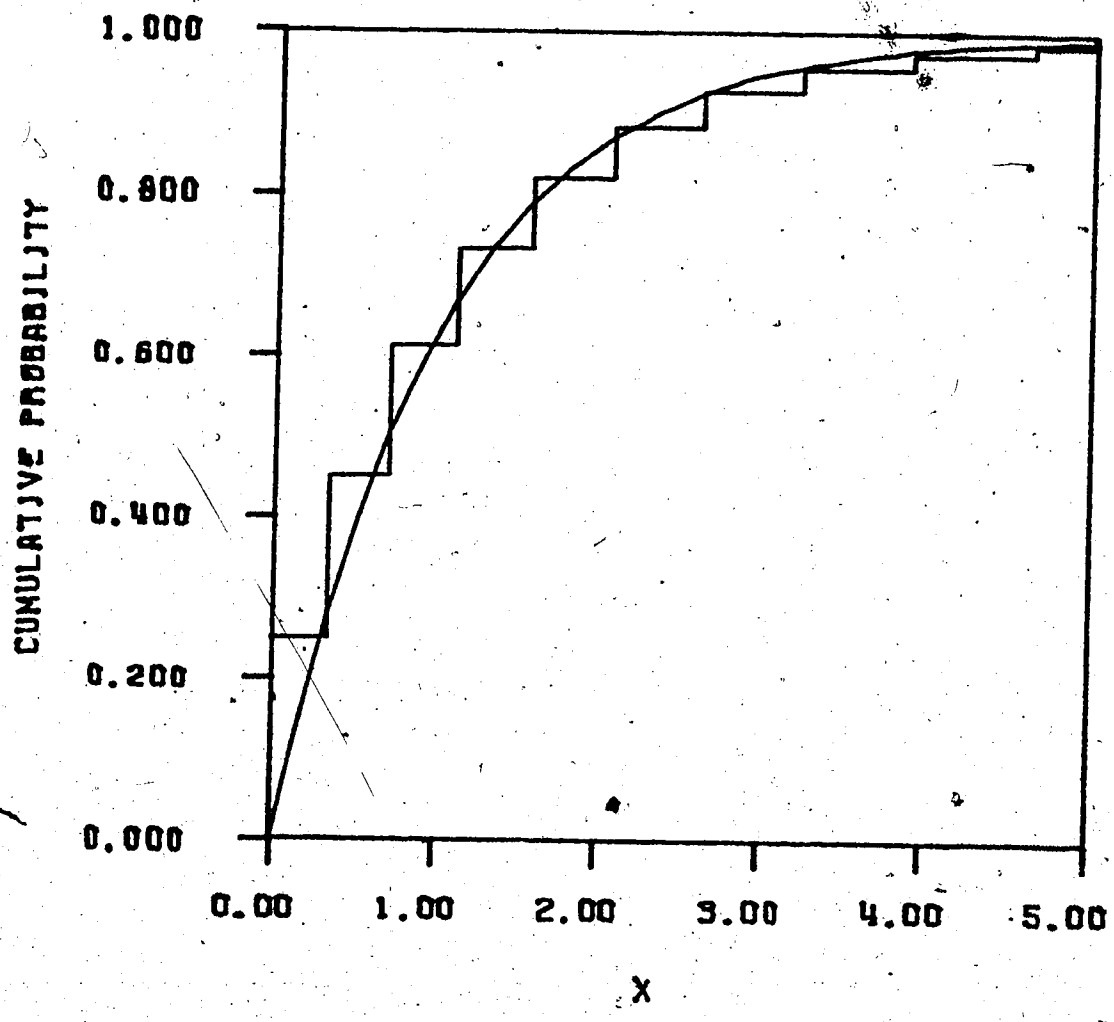
2.3 Graphic Comparison of the First Zero and Exponential Distributions. The above theorem guarantees convergence of $m(e^{\beta D}-1)$ to the Exponential distribution in limiting situations. For practical purposes it is important to know how fast this convergence takes place. The following graphs indicate the kind of approximation that can be expected for $\theta = 0$, $\beta = 1$, and various values of X_1 and Δ. As can be seen, the approximation is reasonably good for even small values of X_1 (ie. values as central as LD75) and large values of Δ (ie. values as large as $.5/\beta$). As expected the fit improves as either either X_1 gets larger or Δ gets smaller. When both occur, a very good approximation is obtained (eg. X_1 = LD99 and $\Delta = .02/\beta$). The lack of fit for either X_1 central or Δ large seems to be primarily due to the situation of approximating a discrete distribution by a continuous one.

FIGURE 2.3.1



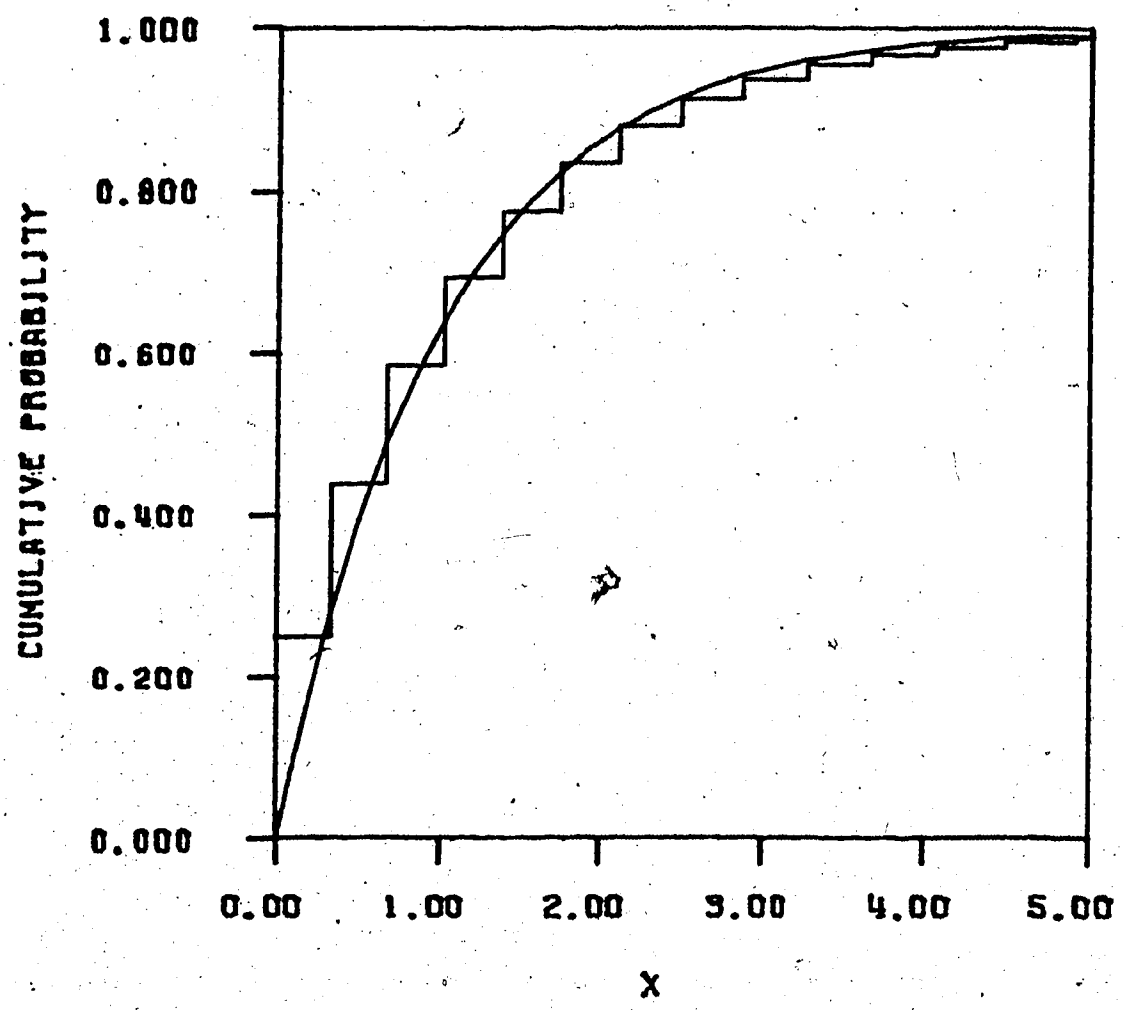
1-EXP(-X) (CONTINUOUS) COMPARED TO P(0.514(EXP(D)-1)<X) (DISCRETE) WHEN X1 = LD75 AND DELTA = 0.5

FIGURE 2.3.2



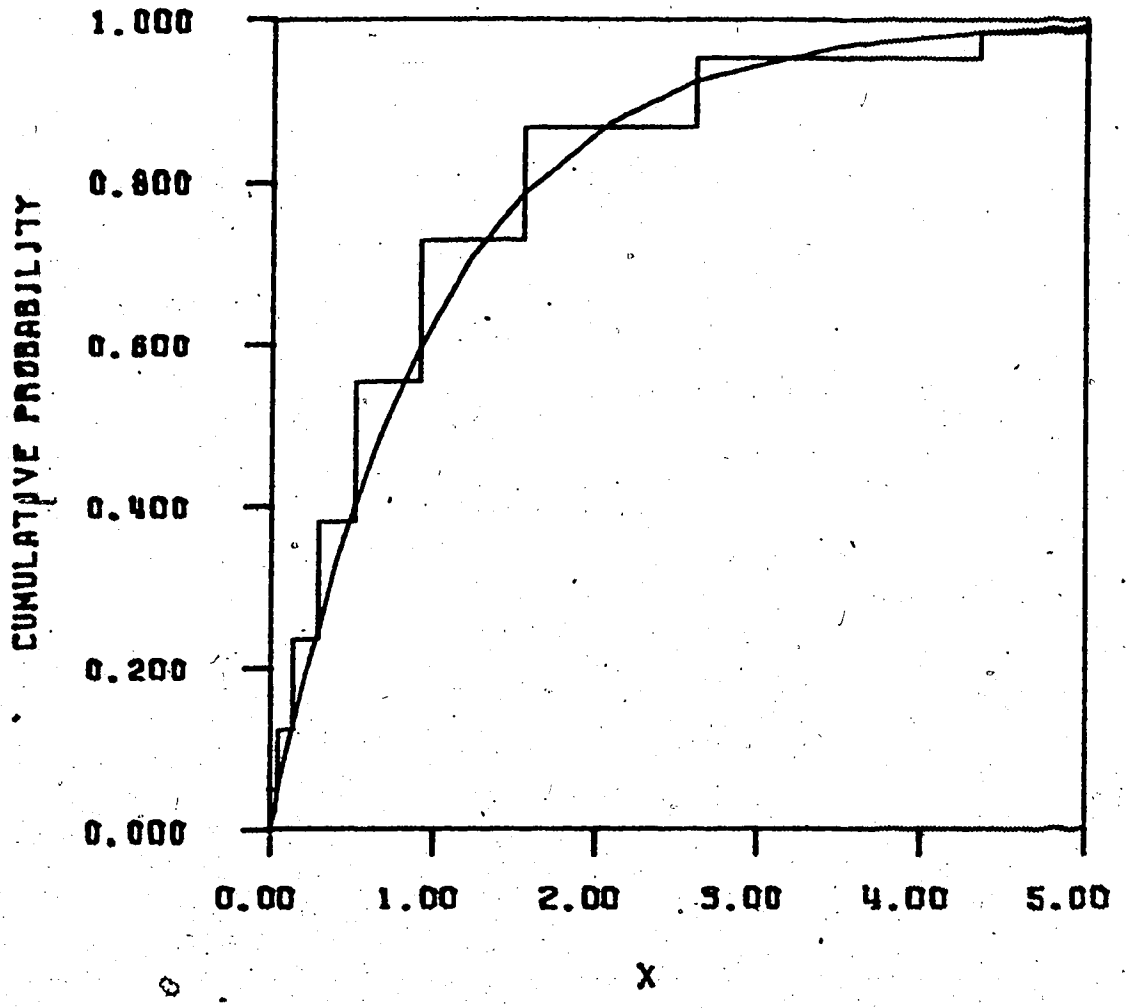
1-EXP(-X) (CONTINUOUS) COMPARED
TO P(3.171(EXP(D)-1)<X) (DISCRETE)
WHEN X1 = LD75 AND DELTA = 0.1

FIGURE 2.3.3



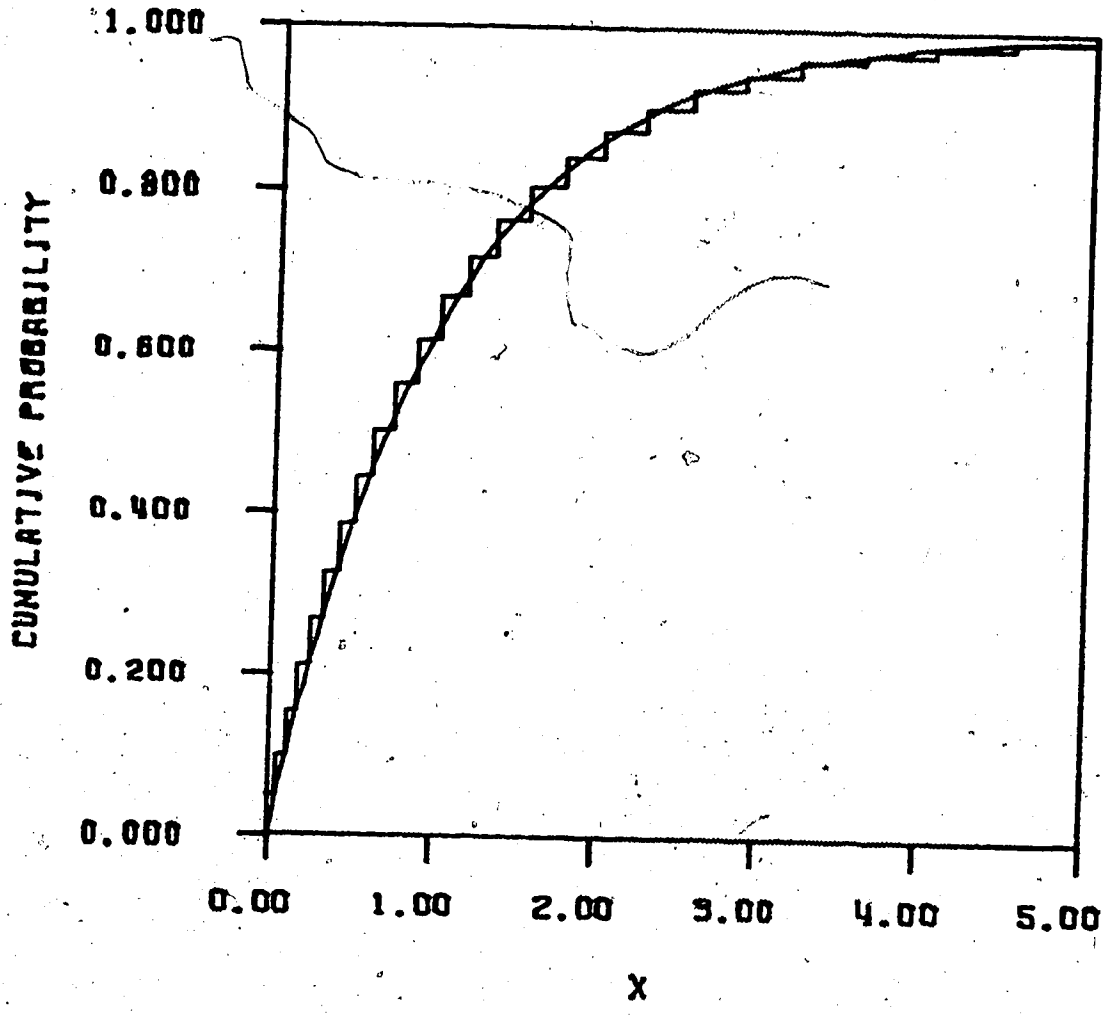
1-EXP(-X) (CONTINUOUS) COMPARED TO P(16.50(EXP(D)-1)<X) (DISCRETE) WHEN X1 = L075 AND DELTA = .02

FIGURE 2.3.4



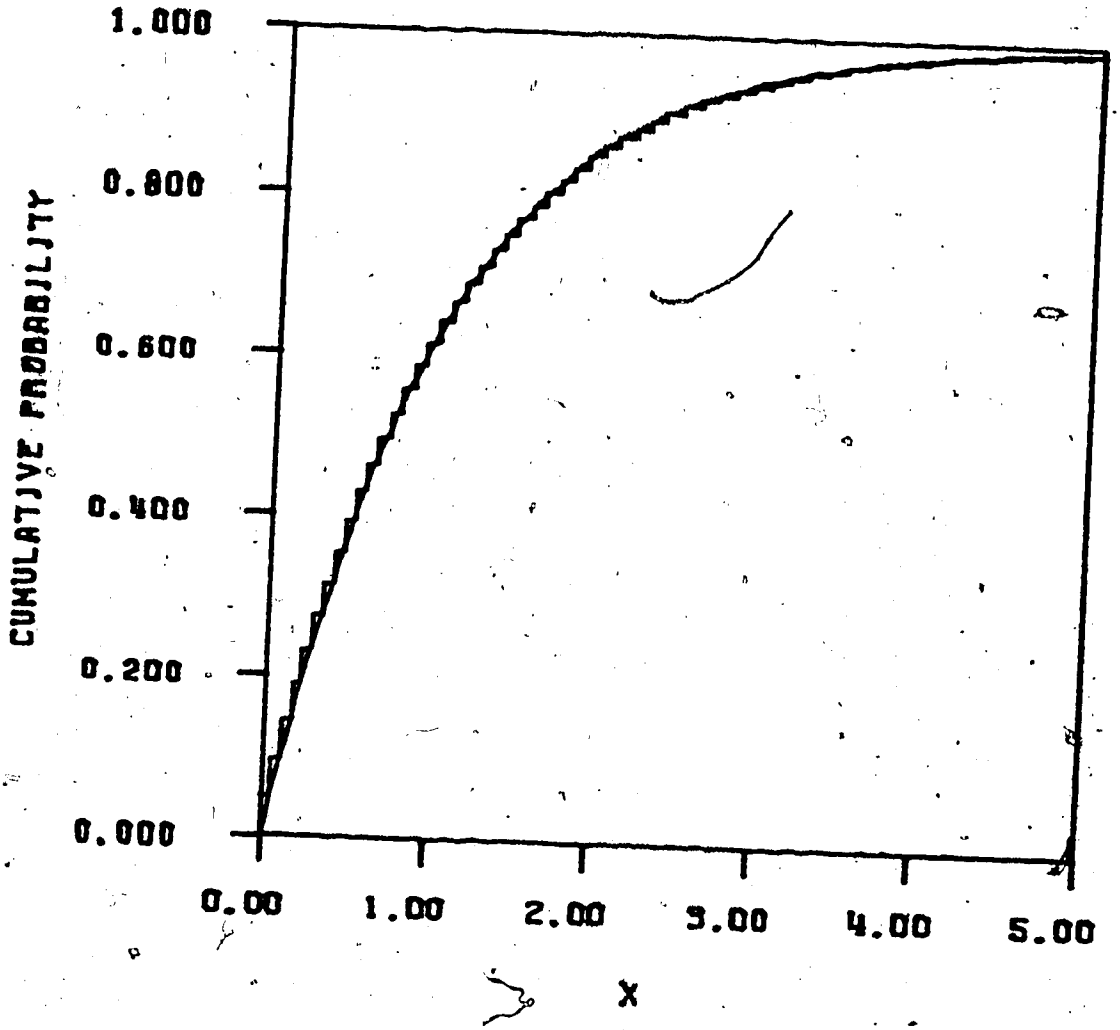
1-EXP(-X) (CONTINUOUS) COMPARED
TO P(.0811(EXP(D)-1)<X) (DISCRETE)
WHEN X1 = LD95 AND DELTA = 0.5

FIGURE 2.3.5



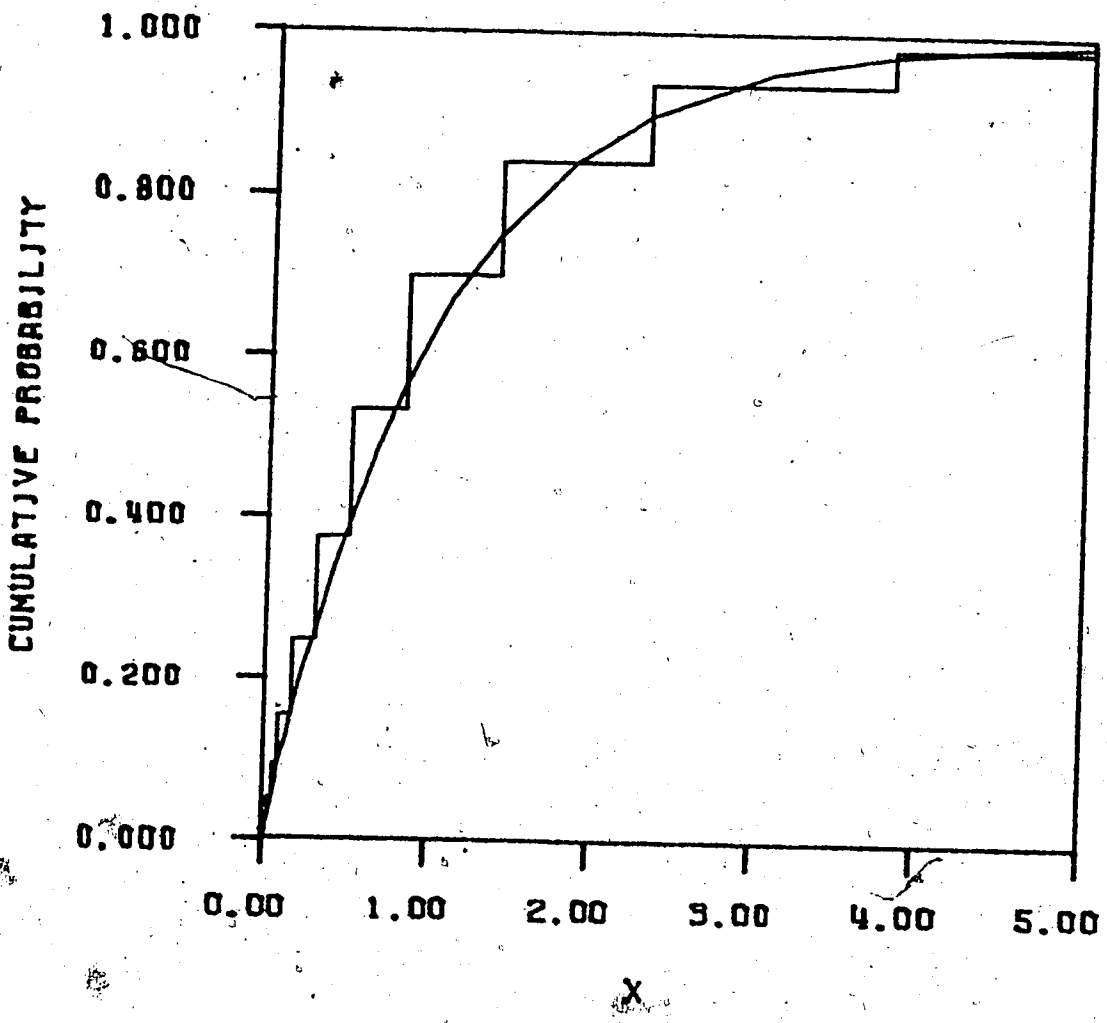
1-EXP(-X) (CONTINUOUS) COMPARED TO P(0.501(EXP(D)-1)<X) (DISCRETE) WHEN X1 = LOG5 AND DELTA = 0.1

FIGURE 2.3.6



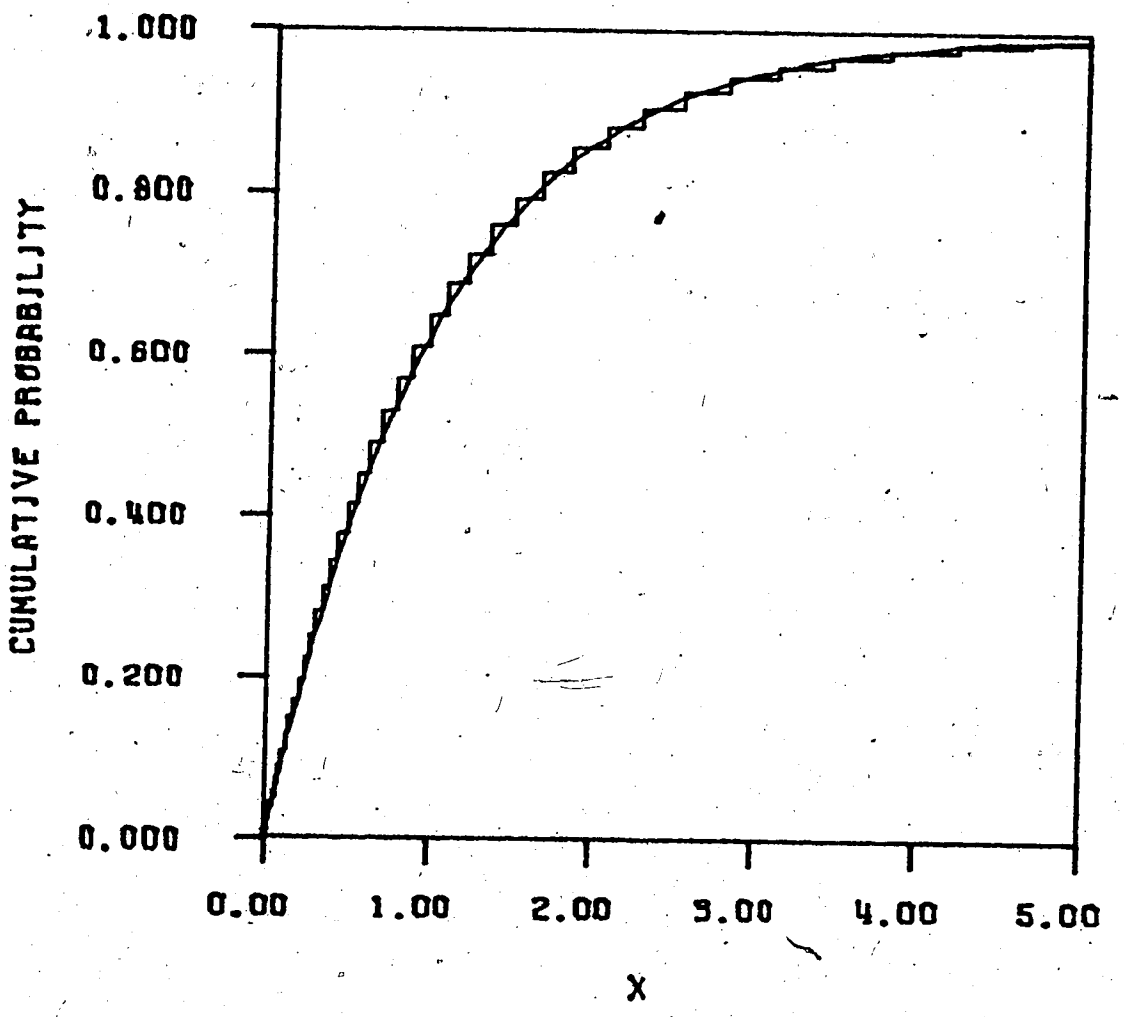
1-EXP(-X) (CONTINUOUS) COMPARED TO P(2.606(EXP(D)-1)<X) (DISCRETE) WHEN X1 = LOG5 AND DELTA = .02

FIGURE 2.3.7



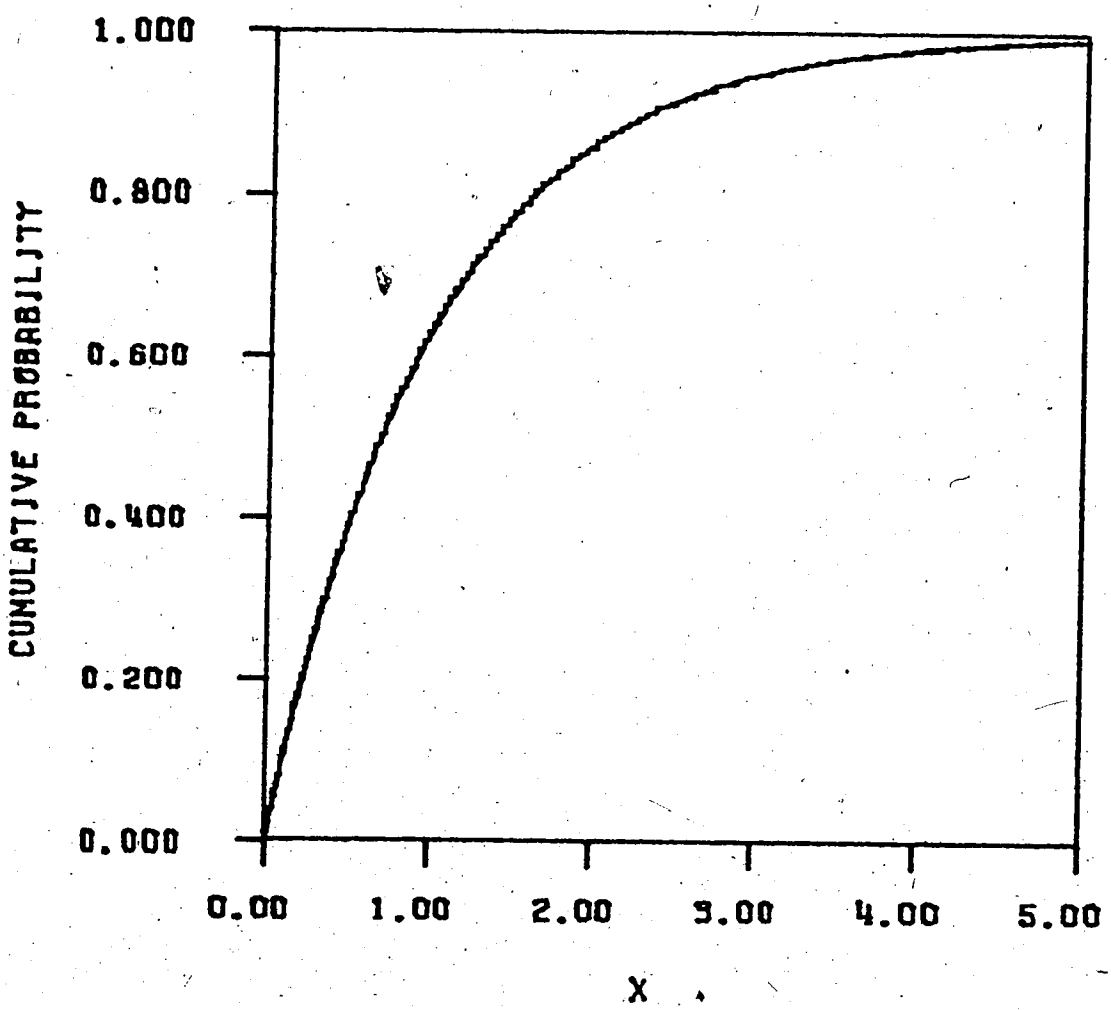
1-EXP(-X) (CONTINUOUS) COMPARED TO P(.0156(EXP(D)-1)<X) (DISCRETE) WHEN X1 = LOG9 AND DELTA = 0.5

FIGURE 2.3.8



1-EXP(-X) (CONTINUOUS) COMPARED
TO P(.0961(EXP(D)-1)<X) (DISCRETE)
WHEN X1 = LOG9 AND DELTA = 0.1

FIGURE 2.3.9



1-EXP(-X) (CONTINUOUS) COMPARED
TO P(0.500(EXP(D)-1)<X) (DISCRETE)
WHEN X1 = LOG9 AND DELTA = .02

2.4 Weak Convergence of $\beta(X_N-\theta)+\ln(e^{\beta\Delta}-1)$ to Extreme Value. The results of section 2.2 hold regardless of the relative rates of convergence of X_1 to infinity and Δ to zero. If in fact this relative convergence takes place under certain conditions, another limiting distribution can be shown to apply. Recall that

$$(2.4.1)\quad D = X_1 - X_N$$

and

$$(2.4.2)\quad m = e^{-\beta(X_1-\theta)}/(e^{\beta\Delta}-1).$$

Corollary 2.4.1: Let the constant z be given. Then as X_1 tends to infinity and Δ tends to 0 in such a way that m tends to 0 we have that

$$P(\beta(X_N-\theta)+\ln(e^{\beta\Delta}-1) \le z) \to \exp(-e^{-z}).$$

Proof: Putting $x=e^{-z}$ we have that

$$1-e^{-x} = \lim P(m(e^{\beta D}-1) \le x) \quad \text{[from Theorem 2.2.1]}$$

$$= \lim P(me^{\beta D} \le x) \quad \text{[since } m \to 0\text{]}$$

$$= \lim P(me^{\beta(X_1 - X_N)} \leq x) \quad \text{[from (2.4.1)]}$$

$$= \lim P(e^{-\beta(X_N - \theta)}/(e^{\beta\Delta} - 1) \leq x) \quad \text{[from (2.4.2)]}$$

$$= \lim P(-\beta(X_N - \theta) - \ln(e^{\beta\Delta} - 1) \leq -z).$$

Hence $P(\beta(X_N - \theta) + \ln(e^{\beta\Delta} - 1) \leq z) \to \exp(-e^{-z})$.

$\exp(-e^{-z})$ is the standard form of the Extreme Value distribution (sometimes called Gumbel's Extreme Value distribution or the Type I Extreme Value distribution).

To understand the implications of this result we should look more closely at the condition that $m \to 0$. From (2.4.2) and using the fact that $(e^{\beta\Delta} - 1)/\beta\Delta \to 1$ as $\Delta \to 0$ we see that

$$m \to 0 \quad \text{iff} \quad \Delta e^{\beta X_1} \to \infty \quad \text{iff} \quad \beta X_1 + \ln(\Delta) \to \infty.$$

These equivalent conditions indicate more clearly the relative sizes of X_1 and Δ. In general terms the requirement may be expressed by stating that Δ may not converge to 0 too quickly.

One further consideration should be made. In practice Theorem 2.2.1 will be interpreted to mean that since

$$\lim P(m(e^{\beta D}-1) \leq z) = 1-e^{-z}$$

we may conclude, for finite values of X_1 and nonzero values of Δ, that

(2.4.3) $P(m(e^{\beta D}-1) \leq z) \doteq 1-e^{-z}$.

Using (2.4.1) we can restate (2.4.3) in the equivalent form

(2.4.4) $P(X_N \leq z) \doteq \exp-\{\exp-\beta(z-\theta)-\exp-\beta(X_1-\theta)\}/(e^{\beta\Delta}-1)$

or more simply

(2.4.5) $P(X_N \leq z) \doteq \exp-\{\exp-\beta(z-t) - \exp-\beta(X_1-t)\}$

where

(2.4.6) $t = \theta - (\ln(e^{\beta\Delta}-1))/\beta$.

This is the form of a Truncated Extreme Value random variable which is truncated above at X_1. That is (2.4.5) represents

(2.4.7) $P(X_N \leq z \mid X_N \leq X_1)$

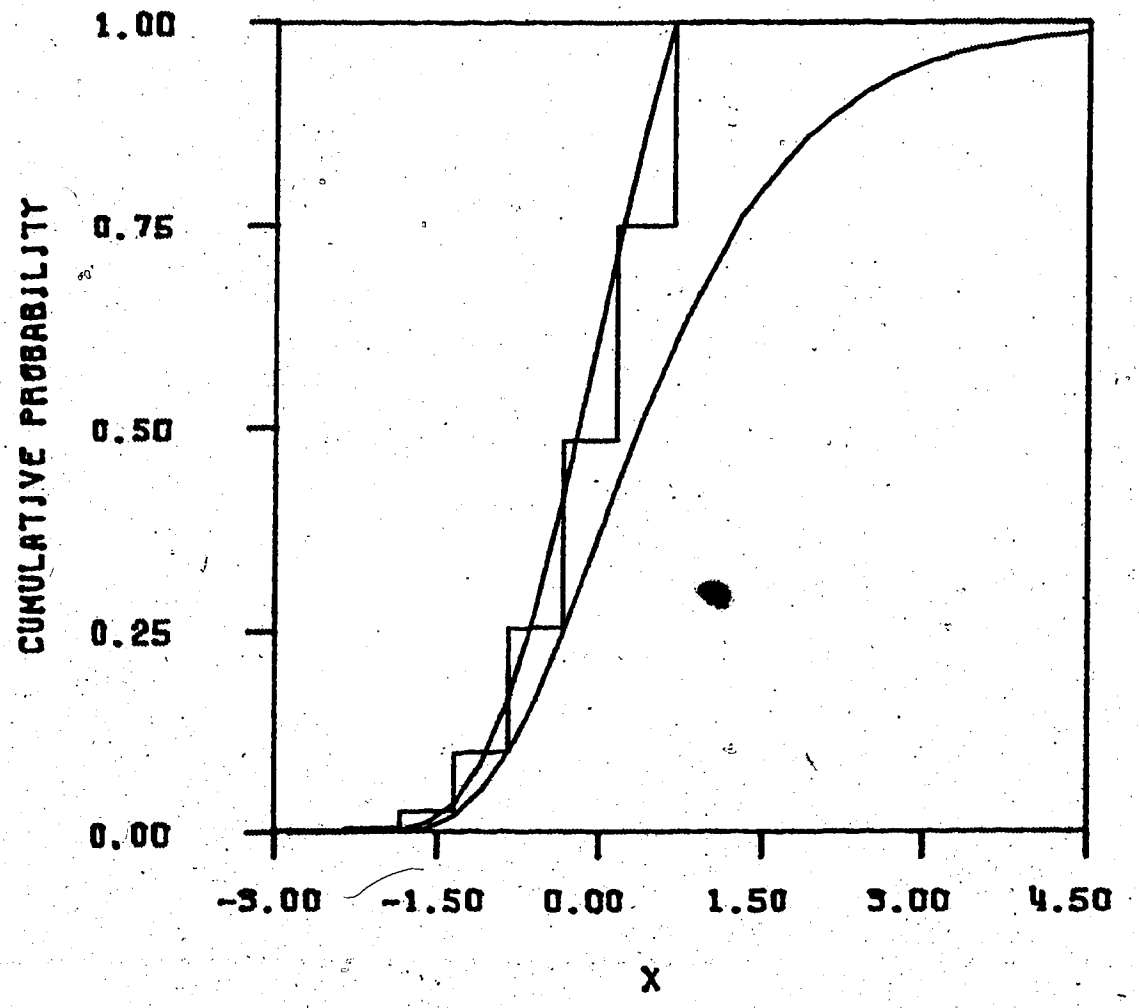
for an Extreme Value random variable X_N with location parameter t and scale parameter β.

2.5 Graphic Comparison of the First Zero and Extreme Value Distributions. The above theorem guarantees convergence of $\beta(X_N-\theta)+\ln(e^{\beta\Delta}-1)$ to Extreme Value in certain limiting situations. Again, we have graphed the two distributions on the following pages to indicate the kind of fit that can be expected for finite cases. As for the graphs comparing the Exponential and First Zero distributions, we have assumed θ and β to be 0 and 1 respectively. As can be seen, the approximation is closer for large values of X_1 and large values of Δ (which yield a small value of m). In the best fitting graph, X_1 is equal to the LD99 and Δ is equal to .5. Thus the corresponding value of m is 0.0156. Compare this to the fit for the cases X_1=LD99 and Δ=.02 (giving m=.5000), X_1=LD75 and Δ=.5 (giving m=.5138), and X_1=LD75 and Δ=.02 (giving m=16.50). It becomes quite evident that the fit deteriorates rapidly as m increases.

In order to compare this approximation to that obtained from the exponential form we have on the same graph included the Truncated Extreme Value approximation of (2.4.5). As expected, in all cases the Truncated approximation is better than the nontruncated one. Only in two cases, namely X_1=LD95 and LD99 and Δ=.5 is the nontruncated fit competetive. We would therefore expect the Extreme Value approximation to have limited applications. We shall see, however, in certain situations this

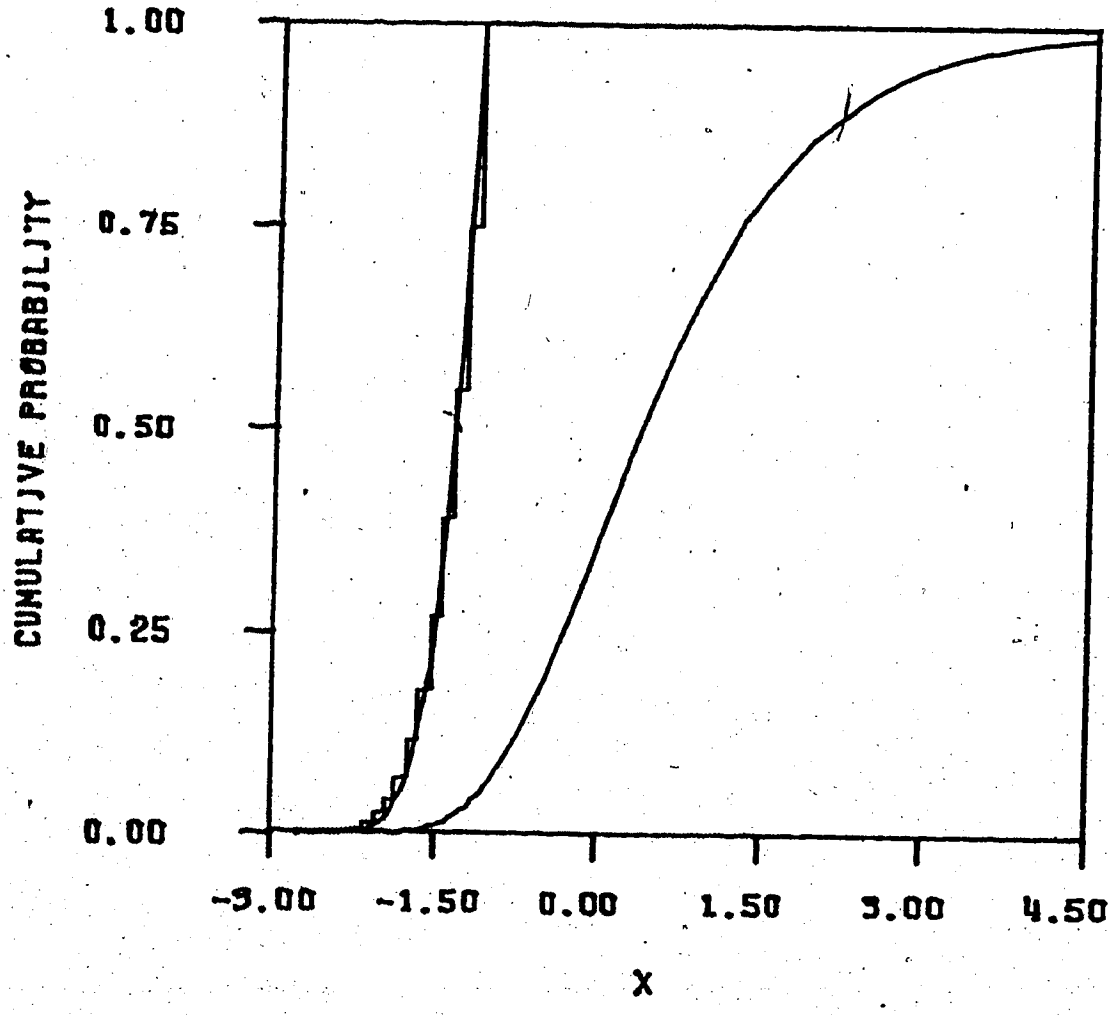
approximation does prove surprisingly useful.

FIGURE 2.5.1



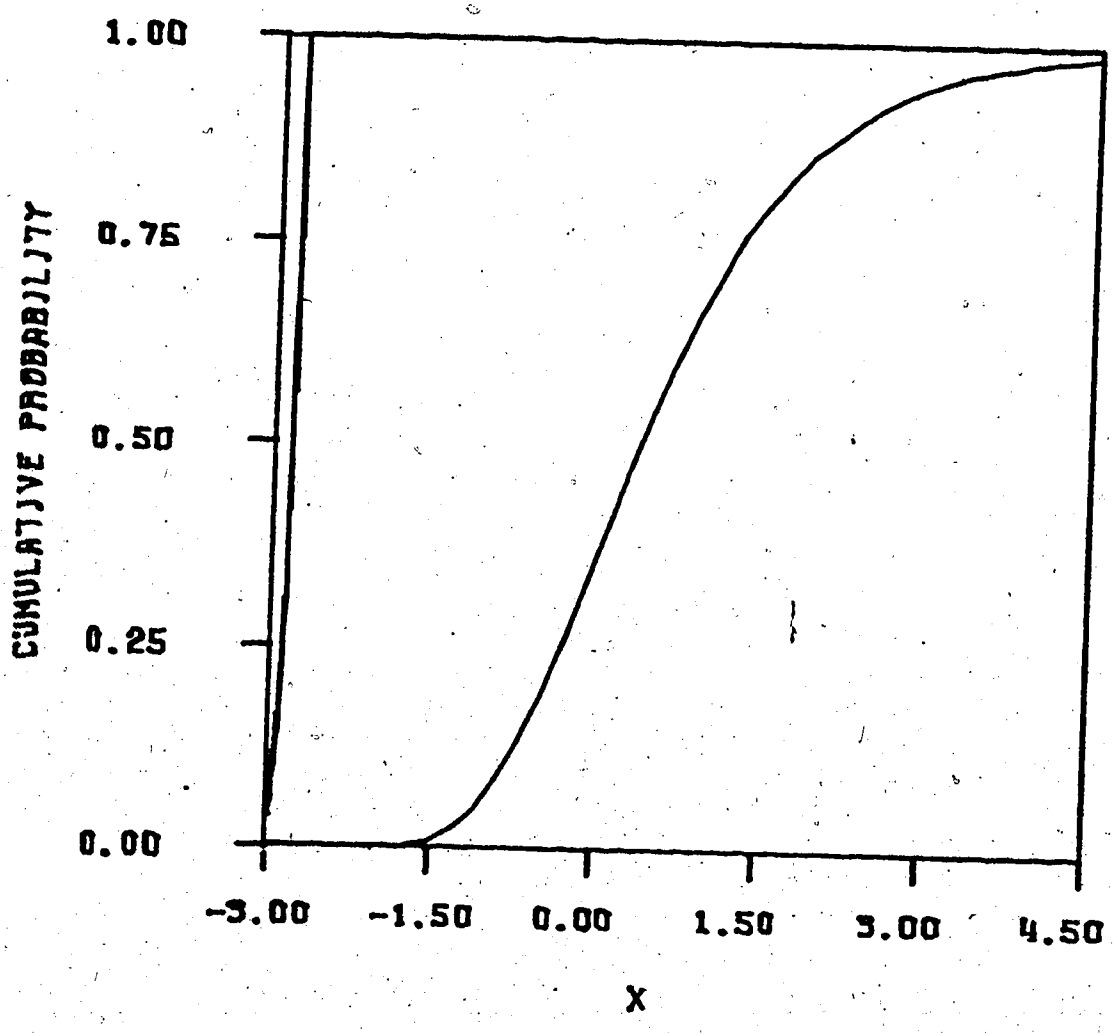
EXP(-EXP(X1-X)) (TRUNCATED) AND
EXP(-EXP(-X)) (CONTINUOUS) COMPARED
TO $P(X_N+LN(EXP(0.5)-1)<X)$ (DISCRETE)
WHEN X1 = LD75 AND DELTA = 0.5

FIGURE 2.5.2



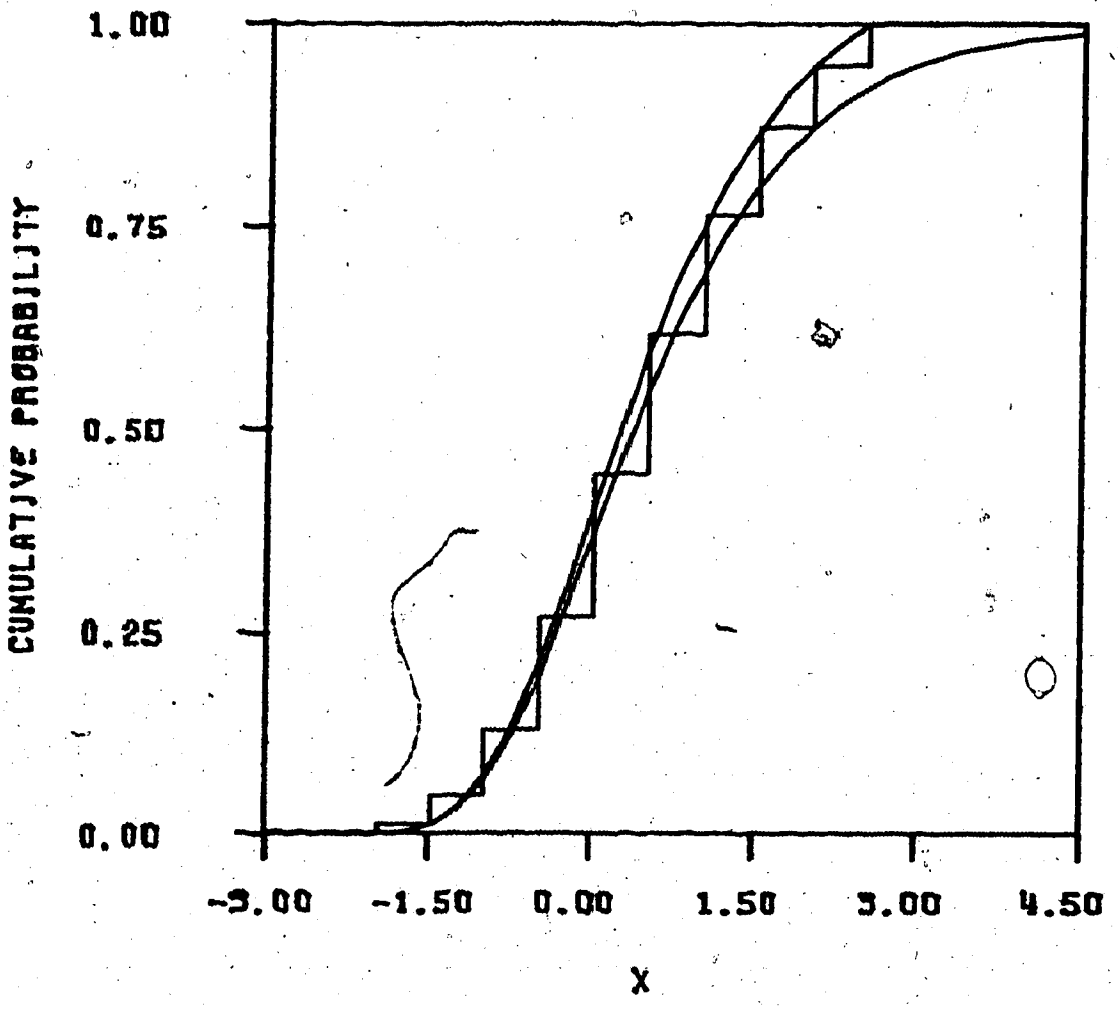
EXP(-EXP(X1-X)) (TRUNCATED) AND
EXP(-EXP(-X)) (CONTINUOUS) COMPARED
TO $P(X_N+LN(EXP(0.1)-1)<X)$ (DISCRETE)
WHEN X1 = LO75 AND DELTA = 0.1

FIGURE 2.5.3



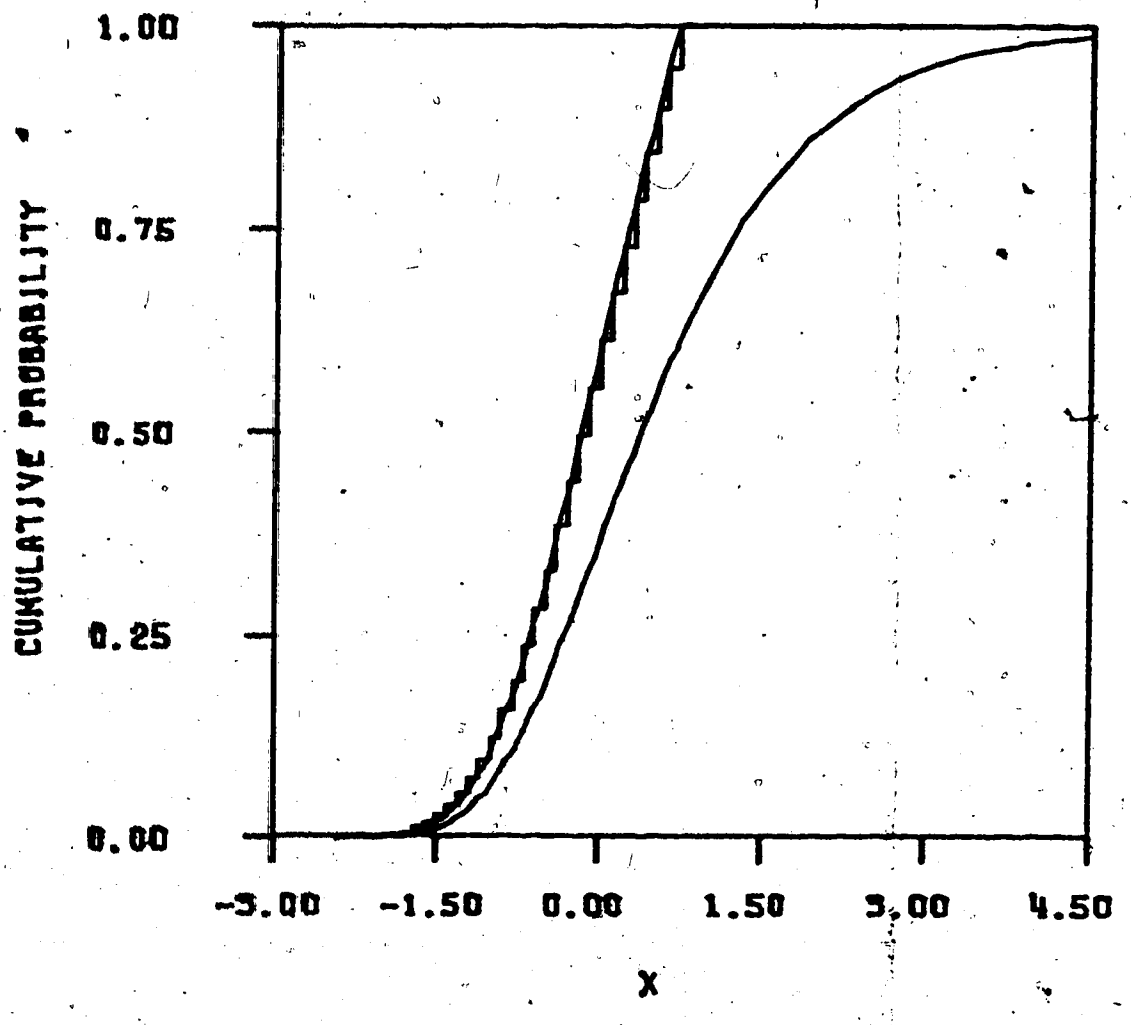
EXP(-EXP(X1-X)) (TRUNCATED) AND
EXP(-EXP(-X)) (CONTINUOUS) COMPARED
TO $P(X_N + LN(EXP(.02)-1) < X)$ (DISCRETE)
WHEN X1 = LD75 AND DELTA = .02

FIGURE 2.5.4



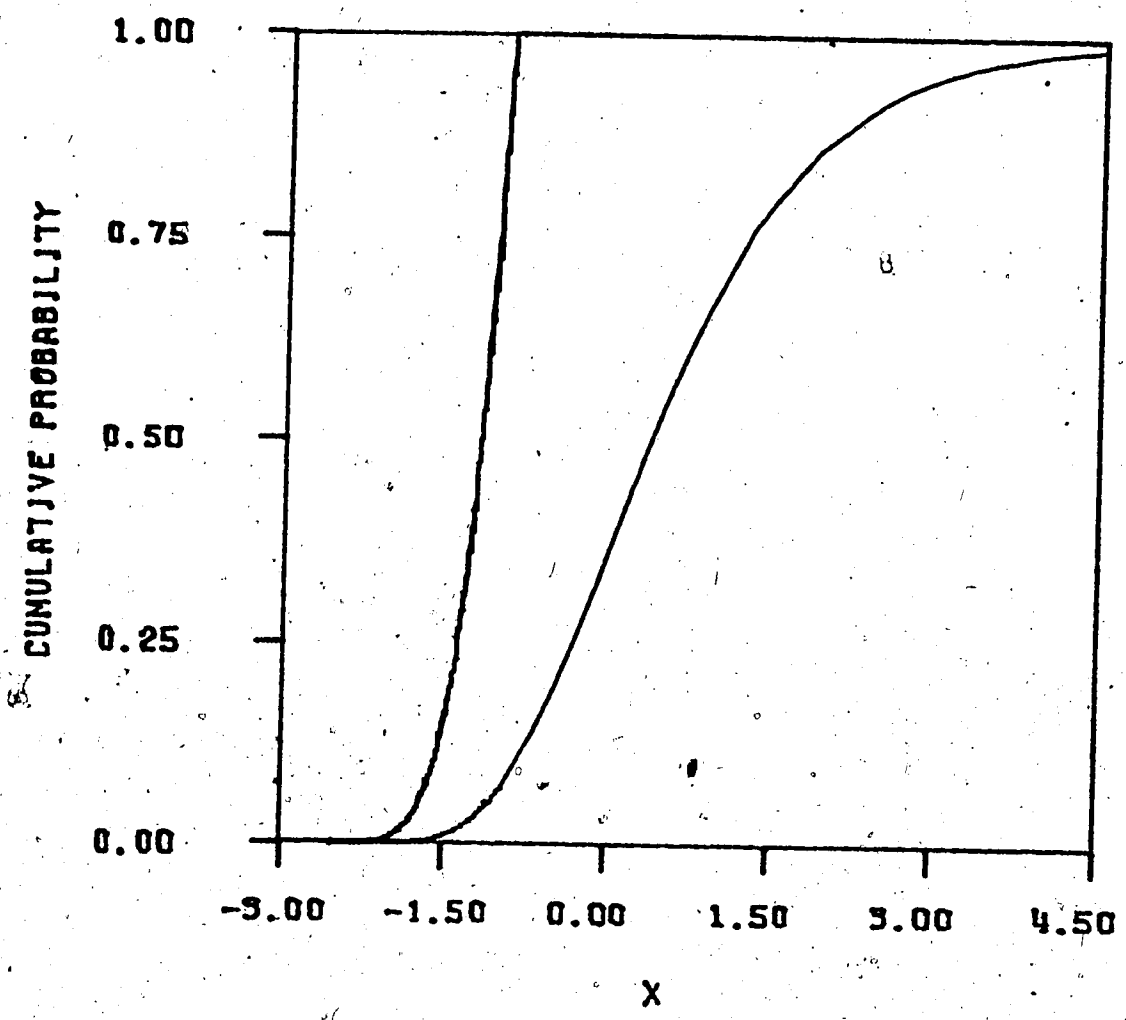
EXP(-EXP(X1-X)) (TRUNCATED) AND
EXP(-EXP(-X)) (CONTINUOUS) COMPARED
TO $P(X_N+LN(EXP(0.5)-1)<X)$ (DISCRETE)
WHEN X1 = LD95 AND DELTA = 0.5

FIGURE 2.5.5



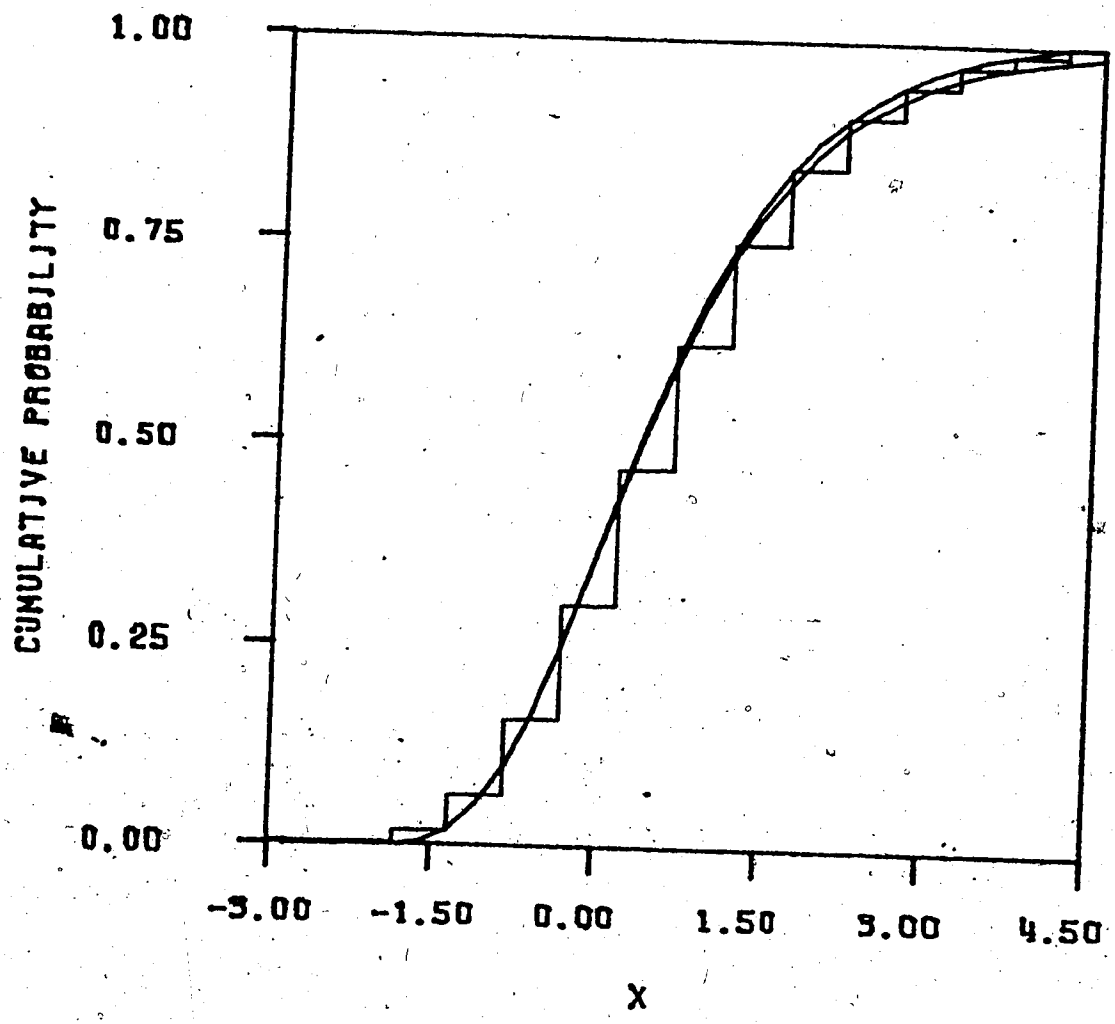
EXP(-EXP(X1-X)) (TRUNCATED) AND
EXP(-EXP(-X)) (CONTINUOUS) COMPARED
TO $P(X_N+LN(EXP(0.1)-1)<X)$ (DISCRETE)
WHEN X1 = LOG5 AND DELTA = 0.1

FIGURE 2.5.6



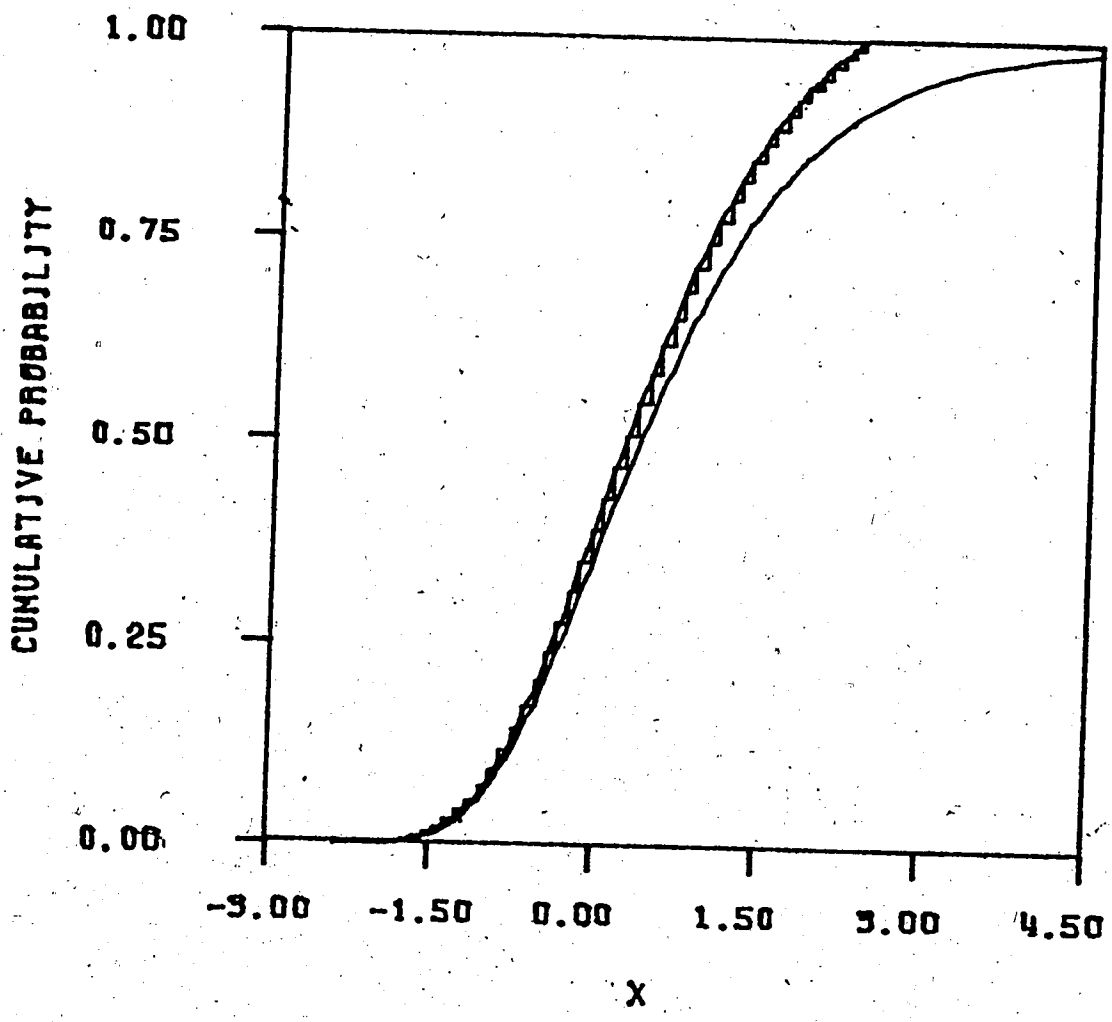
EXP(-EXP(X1-X)) (TRUNCATED) AND
EXP(-EXP(-X)) (CONTINUOUS) COMPARED
TO $P(X_N+LN(EXP(.02)-1)<X)$ (DISCRETE)
WHEN X1 = LOG5 AND DELTA = .02

FIGURE 2.5.7



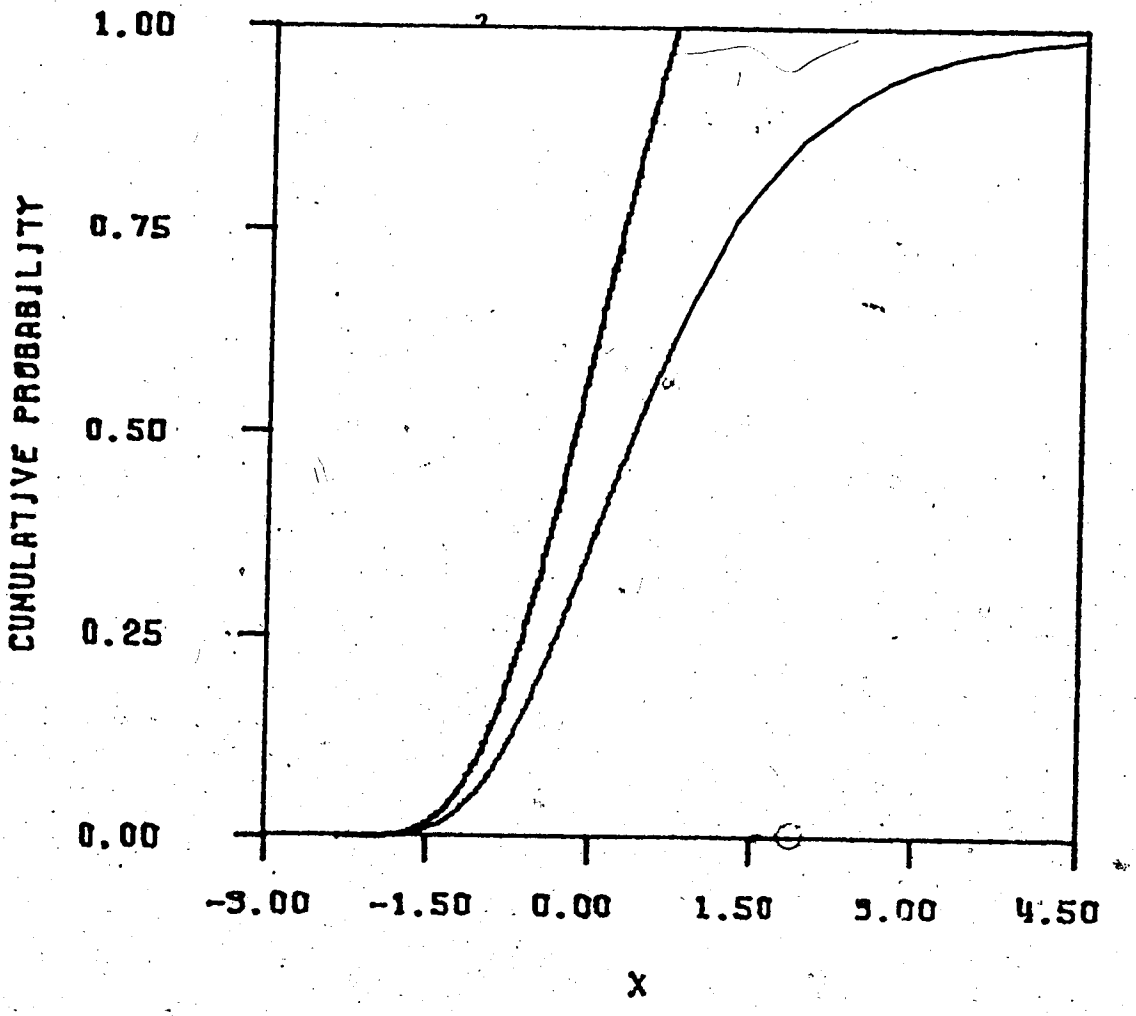
EXP(-EXP(X1-X)) (TRUNCATED) AND
EXP(-EXP(-X)) (CONTINUOUS) COMPARED
TO $P(X_N+LN(EXP(0.5)-1)<X)$ (DISCRETE)
WHEN X1 = LD99 AND DELTA = 0.5

FIGURE 2.5.8



EXP(-EXP(X1-X)) (TRUNCATED) AND
EXP(-EXP(-X)) (CONTINUOUS) COMPARED
TO $P(X_N+LN(EXP(0.1)-1)<X)$ (DISCRETE)
WHEN X1 = LOG9 AND DELTA = 0.1

FIGURE 2.5.9



EXP(-EXP(X1-X)) (TRUNCATED) AND
EXP(-EXP(-X)) (CONTINUOUS) COMPARED
TO $P(X_N+LN(EXP(.02)-1)<X)$ (DISCRETE)
WHEN X1 = LOG9 AND DELTA = .02

CHAPTER III

Estimating the Parameters

3.1 Introduction. The main reason for approximating a distribution is to facilitate the process of estimating the parameters. We will be concerned with three parameters: β (or perhaps $1/\beta$), θ, and r where r is a p-fractile other than θ. For example, if p=.75 then r=LD75. If p=.5, then r=LD50= θ. Since the logistic distribution is a two parameter distribution, any two of these parameters determine the third. Usually of interest are the scale parameter and one location parameter. We will also consider the simpler problem of estimating θ and r when β is known. There are three sources of estimates: the Exact First Zero Distribution, the Exponential approximation, and the Extreme Value approximation. In addition, for each distribution, there are various types of estimates. These include maximum likelihood (ML) estimates, moment estimates, and uniformly minimum variance unbiased (UMVU) estimates. Thus if we talk about the Exponential UMVUE, we are referring to the UMVU estimate obtained from the Exponential approximation. Note that this is not a "true" UMVUE. It is UMVU for the Exponential distribution but undoubtedly bias will be introduced from the finite

approximation. By the same token, the Exponential MLE will be asymptotically unbiased with respect to estimating its own parameters but may not have this property with respect to the First Zero parameters.

Each of the next three sections in this chapter is devoted to deriving estimates from each of the distributions: section 3.2 covers estimates from the Exact First Zero distribution, section 3.3 discusses Exponential estimates, and section 3.4 describes Extreme Value estimates. Their relative performance will be evaluated in the next chapter.

3.2 Exact Maximum Likelihood Estimates. Given the explicit First Zero distribution, it is possible to obtain the Exact Maximum Likelihood Estimates for θ and β (or for r and β). The distribution function for each 0 observed is

$$P(X_N = X_n) = P(Y_1=1, Y_2=1, \ldots, Y_{n-1}=1, Y_n=0)$$

$$= F(X_1)F(X_2)\ldots F(X_{n-1})[1-F(X_n)]$$

$$= \{\prod_{i=1}^{n} F(X_i)\}\exp -\beta(X_n-\theta)$$

where F(x) is the logistic distribution function

$$F(x) = 1/[1+\exp -\beta(x-\theta)].$$

For k such iterations with starting points

$$X_{1_1}, X_{1_2}, \ldots, X_{1_k},$$

increment sizes $\Delta_1, \Delta_2, \ldots, \Delta_k$,

and first zeros at $X_{n_1}, X_{n_2}, \ldots, X_{n_k}$

the likelihood function is

$$L = P(X_{N_1} = X_{n_1}, X_{N_2} = X_{n_2}, \ldots, X_{N_k} = X_{n_k})$$

$$= \{\prod_{j=1}^{k} \prod_{i=1}^{n_j} F(X_{i_j})\} \exp -\beta \sum_{j=1}^{k} (X_{n_j} - \theta).$$

This leads to the log likelihood function

$$\ln(L) = \sum_{j=1}^{k} \sum_{i=1}^{n_j} \ln(F(X_{i_j})) - \beta \sum_{j=1}^{k} (X_{n_j} - \theta).$$

Taking partial derivatives with respect to θ and β gives

$$\frac{\partial \ln(L)}{\partial \theta} = -\sum_{j=1}^{k} \beta \sum_{i=1}^{n_j} F(X_{i_j}) \exp -\beta(X_{i_j} - \theta) + k\beta$$

and

$$\frac{\partial \ln(L)}{\partial \beta} = \sum_{j=1}^{k} \sum_{i=1}^{n_j} X_{i_j} F(X_{i_j}) \exp -\beta(X_{i_j} - \theta) - \sum_{j=1}^{k} (X_{n_j} - \theta).$$

Setting these equal to 0 and reducing leads to the equations

$$(3.2.1) \quad \sum_{j=1}^{k} \sum_{i=1}^{n_j} F(X_{i_j}) - \sum_{j=1}^{k} (n_j - 1) = 0$$

and

$$(3.2.2) \quad \sum_{j=1}^{k} \sum_{i=1}^{n_j} X_{i_j} F(X_{i_j}) - \sum_{j=1}^{k} \sum_{i=1}^{n_j - 1} X_{i_j} = 0.$$

These cannot be solved explicitly but are manageable numerically. The standard procedure is to do a two parameter Newton-Raphson recursion. If β is known, then a one parameter recursion may be used on (3.2.1) to find the value of θ.

In practice, the values of X_1 and/or Δ will be changed during the course of the experiment. However, for the sake of the comparison we will be doing in the next chapter, we also consider the case with the further restrictions that all the starting points and all the increment sizes are equal. Under these conditions the process is simplified noticeably and by defining

$$n = \max \{n_1, n_2, \ldots, n_k\}$$

we can then define the values for $1 \leq i \leq n$

$$w_i = \text{the number of } n_j\text{'s that are} \geq i$$

$$= \sum_{j=1}^{k} I[n_j \geq i]$$

where

$$I[n_j \geq i] = \begin{cases} 1 \text{ if } n_j \geq i \\ 0 \text{ if } n_j < i. \end{cases}$$

This reduces (3.2.1) and (3.2.2) to

$$(3.2.3)\quad \sum_{i=1}^{n} w_i F(X_i) - \sum_{j=1}^{k} (n_j - 1) = 0$$

and

$$(3.2.4)\quad \sum_{j=1}^{k} X_{n_j} - \sum_{i=1}^{n} w_i X_i (1-F(X_i)) = 0.$$

If we denote the left side of (3.2.3) by G (considered as a function of θ and β) and write G_θ as the partial derivative of G with respect to θ, then if β is known and θ_1 is an estimate for θ, the next Newton-Raphson recursive estimate for θ is

$$\theta_2 = \theta_1 - G/G_\theta$$

where G and G_θ are evaluated at θ_1.

In the same way, denoting the left hand side of (3.2.4) by H, if θ_1 and β_1 are estimates for θ and β then the next estimates are

$$\theta_2 = \theta_1 + (HG_\beta - GH_\beta)/(G_\theta H_\beta - G_\beta H_\theta)$$

and

$$\beta_2 = \beta_1 + (GH_\theta - HG_\theta)/(G_\theta H_\beta - G_\beta H_\theta)$$

where again the right hand sides are evaluated at θ_1, β_1. For the logistic distribution function F we have

$$\frac{\partial F}{\partial \theta} = -\beta F(x)(1-F(x)) \text{ and } \frac{\partial F}{\partial \beta} = (x-\theta)F(x)(1-F(x)).$$

Using these we can obtain the quantities

$$G_\theta = \sum w_i (X_i)(1-F(X_i))$$

$$G_\beta = \sum w_i (X_i-\theta)F(X_i)(1-F(X_i))$$

$$H_\theta = -\sum w_i X_i F(X_i)(1-F(X_i))$$

$$H_\beta = \sum w_i X_i (X_i-\theta)F(X_i)(1-F(X_i))$$

where all four sums are taken for $1 \leq i \leq n$. The same procedure can be followed with unequal starting points and increment sizes. The equations are similar with the w's replaced by a second summation sign.

This method is virtually identical to Finney's method. The only difference is that the sample size at each X_i is variable and the samples tend to be closer together than in the classical case. Otherwise the maximum likelihood equations are the same and so must also be the solutions. The difference in the iteration scheme is due to the fact

that Finney uses a first term expansion of the distribution function before deriving the recursion.

The equations of course are much simpler for the one parameter recursion that is used when β is known.

3.3 Exponential Estimates. First we will consider the case when β is known. Theorem 2.2.1 shows that under the proper conditions

$$P(m(e^{\beta D}-1) < z) \to 1 - e^{-z}$$

so for this section we will assume that

(3.3.1) $P(e^{\beta D}-1 < z) = 1 - e^{-mz}$.

If X_1 and Δ are subscripted by i, we will write

$$m_i = e^{-\beta(X_{1_i}-\theta)}/(e^{\beta\Delta_i}-1)$$

The density derived from (3.3.1) is

(3.3.2) $f(z) = me^{-mz}$.

For k such variables with all starting points equal and all increment sizes equal (and hence only one common value for m) we have the joint density

(3.3.3) $L = f(z_1, z_2, \ldots, z_k)$

$$= m^k \exp -m \sum_{i=1}^{k} z_i.$$

We are interested in estimates of ln(m). Since the sum of k independent Exponential variables with mean 1/m is a Gamma random variable with mean k/m and variance k/m^2, we may use the fact that the expected value of the log of this random variable is

$$E[\ln \sum_{i=1}^{k} z_i] = -\ln(m) + \psi(k)$$

where $\psi(k)$ is the Digamma function which for an integer k is equal to

$$\psi(k) = \begin{cases} -\gamma \text{ if } k=1 \\ -\gamma + \sum_{i=1}^{k-1} 1/i \text{ if } k>1. \end{cases}$$

[Note: γ = Euler's constant = .5772156645...]

Recalling that

$$m = e^{-\beta(X_1-\theta)}/(e^{\beta\Delta}-1)$$

we have that

$$E[\ln \sum_{i=1}^{k} z_i] = \beta(X_1 - \theta) + \ln(e^{\beta\Delta}-1) + \psi(k)$$

and so if we put $D_i = X_1 - X_{n_i}$ and $e^{\beta D_i}-1 = z_i$ we have that

$$(3.3.4)\quad \tilde{\theta} = X_1 + [\ln(e^{\beta\Delta}-1)+\psi(k)-\ln\sum_{i=1}^{k}(e^{\beta D_i}-1)]/\beta$$

is an unbiased estimate of θ. Since $\tilde{\theta}$ is a function of the complete sufficient statistic, it follows that $\tilde{\theta}$ is a UMVUE of θ.

We can also find the maximum likelihood estimate for θ. Taking the log of (3.3.3) and using subscripts on m to allow for different starting points and increment sizes gives

$$(3.3.5)\quad \ln(L) = \sum_{i=1}^{k}\ln(m_i) - \sum_{i=1}^{k} m_i z_i.$$

Taking the partial derivative of ln(L) w.r.t. θ gives

$$\frac{\partial \ln(L)}{\partial\theta} = K\beta - \beta\sum_{i=1}^{k} m_i z_i.$$

Setting this equal to 0 and solving for θ yields

$$(3.3.6)\quad \hat{\theta} = [\ln(k)-\ln\sum_{i=1}^{k}\{e^{-\beta X_{1_i}}(e^{\beta D_i}-1)/(e^{\beta\Delta_i}-1)\}]/\beta.$$

This estimate of course can be used even with unequal starting points and increment sizes. However, in order to compare it with the UMVUE, let us assume that starting points and increment sizes are the same. Then (3.3.6) reduces to

$$(3.3.7)\quad \hat{\theta} = [\ln(k) - \ln \sum_{i=1}^{k} \{e^{-\beta X_1} (e^{\beta D_i} - 1)/(e^{\beta \Delta} - 1)\}]/\beta$$

$$= X_1 + [\ln(e^{\beta\Delta} - 1) + \ln(k) - \ln \sum_{i=1}^{k} (e^{\beta D_i} - 1)]/\beta.$$

The difference between the UMVUE and the MLE is

$$\text{UMVUE} - \text{MLE} = [\psi_k(k) - \ln(k)]/\beta$$

which is a contant so Var(UMVUE) = Var(MLE) and the bias of the MLE can actually be calculated.

When β is not known, the distribution (3.3.1) should be rewritten

$$(3.3.8)\quad P(D < d) = 1 - \exp -m(e^{\beta d} - 1)$$

and the corresponding density is

$$(3.3.9)\quad f(d) = \beta\, m e^{\beta d} \exp -m(e^{\beta d} - 1)$$

so the new log likelihood for k such variables is

$$(3.3.10)\quad \ln(L) = k\ln(\beta) + \sum_{i=1}^{k} \ln(m_i) + \beta \sum_{i=1}^{k} d_i - \sum_{i=1}^{k} m_i (e^{\beta d_i} - 1).$$

Since we already have the MLE for θ (3.3.6) we need only solve for β. (3.3.6) gives an explicit solution for $\hat{\theta}$. Thus

when we take the partial derivative of (3.3.10) and set it equal to 0, we may substitute (3.3.6) into the equation leaving it a function only of β, the d's, Δ's, and X_1's. Thus the most difficult calculations require only a single parameter recursion to ve for β. This value may then be substituted into (3.3.6) to find $\hat{\theta}$. Rather than give these equations, we will instead consider the neater solutions when all the X_1's and Δ's are equal. In this case (3.3.10) becomes

$$(3.3.11)\quad \ln(L) = k\ln(\beta) + k\ln(m) + \beta \sum_{i=1}^{k} d_i - m \sum_{i=1}^{k} (e^{\beta d_i} - 1)$$

and taking the partial derivative w.r.t. β yields

$$(3.3.12)\quad \frac{\partial \ln(L)}{\partial \beta} = k/\beta + (k/m)\frac{\partial m}{\partial \beta} + \sum_{i=1}^{k} d_i$$

$$- \frac{\partial m}{\partial \beta} \sum_{i=1}^{k} (e^{\beta d_i} - 1) - m \sum_{i=1}^{k} d_i e^{\beta d_i}.$$

Substituting (3.3.7) into m gives

$$\hat{m} = e^{\hat{\beta}(x_1 - \hat{\theta})} / (e^{\hat{\beta}\Delta} - 1)$$

$$= k / \sum_{i=1}^{k} (e^{\hat{\beta} d_i} - 1)$$

and substituting this into (3.3.12) gives

$$(3.3.13)\quad \frac{\partial \ln(L)}{\partial \beta} = k/\beta + \sum_{i=1}^{k} d_i - k\Big(\sum_{i=1}^{k} d_i e^{\beta d_i}\Big)\Big/\sum_{i=1}^{k} (e^{\beta d_i} - 1).$$

Setting this equal to 0 gives an equation which may be solved for $\hat{\beta}$ numerically.

3.4 Extreme Value Estimates. From Corollary 2.4.1 we know that under certain conditions

$$P(\beta(X_N - \theta) + \ln(e^{\beta\Delta}-1) < z) \to \exp-e^{-z}.$$

For this section we will assume that

(3.4.1) $$P(X_N < x) = \exp-\exp-\beta(x - \{\theta - [\ln(e^{\beta\Delta}-1)]/\beta\}).$$

Putting $s = \theta - [\ln(e^{\beta\Delta}-1)]/\beta$

we can reparametrize (3.4.1) to the form

(3.4.2) $$P(X_N < x) = \exp-\exp-\beta(x-s).$$

This is simply an Extreme Value distribution (sometimes called a Type I Extreme Value distribution) with mean $s + \gamma/\beta$ and variance $\pi^2/(6\beta^2)$. The estimates we are interested in are the moment estimates, found by solving

(3.4.3) $\tilde{\beta} = \pi/(6 \text{ times the sample variance})^{\frac{1}{2}}$

and

(3.4.4) $\tilde{s} = \text{sample mean} - \gamma/\tilde{\beta}.$

This last equation can be solved for $\tilde{\theta}$ giving

(3.4.5) $\tilde{\theta}$ = sample mean - $[\gamma - \ln(e^{\tilde{\beta}\Delta}-1)]/\tilde{\beta}$.

We will not consider any Maximum Likelihood estimates from the Extreme Value distribution for two major reasons. First, the moment estimates for $1/\beta$ and s given above are approximately 55% and 95% efficient respectively [12]. While this may be low as far as estimating β is concerned, the high efficiency of the location parameter makes it very competetive, since the bias due to lack of fit will dominate the effect of a 5% loss of efficiency. The second reason is that the ML estimates from the Extreme Value approximation are roughly as computationally difficult as those from the Exponential approximation, and since the Exponential approximation is better, the ML estimates based thereon should also be more desirable. It is primarily the simplicity of the moment estimates that makes them so attractive. We will see that they also perform surprisingly well under certain sampling situations.

We could of course calculate estimates from the Truncated Extreme Value approximation. However, since this was simply a transformation of the Exponential approximation, it is therefore no surprise to find that the UMVUE of θ when β is known and the ML estimates in the general case are identical to those from the Exponential approximation, and we will not reproduce them here.

CHAPTER IV

Relative Performance of Estimates

4.1 Introduction. In Chapter III we presented a rather large list of possible estimates which could be used. We have actually looked at several others but because of their poor overall performance we did not feel they were worth including in the development or comparisons. The estimates can be classified into two natural groupings; estimates of θ or r when β is known and estimates of θ, r, and β in the general case. Section 4.2 will treat the first group and section 4.3 will concern itself with the second group. In addition there is the natural question of what would happen if the model were incorrect. That is, what if instead of having the assumed logit model, the actual underlying response function were probit? Such a question is obviously important and will be considered in section 4.4. We will then end the chapter with a comparison of First Zero estimates and classical logit analysis estimates in one particular testing situation.

The nature of the estimates generally made it impossible to get the explicit moments of the sample estimates. As a result most of the comparisons that were made were done by means of Monte-Carlo simulations. A

pseudo-random number generator, the one supplied by the APL installation at the University of Alberta, was used to simulate the large samples needed to be able to compare the bias and variance of the different estimates. Wherever possible we used paired comparisons and we also used different starting seeds on different runs in order to make the results of separate simulations "independent". We also kept track of the starting seeds for each simulation with the result that each of the simulations is completely reproducible.

For the sake of standardizing the comparison procedure, we will always have the starting points equal and increment sizes equal. We do this for two reasons. First, having a randomly varying starting point and increment size would add variance to the estimates that might obscure relative performance. Second, determining an optimal method of varying X_1 and Δ sequentially is not a simple process, and very likely the method itself would depend on the type of estimate. This consideration will be discussed again in the next chapter in the sections dealing with recommendations and further research.

The underlying response function will be the standard logistic function

$$F(x) = 1/(1 + e^{-x})$$

which has θ and β equal to 0 and 1 respectively. We tested for three different starting points: LD75, LD95, and LD99 whose numeric values are ln 3, ln 19, and ln 99. Three increment sizes were used as well: .02, .1, and .5. With shorter programs we also used three different sample sizes 5, 10, and 20. For longer programs fewer sample sizes were used. Here sample size refers to the number of 0's in the sample and not the actual number of observations.

4.2 Estimates when β is Known. When β is known, it is irrelevant which root is to be estimated. We also have the atypical statistical situation of having no penalty for extrapolation. This follows since if r is the p-fractile root (ie. $F(r)=p$), then

$$r = \theta + \{\ln(p/[1-p])\}/\beta.$$

Hence if $\hat{\theta}$ is any estimate of θ then

$$\hat{r} = \hat{\theta} + \{\ln(p/[1-p])\}/\beta$$

is an estimate of r with

$$\text{Bias}(\hat{r}) = \text{Bias}(\hat{\theta}) \quad \text{and} \quad \text{Var}(\hat{r}) = \text{Var}(\hat{\theta}).$$

Thus we may talk simply of the bias of an estimate without referring to the root it is estimating.

Table 4.2.1 summarizes the results of twenty-seven separate simulations - one simulation for each of the starting points, increment sizes, and sample sizes. Four estimates were considered: the Exact MLE, the Exponential MLE, the Exponential UMVUE, and the Extreme Value Moment Estimate. For each simulation, one thousand samples were generated and the four estimates calculated for that

TABLE 4.2.1 COMPARISON OF BIAS AND VARIANCE (IN BRACKETS) OF ESTIMATES WHEN BETA IS KNOWN.

		SAMPLE SIZE 5				SAMPLE SIZE 10				SAMPLE SIZE 20			
	TYPE OF ESTIMATE	EXACT MLE	EXP MLE	EXP UMV	EV MOM	EXACT MLE	EXP MLE	EXP UMV	EV MOM	EXACT MLE	EXP MLE	EXP UMV	EV MOM
X_1	Δ												
LD75	.02	-.07 (.22)	.07 (.22)	-.03 (.22)	-3.44 (.00)	-.07 (.13)	.07 (.13)	.02 (.13)	-3.44 (.00)	-.03 (.07)	.03 (.07)	.00 (.07)	-3.44 (.00)
LD75	.1	-.03 (.24)	.04 (.24)	-.06 (.24)	-1.99 (.01)	-.06 (.15)	.07 (.15)	.02 (.15)	-1.97 (.01)	-.04 (.08)	.04 (.08)	.02 (.08)	-1.97 (.00)
LD75	.5	-.02 (.29)	.09 (.29)	-.01 (.29)	-.76 (.09)	-.03 (.17)	.07 (.19)	.02 (.18)	-.74 (.04)	-.03 (.09)	.05 (.10)	.02 (.10)	-.72 (.02)
LD95	.02	-.06 (.18)	.06 (.18)	-.04 (.18)	-1.83 (.01)	-.04 (.11)	.04 (.11)	-.01 (.11)	-1.83 (.01)	-.03 (.06)	.03 (.06)	.01 (.06)	-1.83 (.00)
LD95	.1	-.05 (.19)	.07 (.19)	-.04 (.19)	-.82 (.06)	-.04 (.10)	.04 (.10)	-.01 (.10)	-.79 (.03)	-.01 (.06)	.02 (.06)	-.01 (.06)	-.80 (.02)
LD95	.5	-.01 (.24)	.08 (.26)	-.02 (.26)	-.18 (.18)	-.05 (.15)	.09 (.16)	.04 (.16)	-.12 (.11)	-.02 (.08)	.03 (.09)	.01 (.09)	-.13 (.06)
LD99	.02	-.07 (.18)	.07 (.18)	-.03 (.18)	-.82 (.06)	-.04 (.11)	.04 (.11)	-.01 (.11)	-.81 (.03)	-.03 (.05)	.03 (.05)	.00 (.05)	-.80 (.02)
LD99	.1	-.07 (.19)	.09 (.19)	-.02 (.19)	-.28 (.15)	-.04 (.11)	.05 (.11)	[illegible]	-.27 (.08)	-.02 (.05)	.02 (.05)	.00 (.05)	-.26 (.04)
LD99	.5	-.03 (.24)	.11 (.26)	.00 (.26)	.03 (.26)	-.03 (.14)	.08 (.15)	[illegible]	.04 (.14)	-.03 (.07)	.05 (.08)	.02 (.08)	.07 (.07)

sample. From the table it is apparent that the Exact and Exponential MLE's are essentially the same with regard to both absolute bias and variance, except perhaps when Δ is large, in which case the Exact MLE might have slightly smaller variance. The Exponential UMVUE has the same variance as the Exponential MLE and it has less bias than the other two. The Extreme Value Moment Estimate is never really competitive, since the only instances that its bias is acceptably small its variance is as high as that of the other estimates. The Extreme Value and Exponential estimates are all very straighforward to calculate explicitly, while the Exact estimates require a recursion to locate the root of the ML equation. As a result, the Exponential UMVUE seems to have the edge as far as desirability is concerned, but it may only be used when all starting points and increment sizes are equal. Otherwise, for a general testing situation where for one reason or another the starting points or increment sizes are changed, the Exponential MLE would seem to be the best choice. The one exception to this might be in the situation where large values of Δ were to be used, and then the slight decrease in variance might justify the extra computation necessary to use the Exact MLE.

4.3 Estimates when β is not known. In the general case, we will only consider three estimates: the Exact MLE, the Exponential MLE, and the Extreme Value Moment Estimates. The Exponential UMVUE may only be used when β is known. Four quantities must be taken into account when comparing different estimates: the starting point, increment size, sample size, and also the root to be estimated since different estimates will have different abilities to extrapolate. A fifth factor which may be quite critical in practice is the computational aspects of the estimate. The Exact estimates require a two parameter recursion to solve for the estimates, while the Exponential estimates require only a one parameter recursion and, simplest of all, the Extreme Value estimates may be calculated explicitly. For this reason, the Exact estimates are the most sensitive to choice of starting approximations. As a case in point, for one simulation with starting point LD95, increment size .02, and sample size 10 we used the starting approximations of 0 and 1 (the true values) for θ and β respectively. Even so, we had to generate 2369 samples before we found 1000 for which the procedure converged! The Exponential estimates are much more likely to yield a result. In the above example, 1000 of the first 1115 samples yielded solutions for the Exponential ML estimates. What we finally ended up doing was to calculate the Exponential estimates

for the sample and then use these values as the starting approximations for the Exact estimate procedure. When this was done, the proportion of samples that yielded Exact estimates increased dramatically. We did not find a single case when the Exact procedure converged and the Exponential procedure diverged. The problem of divergence generally decreased as Δ and X_1 increased. The Extreme Value estimates were undefined only when all the stopping points were equal, a rare occurrence especially when the sample sizes were at least 10. We arbitrarily decided that a procedure would be considered to have diverged when the value of $\hat{\beta}$ had gone below .1 or above 10. We only compared the estimates when all three converged. This tends to favor firstly the Exact estimates and secondly the Exponential estimates since they were not penalized in any way for diverging. We had considered giving the limit values of either .1 or 10 to $\hat{\beta}$ when the procedure diverged, and this would have had the effect of reversing the advantages with the Extreme Value coming first and the Exponential coming second. This question of divergence will be mentioned again in the next chapter when the question of how this affects First Zero techniques with respect to Classical methods under cost restrictions is discussed.

Another point we should mention is that of adding a Continuity Correction Factor (CCF) to the values of D in

the Exponential and Extreme Value approximations. We found that a CCF did not help either the fit or the estimates in the Extreme Value case and so we did not include one there. Using a CCF in the Exponential estimate for r when β was known actually hurt their performance and again we did not include one. However, in the general case it becomes apparent that leaving out the CCF adversely affects the performance of the estimates. This is primarily due to the procedure for estimating β, which is why the CCF was not necessary for the case when β was known. Adding the CCF slightly increases the bias of the estimate of β and decreases its variance. These two factors combine to significantly reduce the variance of the estimates of the root r. For these reasons, the Exponential MLE will be calculated using the corrected values. To each value of D we add the quantity of $\Delta/2$ before the Exponential estimates are calculated.

Tables 4.3.1 and 4.3.2 summarize the results of eighteen simulated sampling situations. In each simulation samples were generated until 1000 were found for which all three estimates converged. For each sample, all three estimates were calculated and also the difference between the Exact and Exponential MLE's. Table 4.3.1 contains the results for samples containing 10 zeros and 4.3.2 for samples containing 20 zeros. For each sample estimates were

TABLE 4.3.1 COMPARISON OF BIAS AND VARIANCE (IN BRACKETS) OF ESTIMATES WHEN BETA IS NOT KNOWN AND THE NUMBER OF ZEROS IN EACH SAMPLE IS 10

X_1	Δ	QUANTITY ESTIMATED	TYPE OF ESTIMATE: EXACT MLE	DIFF	EXP MLE	EV MOM
LD75	.02	β	3.22 (6.27)	.262 (.214)	2.96 (4.73)	20.6 (36.0)
LD75	.02	LD75	-.057 (.073)	.084 (.019)	-.141 (.051)	-.072 (.001)
LD75	.1	β	1.82 (4.07)	.438 (.280)	1.38 (2.44)	5.15 (3.35)
LD75	.1	LD75	-.026 (.351)	.185 (.160)	-.211 (.096)	.215 (.016)
LD75	.5	β	.502 (.958)	.386 (.177)	.115 (.381)	[illegible]
LD75	.5	LD50	.054 (.364)	.495 (.091)	-.441 (.550)	-.012 (.133)
LD75	.5	LD75	.140 (1.12)	.291 (.251)	-.152 (.395)	-.313 (.069)
LD95	.02	β	1.45 (2.82)	.085 (.009)	1.36 (2.57)	5.08 (3.30)
LD95	.02	LD95	-.004 (.304)	.028 (.003)	-.032 (.256)	-.261 (.013)
LD95	.1	β	.420 (.499)	.086 (.008)	.334 (.422)	1.29 (.279)
LD95	.1	LD75	.050 (.822)	.120 (.006)	.070 (.926)	.514 (.105)
LD95	.1	LD95	.030 (.801)	.030 (.003)	.000 (.732)	-.489 (.038)

X_1	Δ	QUANTITY ESTIMATED	TYPE OF ESTIMATE: EXACT MLE	DIFF	EXP MLE	EV MOM
LD95	.5	β	.228 (.285)	.199 (.028)	.029 (.169)	.288 (.109)
LD95	.5	LD75	.032 (.168)	.230 (.006)	-.199 (.174)	.058 (.145)
LD95	.5	LD95	.015 (.950)	-.070 (.013)	.055 (.969)	-.291 (.140)
LD99	.02	β	.432 (.540)	.018 (.000)	.414 (.523)	1.39 (.313)
LD99	.02	LD95	.078 (.363)	.022 (.000)	.056 (.343)	.400 (.081)
LD99	.02	LD99	.001 (.639)	.004 (.000)	-.003 (.633)	-.524 (.034)
LD99	.1	β	.216 (.208)	.045 (.001)	.171 (.187)	.462 (.121)
LD99	.1	LD95	-.047 (.159)	.038 (.000)	.010 (.155)	-.044 (.094)
LD99	.1	LD99	-.016 (1.14)	-.015 (.001)	-.001 (1.13)	-.509 (.126)
LD99	.5	β	.201 (.199)	.165 (.017)	.036 (.122)	.131 (.101)
LD99	.5	LD95	-.070 (.456)	-.007 (.005)	-.063 (.439)	-.008 (.209)
LD99	.5	LD99	-.169 (1.49)	-.222 (.030)	.054 (1.51)	-.100 (.559)

TABLE 4.3.2 COMPARISON OF BIAS AND VARIANCE (IN BRACKETS) OF ESTIMATES WHEN BETA IS NOT KNOWN AND THE NUMBER OF ZEROS IN EACH SAMPLE IS 20

X_1	Δ	QUANTITY ESTIMATED	TYPE OF ESTIMATE: EXACT MLE	DIFF	EXP MLE	EV MOM
LD75	.02	β	2.92 (6.00)	.317 (.191)	2.60 (4.33)	21.2 (23.5)
LD75	.02	LD75	-.032 (.051)	.090 (.025)	-.121 (.025)	-.066 (.001)
LD75	.1	β	.964 (1.98)	.302 (.135)	.661 (1.16)	4.79 (1.74)
LD75	.1	LD75	.003 (.192)	.202 (.078)	-.199 (.078)	-.212 (.008)
LD75	.5	β	.237 (.346)	.310 (.049)	-.073 (.155)	.933 (.100)
LD75	.5	LD50	-.002 (.159)	.530 (.064)	-.532 (.336)	.202 (.059)
LD75	.5	LD75	.078 (.576)	.238 (.108)	-.160 (.233)	-.314 (.030)
LD95	.02	β	.721 (1.16)	.061 (.003)	.660 (1.06)	4.68 (1.48)
LD95	.02	LD95	.041 (.251)	.030 (.002)	.011 (.216)	-.258 (.006)
LD95	.1	β	.168 (.224)	.076 (.002)	.092 (.189)	1.20 (.123)
LD95	.1	LD75	-.009 (.382)	.140 (.004)	-.149 (.447)	-.138 (.000)
LD95	.1	LD95	.070 (.370)	.020 (.001)	.050 (.352)	-.470 (.020)

X_1	Δ	QUANTITY ESTIMATED	TYPE OF ESTIMATE: EXACT MLE	DIFF	EXP MLE	EV MOM
LD95	.5	β	.107 (.109)	.191 (.010)	-.084 (.065)	.260 (.040)
LD95	.5	LD75	.025 (.077)	.244 (.003)	-.219 (.084)	.075 (.068)
LD95	.5	LD95	.000 (.380)	-.115 (.010)	.115 (.425)	-.272 (.068)
LD99	.02	β	.179 (.196)	.016 (.000)	.163 (.190)	1.28 (.121)
LD99	.02	LD75	.029 (.153)	.024 (.000)	.005 (.158)	.399 (.041)
LD99	.02	LD99	.019 (.261)	.003 (.000)	.016 (.260)	-.511 (.018)
LD99	.1	β	.105 (.088)	.043 (.001)	.061 (.078)	.405 (.049)
LD99	.1	LD95	.007 (.060)	.038 (.000)	-.031 (.059)	-.057 (.043)
LD99	.1	LD99	-.041 (.332)	-.024 (.001)	-.017 (.340)	-.507 (.060)
LD99	.5	β	.092 (.062)	.151 (.006)	-.059 (.040)	.072 (.034)
LD99	.5	LD95	-.050 (.186)	-.024 (.003)	-.026 (.188)	.012 (.111)
LD99	.5	LD99	-.112 (.556)	-.267 (.022)	.155 (.602)	-.057 (.280)

calculated for β and the two closest roots to the sample points, these being the starting point and the next smallest root. In general we found that extrapolation very far beyond the sampling region yielded high variances and they have not been included in the tables. When the starting point is either LD75 or LD95 and Δ = .02, the sampling region stays very close to the starting point and in these cases we only gave estimates for these roots.

From the tables, the following general remarks may be made:

(i) In all cases, the Exponential estimate of β is better than the Exact. It has both less absolute bias and smaller variance.

(ii) The Extreme Value estimate of the root has less Mean Square Error (MSE) than either of the other estimates in all estimates based on samples containing 10 zeros, and only loses out for 20 zeros when X_1 = LD99 and Δ = .02. It also has less bias when X_1 = LD99 and Δ = .5 for 20 zeros.

(iii) For Δ = .02 and $X_1 \geq$ LD95 the Exponential and Exact estimates are virtually indistinguishable with the Exponential perhaps having a slight edge. The results are similar for X_1 = LD99 and Δ = .1.

(iv) As the number of zeros in the sample increases, the bias of the Exact MLE must of course converge to zero. It is apparent that the Exponential MLE will also converge to

a value very close to zero in most cases since the approximation is very good for $X_1 \geq$ LD95 and $\Delta \leq .1$. However the bias of the Extreme Value does not decrease as the number of zeros increases, but instead remains essentially constant. Thus we could actually calculate under a fixed sampling situation for what number of zeros the MSE of the Exact or Exponential estimates would become less than that of the Extreme Value. However, for X_1 large (say at least LD95) and Δ large (eg. .5) this would require a very large sample before the ML estimates achieved this goal.

Although it is not given in the tables, solutions for both the Exact and Exponential estimates are not likely to be found when X_1 = LD75 and Δ = .02. In our simulation for 10 zeros in the sample, 2366 samples were generated before 1000 were found that yielded solutions for both estimation procedures. When the number of zeros in the sample was increased to 20, 1000 of the first 1649 samples gave convergent solutions. The problem diminished as X_1 and/or Δ and/or the number of zeros increased. The reason for this can be seen since when X_1 is central and Δ is small, the samples tend to get selected from a very small region. This is asymptotically optimum for estimating the root but for smaller sample sizes it allows considerable variation in the estimate of β. Recall that we set arbitrary limits on

the permissible values of β at 1 and 10. For such a small sampling range the probability of $\hat{\beta}$ falling outside this range becomes significantly large. Increasing X_1 and/or Δ increases the sampling range and reduces the problem. Increasing the sample size reduces the variance of the estimates and therefore reduces the probability of non-convergence.

4.4 Performance of Estimates in Probit Analysis. When the response function is not logistic, it is important to know how the estimates of the parameters will be affected by applying logit analysis to a probit model. For our simulations using the logistic distribution we used the model with θ equal to 0 and β equal to 1. This produced a distribution with mean 0 and variance $\pi^2/6$ (= 1.6449...). For our Normal response function we will use a Normal distribution with this same mean and variance so that the biases, variances, and mean squared error of the estimate will be in a sense comparable to those in the tables of the previous section. The increment sizes will remain the same but of course the 75th, 95th, and 99th percentiles change. Their values for the above Normal distribution are .865, 2.11, and 2.98 respectively. These values are much closer to zero than were those from the logistic distribution, due of course to the lighter tails of the Normal distribution. An alternate method of comparing the two response functions would be to choose a Normal distribution with mean 0 and the same 95th percentile as the logistic's. If the prime root of interest were known, this would perhaps be a better method, but since we were interested in a range of values, we decided to set the means and variances equal.

As in the last section, we estimated two of LD50, LD75, LD95, and LD99, depending on the starting point. We

have not performed a full analysis, but have only included those combinations of starting points and increment sizes for which one of the Exponential or Extreme Value estimates performed well enough to be used in actual practice. Because of the similarity of the Exponential and Exact estimates, as well as the computational difficulty of the latter, we have omitted it in the comparison.

Table 4.4.1 summarizes the results of the simulation. From the table, and comparing corresponding values from Table 4.3.1, several observations may be made:

(i) The bias of the estimates is surprisingly small considering the difference in the models. Of course these biases will not approach 0 as the sample size increases as they would in the logit model, but in many cases the number of zeros in the sample must be very large before the square of the bias becomes a major factor in the Mean Squared Error (MSE).

(ii) The variance of the probit estimates is generally smaller than for the logit estimates. This can be attributed to the shape of the curves and the fact that the extreme quantiles of this Normal distribution are much closer together than the logistic extremes.

(iii) The MSE of the Extreme Value estimates is less than the MSE of the Exponential estimates in all cases. This is due to the lower variance of the EV estimates. However, in

TABLE 4.4.1 BIAS AND VARIANCE (IN BRACKETS) OF EXPONENTIAL AND EXTREME VALUE ESTIMATES WHEN THE ACTUAL UNDERLYING DISTRIBUTION IS NORMAL. SAMPLES CONTAIN 10 ZEROS.

			TYPE OF ESTIMATE			TYPE OF ESTIMATE	
			EXP MLE	EV MOM		EXP MLE	EV MOM
X_1	Δ	QUANTITY ESTIMATED			QUANTITY ESTIMATED		
LD75	.1	LD50	-.164 (1.21)	.496 (.026)	LD75	-.134 (.166)	-.187 (.013)
LD75	.5	LD50	-.430 (.444)	.118 (.102)	LD75	-.092 (.372)	-.224 (.053)
LD95	.02	LD75	.059 (1.43)	.740 (.024)	LD95	.000 (.178)	-.216 (.008)
LD95	.1	LD75	-.060 (.236)	.259 (.058)	LD95	.069 (.432)	-.318 (.023)
LD95	.5	LD75	-.204 (.090)	.014 (.074)	LD95	.139 (.503)	-.067 (.088)
LD99	.02	LD95	-.003 (.069)	.092 (.027)	LD99	.104 (.676)	-.288 (.016)
LD99	.1	LD95	-.058 (.074)	-.114 (.042)	LD99	.084 (.359)	-.219 (.075)
LD99	.5	LD95	.037 (.257)	.070 (.119)	LD99	.521 (.818)	.349 (.292)

this case the Exponential estimates do not have the advantage of smaller asymptotic bias and in certain sampling situations it is likely that the MSE of the Extreme Value estimates would always be less than that of the Exponential estimates.

(iv) The bias is a function of the mean and variance of the response function and also X_1, Δ, and the root to be estimated. Thus, by changing X_1 and Δ appropriately the estimates could be made to be unbiased in the probit model without losing their asymptotic properties in the logit model. We will mention this fact again in the next chapter in the section discussing further possible research.

4.6 Comparison of First Zero and Classical Estimates. It is necessary to know not only how the First Zero estimates perform in relation to one another, but also how they perform with respect to the classical analysis estimates. This could be thought of as comparing the sampling procedures, since the Exact MLE is theoretically the classical estimate adjusted for the First Zero sampling technique. To do this we ran three simulations according to reasonably standard procedures as recommended by Finney in his book "Probit Analysis". We sampled at four different percentiles in each simulation and took equal size samples at each of the four doses. However, comparing the two types of estimates does pose some problems. Classical analysis has fixed sample size and a variable number of zeros in each sample. First Zero analysis has a fixed number of zeros and a variable sample size. We decided to compare samples where the number of zeros in the First Zero sample was set equal to the expected number of zeros in the Classical sample, modelling the situation where the cost of a death is a major component of the loss function. Also necessary for comparison purposes is the expected First Zero sample size and this is also provided in the table. Both sampling methods are most effective when the sampling points bracket the point to be estimated. For this reason we restricted our attention to the case of estimating LD95.

and starting at LD99 for the First Zero estimates. The First Zero values are reproduced here again from Table 4.3.2 to facilitate the comparison. We considered only samples containing 20 zeros in the First Zero analysis and samples having a mean of 20 zeros in the classical analysis. We also included the estimates of β in the comparison, making β and LD95 the parameters of interest.

The results are summarized in Table 4.5.1. From the table, several comments may be made. Some of these are:

(i) For a fixed number of zeros and approximately the same sample size, each of the First Zero estimates of both β and LD95 are better than the corresponding Classical estimates. The only exception to this is the Extreme Value estimate of β when $\Delta = .1$.

(ii) Since the Exact ML estimates are essentially the same as the Classical ones, it would seem that that the First Zero procedure might be a more efficient sampling technique for estimating extreme quantiles in logit analysis, at least when the number of zeros is a limiting factor in determining the sampling method.

(iii) It appears that under certain sampling situations, the Extreme Value moment estimates can provide a significant increase in efficiency over the usual Maximum Likelihood methods for even reasonably large samples. By the same token, in many instances the Exponential estimates

TABLE 4.5.1

BIAS AND VARIANCE (IN BRACKETS) OF ESTIMATES OF β AND LD95. FIRST ZERO SAMPLES CONTAIN 20 ZEROS. CLASSICAL ANALYSIS SAMPLES HAVE A MEAN OF 20 ZEROS PER SAMPLE.

FIRST ZERO ESTIMATES

TYPE OF ESTIMATE	X_1	Δ	ESTIMATE OF β	ESTIMATE OF LD95	MEAN # OBS PER SAMPLE
EXACT MLE	LD99	.1	.105 (.088)	.007 (.060)	424.6
EXP MLE	LD99	.1	.061 (.078)	-.031 (.058)	424.6
EV MOM	LD99	.1	.405 (.049)	-.057 (.043)	424.6
EXACT MLE	LD99	.5	.092 (.062)	-.050 (.186)	161.0
EXP MLE	LD99	.5	-.059 (.040)	-.026 (.188)	161.0
EV MOM	LD99	.5	.072 (.034)	.012 (.111)	161.0

CLASSICAL ANALYSIS ESTIMATES

SAMPLING METHOD	ESTIMATE OF β	ESTIMATE OF LD95	# OF OBS PER SAMPLE
400 OBS AT LD92,94,96,98	.119 (.256)	-.053 (.107)	400
50 OBS AT LD81,87,93,99	.147 (.223)	-.031 (.195)	200
10 OBS AT LD20,40,60,80	.127 (.194)	.140 (2.14)	40

are as good or better than Exact or Classical estimates with the added bonus of being easier to calculate. The Extreme Value estimates are by far the most attractive computationally, however.

CHAPTER V

Conclusions

5.1 Cost, Loss, and Risk Considerations. The First Zero sampling technique is desirable for two reasons: sampling is done near the root of interest and the number of zeros in the sample can be controlled. As mentioned previously, by changing the values of X_1 and Δ, the proportion of zeros to observations in the sample and the MSE of the estimates can be varied. This becomes important when the relative costs of taking an observation and having a zero are considered. As an example, let us say that the cost per observation is C_1 and the additional cost of a zero is C_2 (as in the case when a zero corresponds to a death). If the total cost of the experiment was to be C and the number of observations were N_1 and the number of zeros were N_2, then we would want to minimize the MSE (or perhaps some other loss function) subject to

$$N_1C_1 + N_2C_2 \leq C.$$

In practice, it is rare that both N_1 and N_2 would be known before the experiment begins; generally one is fixed and the other is variable. Hence, another possibility is to minimize the MSE subject to the alternate constraint

$$E(N_1)C_1 + E(N_2)C_2 \leq C$$

where $E(X)$ is the expected value of the random variable X.

In First Zero sampling it is then necessary to know the expected number of observations per zero. For the values we have discussed these quantities have been calculated and are presented in Table 5.1.1. For classical sampling, the total number of observations would be set and the expected number of zeros calculated.

Let us illustrate the above by means of a rather extensive example using the latter of the two above constraint conditions. We assume we wish to estimate LD95. Further we assume that C_1=1, C_2=5, and C=300. We cannot do a complete analysis of the optimal sampling strategy for each estimate, but we shall try to give a representative survey of the competing estimates. To calculate the expected cost, we had to fix the number of zeros in the First Zero samples and calculate the expected number of observations, while in the Classical samples the number of observations was fixed and the expected number of zeros calculated. For the sampling method we indicate the starting point and increment size for First Zero sampling and the dose levels and number of replicates at each level for the Classical technique. The results are summarized in Table 5.1.2. The MSE was calculated by generating 1000 samples for each of the estimates. The simulations used different seeds and thus may be considered independent. Again estimates were not penalized in the case of

TABLE 5.1.1

EXPECTED NUMBER OF OBSERVATIONS PER ZERO IN THE LOGIT MODEL

X_1	INCREMENT SIZE .02	.1	.5
LD75	3.84	3.42	2.63
LD95	15.6	10.0	5.12
LD99	47.0	21.2	8.05

TABLE 5.1.2

COMPARISON OF MSE OF VARIOUS ESTIMATES OF LD95 WITH COST RESTRAINTS

TYPE OF ESTIMATE	SAMPLING METHOD	$E(N_1)$	$E(N_2)$	E(COST)	MSE
EXPONENTIAL	LD95, .02	218	14	288	.259
EXPONENTIAL	LD99, .1	233	11	288	.126
EXPONENTIAL	LD99, .5	185	23	300	.159
EXT VALUE	LD95, .02	218	14	288	.076
EXT VALUE	LD99, .1	233	11	288	.092
EXT VALUE	LD99, .5	185	23	300	.099
CLASSICAL	60@LD92,94,96,98	240	12	300	.253
CLASSICAL	50@LD81,87,93,99	200	20	300	.203
CLASSICAL	21@LD20,40,60,80	84	42	294	.905
CLASSICAL	120@LD92,98	240	12	300	.167
CLASSICAL	100@LD82,98	200	20	300	.155
CLASSICAL	42@LD10,90	84	42	294	.380

divergence, since divergent solutions were ignored. This question is important enough to warrant further attention. Both First Zero and Classical techniques will not yield solutions for certain samples. The only general statement that can be made is that the Extreme Value estimates diverge less in all situations in Table 5.1.2 than any of the other estimates. Between the Exponential and Classical estimates it depends on the situation; some Exponential estimates diverge less than some Classical estimates and vice versa. The bottom line perhaps is comparing those cases with the least MSE for each technique. In this case the Exponential both had smaller MSE and diverged less than the Classical estimates.

From the table, several observations may be made:

(i) The Extreme value estimate is clearly the winner in this situation. It is also remarkably unaffected by choice of starting point and increment size. Although the combination giving the smallest MSE was X_1=LD95 and Δ =.02, the major part of the MSE was the bias of the estimate. Thus perhaps one of the other combinations would be preferrable in a larger experiment.

(ii) Although not given in the table, it should be mentioned that the bias of all the estimates except one was quite small. The absolute bias of the Exponential estimates was less than .025, and that of the Classical estimates

less than .1. As mentioned above, the Extreme Value estimate for X_1 =LD95 and Δ =.02 was the worst at -.259, but the other EV estimates had absolute biases less than .05.

(iii) We have included various allocations of observations for the Classical method in patterns roughly similar to those proposed for example by Finney, Wetherill, and Tsutakawa. For this situation, the minimum MSE is achieved by placing two groups of 100 observations at each of LD82 and LD98. Apparently, fewer dose levels with larger numbers of observations per dose seems to be more efficient.

(iv) The Exponential estimate, while not matching the Extreme Value estimate, seems to be better than the Classical estimates. Since both are Maximum Likelihood estimates, this would seem to indicate that First Zero sampling is a more efficient method of placing observations than the Classical one, at least under certain restraint conditions. An obvious modification to Classical sampling would be to vary the number of observations at each dose. This is essentially what is accomplished by Wetherill's UDTR rule and a comparison of the performance of this estimate to First Zero estimates for extreme quantiles would be an interesting topic of further research.

(v) In actual practice, the true value of the sampling doses and spacing will not be known but will be randomly distributed. Their distribution will either be determined

by prior knowledge, or by previous iterations of the root finding process. These random variations introduce another component into the MSE, but the expected MSE is just the expected value of the MSE given these values. It is therefore important that the MSE not change much if the doses or increments are changed. The Extreme Value estimate has this property, and both the Exponential and Extreme Value estimates have relatively stable cost functions, whereas the Classical method does not.

5.2 Sequential Approximation Procedures. Our original aim when we started research in this area was to develop a sequential approximation procedure that improved on the Robbins - Monroe one defined by (1.3.1). In this we were not entirely successful if one requires that the procedure must both (a) have the nth dose contain all the information from the first n-1 observations and (b) use the nth dose as the present estimate of the root in order to be considered a sequential estimation procedure. We do not believe this goal can be achieved without significant loss of efficiency in the estimates. The reason for this is the type of errors that occur at extreme quantiles. For example, sampling near LD95 will result in two types of errors, the one resulting from observing a one which gives an error of .05 with probability .95 and that of observing a zero which gives an error of .95 with probability .05. Thus the error associated with a zero is nineteen times as large as that associated with a one. Any Robbins - Monro type procedure will cause a jump to the right nineteen times as large as the jump to the left when a zero is observed. Hoping to be in the vicinity of the root under these circumstances would require a very small increment size.

However, our methods could be considered "almost" sequential approximation procedures. Anytime after the first zero is observed you will have a continuously updated

estimate of the root. The sampling procedure itself requires sequential sampling. And the choice of X_1 will generally be made in such a way that the sampling will be done in the vicinity of the root. If simplicity is a prime consideration, then the Extreme Value Moment estimates should be given consideration. This procedure only requires recording the sum and sum of squares of the stopping points, and could easily be programmed into a pocket calculator such as the Texas Instruments model 57, 58, or 59. If rigor is required and computing facilities are available then the Exact ML estimates offer full efficiency with perhaps even the added advantage of more efficiency than the classical analysis. In either case the procedure could be programmed to indicate what dose is required at each stage and when the desired accuracy was achieved. The methods are also fairly resistant to incorrect assumptions about the form of the response function which makes them desirable in situations where there are doubts about the model.

5.3 Recommendations. Two cases should be considered here: β known and β unknown. When β is known the best choice would be the Exponential UMVUE since its bias is generally less than the other two. Starting at a fairly central value with a smaller increment size seems to give smaller variance than starting at a more extreme quantile and using a larger increment. If the original starting point is inappropriate X_1 may be changed and the observations used in the Exponential ML estimate in the more general sampling situation.

When β is not known, the choice of estimate depends on more factors. Already mentioned in the previous section is simplicity. Here the Extreme Value estimate wins easily. The choice of Δ is critical since it will govern the number of observations per zero, and the estimate makes no allowance for changing Δ. The original starting point is not a major concern, however, since the starting point is not used in calculating the estimate. X_1 must of course eventually be set to a sufficiently large value to ensure reasonably small bias.

The optimal values of X_1 and Δ will depend on cost considerations and also the unknown parameters θ and β. In practice these parameters will not be known and so X_1 and Δ will have to be changed during the sampling. The general technique would be to sample until a 0 is observed. Based

on the sampling up to that point estimates of the root r and β would be calculated. Using these estimates the optimal values of X_1 and Δ would be found for the next set of observations. Following this procedure would guarantee that X_1 and Δ would converge to their optimal values. What the optimal values would be is an open question which we mention in the next section.

Another consideration is the loss function to be used. If the number of zeros is small to medium and squared error loss is used then again the Extreme Value Moment estimates will likely be the best choice. However, if unbiasedness is important, then one of the other two estimates will be better, especially if the root is fairly central. If the sample is small then a large starting point and large increment size should be used to increase the probability of obtaining a convergent solution. If a large sample is to be used, then a smaller increment should eventually be used in order to concentrate the observations about the root. If β is to be estimated, then either the Exponential MLE (less bias) or the Extreme Value Moment estimate (less MSE under certain conditions) should be used.

Finally, the cost considerations must be taken into account in the choice of X_1 and Δ as outlined in Section 5.1 and these factors are fixed for all the estimates. What determines the choice of estimate will be which one

performs best (whatever the loss function) under the given constraints.

5.4 Further Research. Here we would like to mention briefly some questions that this thesis raises and possible research problems arising from them.

(a) In the case when β is known, it would be useful to know the exact relationship between the MSE and the choice of X_1 and Δ. This would require straightforward but extensive and large scale simulations to obtain either a function or graph of the one as a function of the other two.

(b) As mentioned previously, it would be useful to know the optimal values of X_1 and Δ for estimating the root. Unfortunately these values will be functions of the root to be estimated, the loss function used, the distribution parameters, and the cost restraints. It would be impossible to tabulate such values under all possible combinations of these factors and so a study on the relationships between these factors and the choice of X_1 and Δ would have to be made in order to understand their behavior in the general case.

(c) Along this line it would be useful to distinguish between models while sampling only from the extreme quantiles. To do this a goodness of fit test could be used to determine whether the distribution of the stopping point (for example) was approximately Extreme Value, but what is the limiting First Zero distribution in the probit model? It might be possible to do such a test using many fewer

zeros than are now required if the limiting distributions of the different response functions were known. The advantage here is that the distributions differ the most in the tails and that is precisely where the First Zero method concentrates the observations.

(d) Finally it would be nice to know if the First Zero sampling method is more efficient than classical techniques. Under the requirements that the number of observations/zero be equal to the expected number of observations/zero, is the proposed procedure the best way of selecting a sample from the tails of a response function? Again, this would require a large scale simulation involving running the classical analysis with different sample sizes at each dose and different numbers of doses.

BIBLIOGRAPHY

[1] Bartlett, M. (1946). "A Modified Probit Technique for Small Probabilities", Journal of the Royal Statistical Society Supplement, 8, pp. 113-117.

[2] Berkson, J. (1944). "Application of the Logistic Function to Bioassay", Journal of the American Statistical Association, 39, pp. 357-365.

[3] Berkson, J. (1955). "Maximum Likelihood and Minimum Chi-Squared Estimates of the Logistic Function", Journal of the American Statistical Association, 50, pp. 130-162.

[4] Bliss, C. (1935a). "The Calculation of the Dosage - Mortality Curve", Annals of Applied Biology, 22, pp. 134-167.

[5] Bliss, C. (1935b). "The Comparison of Dosage - Mortality Data", Annals of Applied Biology", 22, 307-333.

[6] Bliss, C. (1938). "The Determination of Dosage - Mortality Curves from Small Numbers", Quarterly Journal of Pharmacology, 11, pp. 192-216.

[7] Blum, J. R. (1954). "Approximation Methods which Converge with Probability One", Annals of Mathematical Statistics, 25, pp. 390-394.

[8] De Jong, R. (1973). "Generalized Analysis of Quantal Dose - Response Curves", Computers and Biomedical Research, 6, pp. 588-595.

[9] Dixon, W. and Mood, A. (1948). "A Method for Obtaining and Analyzing Sensitivity Data", Journal of the American Statistical Association, 43, pp. 109-126.

[10] Finney, D. J. (1964). "Statistical Method in Biological Assay", Second edition, London, Charles Griffin and Co. Ltd.

[11] Finney, D. J. (1971). "Probit Analysis", Third edition, Cambridge University Press.

[12] Johnson, N. and Kotz, S. (1970). "Continuous Univariate Distributions", Houghton Mifflin Co.

[13] Kiefer, J. and Wolfowitz, J. (1952). "Stochastic Estimation of the Maximum of a Regression Function", Annals of Mathematical Statistics, 23, pp. 462-466.

[14] Robbins, H., and Monro, S. (1951). "A Stochastic Approximation Method", Annals of Mathematical Statistics, 22, pp. 400-407.

[15] Tsutakawa, R. (1980). "Selection of Dose Levels for Estimating Percentage Points of Logistic Quantal Response Curve", Applied Statistics, 29, #1, pp. 25-33.

[16] Wetherill, G. B. (1963). "Sequential Estimation of Quantal Responses", Journal of the Royal Statistics

Society, Series B, pp. 1-43.

[17] Wetherill, G. B. (1975). "Sequential Methods in Statistics", Second edition, London, Chapman and Hall Ltd.

'PENDIX

For completeness we include here the program listing of all the APL programs used in the calculations and simulations presented in the thesis. Below is an index to the programs. The programs are listed alphabetically, one per page unless more than one page is required. The index indicates the programs that were used for each table or figure.

Where Used	List of Programs Used
Figures 2.3.1-2.3.9	SINKEXP, GEN
Figures 2.5.1-2.5.9	SINKEV, GEN
Table 4.2.1	THETA, GEN
Table 4.3.1	BETA, GEN, BEXPML
Table 4.3.2	BETA, GEN, BEXPML
Table 4.4.1	NOREV, NORSIM, NORMAL, GENOR
Table 4.5.1	FIN, BETA, GEN, BEXPML
Table 5.1.1	GEN
Table 5.1.2	FIN, EVMOM, EVEX, GEN, BEXPML

```
[0]  X1 BETA DEL;S;SS;T;CNT;XI;I;NTH;NB;TH;B;P;PI;FAC;DEN;
                              A;B;C;D;E;NC;ERR;R;F;G;H;N;WT;DD
[1]  T←⎕AI[2]
[2]  ' '
[3]  'THIS FUNCTION FINDS THE EXACT, EXPONENTIAL, AND EXTR
                              EME'
[4]  'VALUE ESTIMATES FOR BETA, THETA, LD75, LD95, AND LD9
                              9.'
[5]  'SPECIFICATIONS:'
[6]  '   X1     DELTA     SAMPLE SIZE   SIMULATION SIZE
                              SEED'
[7]  6 3 7 2 12 0 15 0 20 0 ⍕X1,DEL,NUMDEATHS,SIMSIZE,⎕RL
[8]  S←SS←E← 6 5 ⍴NC←CNT←0
[9]  P←10000×+\GEN X1,DEL
[10] R←⊛ 1 3 19 99
[11] MAINLOOP:N←1++/(?NUMDEATHS⍴10000)∘.>P
[12] ⍝ CALCULATE THE EXPONENTIAL ESTIMATES
[13] B←BEXPML DD←DEL×N-0.5
[14] TH←X1+(÷B)×⊛NUMDEATHS×(¯1+*B×DEL)÷+/¯1+*B×DD
[15] NC←NC+ERR←(B<0.1)∨B>9.9
[16] →ERR/MAINLOOP
[17] E[1;]←(-1,R)+B,TH+R÷B
[18] ⍝ CALCULATE THE EXACT ESTIMATES
[19] I←0
[20] WT←+/(⍳⌈/N)∘.≤N
[21] XI←X1+DEL×1-⍳⍴WT
[22] LOOP:→(10>I←I+1)/CONTINUE
[23] →(1<NC←NC+1)/MAINLOOP
[24] CONTINUE:PI←1÷1+*-B×XI-TH
[25] A←+/FAC←PI×F←WT×1-PI
[26] H←+/FAC×XI
[27] C←+/FAC×XI×XI
[28] D←+/XI[N]
[29] G←+/XI×F
[30] F←NUMDEATHS-+/F
[31] NC←NC+ERR←0.0001>|DEN←(B×A×C-TH×H)-B×H×H-TH×A
[32] →ERR/MAINLOOP
[33] NTH←TH+(÷DEN)×((H-TH×A)×G-D)+F×C-TH×H
[34] NB←B+(÷DEN)×(F×B×H)+B×A×G-D
[35] NC←NC+ERR←(NB<0.1)∨(NB>10)∨25<|NTH
[36] →ERR/MAINLOOP
[37] →((0.01<|(B←NB)-B)∨0.01<|(TH←NTH)-TH)/LOOP
[38] E[3;]←(-1,R)+B,TH+R÷B
[39] ⍝ CALCULATE THE EXTREME VALUE ESTIMATES
[40] B←((NUMDEATHS×+/DD×DD)-(A←+/DD)*2)÷NUMDEATHS×NUMDEATH
                              S-1
[41] B←(○1)÷(6×B)*0.5
[42] TH←(X1+(0.5×DEL)-A÷NUMDEATHS)+(÷B)×¯0.5772157+⊛¯1+*B×
                              DEL
[43] E[5;]←(-1,R)+B,TH+R÷B
[44] ⍝ CALCULATE THE DIFFERENCES
[45] E[2;]←E[1;]-E[3;]
[46] E[4;]←E[3;]-E[5;]
```

```
[47]  E[6;]←E[5;]-E[1;]
[48]  S←S+E
[49]  SS←SS+E×E
[50]  →(SIMSIZE>CNT←CNT+1)/MAINLOOP
[51]  '                                    BIAS
                                  VARIANCE'
[52]  100ρ'          BETA    THETA     LD75     LD95     LD99
                                                          '
[53]  A← 6 8 ρ'EXPON              EXACT              EX VAL
                                                          '
[54]  A←A, 8 3 ▼S÷N←SIMSIZE
[55]  A,(6 8 ρ' '), 8 3 ▼(SS÷N-1)-(S×S)÷N×N-1
[56]  'CPU TIME ',(▼0.001×⎕AI[2]-T),(10 0 ▼NC),' DIVERGED'
```

```
[0]  B←BEXPML D;K;EBD;SEBD;DBAR;FB;FPB;NEWB;DEBD
[1] ⍝THIS FUNCTION USES A NEWTON-RAPHSON ITERATION
[2] ⍝TO FIND THE ML SOLUTION FOR BETA FROM THE
[3] ⍝EXPONENTIAL APPROXIMATION. SINCE THE VALUE
[4] ⍝OF BETA=0 IS A FALSE SOLUTION, A PRELIMINARY
[5] ⍝SEARCH IS MADE TO FIND A REASONABLE STARTING
[6] ⍝POINT. IF NO SUCH POINT IS FOUND, THE VALUE
[7] ⍝OF BETA≤0.1 OR BETA=10 IS RETURNED.
[8]  K←⍴D
[9]  B←0
[10] AGAIN:B←B+2
[11]  →(B>9.9)/0
[12] LOOP:SEBD←+/EBD←*B×D
[13]  DEBD←+/D×EBD
[14]  DBAR←(+/D)÷K
[15]  FB←(SEBD-K)+(B×DBAR×SEBD-K)-B×DEBD
[16]  →(0<FB)/AGAIN
[17]  FPB←(DBAR×SEBD-K)+(B×DBAR×DEBD)-B×+/EBD×D*2
[18]  NEWB←B-FB÷FPB
[19]  →((B>0.1)∧0.01<|(B←NEWB)-B)/LOOP
```

```
[0]  EVEX;T;X1;DEL;ND;NS;S;SS;CNT;P;I;TH;B;N;B;D;E;ZC;ERR;
                                                R;AV;VAR;SKIP;A
[1]  T←⎕AI[2]
[2]  'THIS FUNCTION COMPARES THE MAXIMUM LIKELIHOOD ESTIMA
                                                TES'
[3]  'FROM THE EXPONENTIAL APPROXIMATION TO THE MOMENT EST
                                                IMATES'
[4]  'FROM THE EXTREME VALUE APPROXIMATION.'
[5]  'ENTER THE STARTING POINT X1:'
[6]  X1←⎕
[7]  'ENTER THE INCREMENT SIZE DELTA:'
[8]  DEL←⎕
[9]  'ENTER THE NUMBER OF DEATHS IN EACH SAMPLE:'
[10] ND←⎕
[11] 'ENTER THE NUMBER OF SAMPLES IN THE SIMULATION:'
[12] NS←⎕
[13] 'ENTER THE RANDOM NUMBER GENERATING SEED:'
[14] ⎕RL←⎕
[15] 'ENTER A 1 IF YOU DO NOT WISH TO SEE INTERMEDIATE RES
                                                ULTS,'
[16] '     A 0 IF YOU DO:'
[17] SKIP←⎕
[18] S←SS←E← 3 5 ⍴ZC←3⍴CNT←0
[19] P←10000×+\GEN X1,DEL
[20] R←⊛ 1 3 19 99
[21] AGAIN:D←DEL×0.5++/(?ND⍴10000)∘.>P
[22] B←BEXPML D
[23] TH←X1+(÷B)×⊛ND×(¯1+⋆B×DEL)÷+/-1-⋆B×D
[24] ZC[1]←ZC[1]+ERR←(B<0.1)∨B>9.9
[25] E[1;]←(1-ERR)×B,TH+R÷B
[26] VAR←0.01⌈((+/D×D)÷ND-1)-((AV←(+/D)÷ND)⋆2)×ND÷ND-1
[27] ZC[2]←ZC[2]+ERR←(B<0.1)∨9.9<B←(○1)÷(6×VAR)⋆0.5
[28] E[2;]←(1-ERR)×B,(X1-AV-DEL÷2)+(÷B)×R+¯0.577216+⊛¯1+⋆B
                                                ×DEL
[29] E[3;]←(0≠E[1;1]×E[2;1])×E[2;]-E[1;]
[30] ZC[3]←ZC[3]+0=E[1;1]×E[2;1]
[31] S←S+E
[32] SS←SS+E×E
[33] →SKIP/JUMP
[34] 6 2 ▼⍉
[35] (3 5 ⍴' '),6 2⍕▼E
[36] JUMP:→(NS>CNT←CNT+1)/AGAIN
[37] (I←1)⍴
[38] A← 3 15 ⍴'EXPONENTIAL ESTEXTREME VAL ESTDIFFERENCE
                                                '
[39] OUTPUT:(5⍴' '),A[I;]
[40] 'QUANTITY ESTIMATED     BETA     THETA      LD75      LD
                                                95      LD99'
[41] (I≠3)/'ACTUAL VALUE       ',9 3 ▼ 1 0 1.099 2.944 4.5
                                                95
[42] 'MEAN OF ESTIMATES ',9 3 ▼S[I;]÷N←NS-ZC[I]
[43] 'VAR OF ESTIMATES  ',9 3 ▼(SS[I;]÷N-1)-(S[I;]⋆2)÷N×N
                                                -1
```

```
[44]  'ALSO THERE WERE ',(⍕ZC[I]),' SAMPLES WHICH GAVE NO S
                                                  OLUTION'
[45]  ' '
[46]  →(3≥I←I+1)/OUTPUT
[47]  'THE CPU TIME REQUIRED WAS ',⍕0.001×⎕AI[2]-T
```

```
[0]  EVMOM;X1;DEL;XN;P;NS;ND;R;S;SS;E;VAR;AV;T;CNT;ZC;B;ER
                                                        R
[1]  'THIS PROGRAM CALCULATES THE ESTIMATES OF BETA, THETA
                                                  , LD75,'
[2]  'LD95, AND LD99 USING THE MOMENT ESTIMATES FROM THE E
                                                  XTREME'
[3]  'VALUE DISTRIBUTION'
[4]  T←⎕AI[2]
[5]  'ENTER THE STARTING POINT X1:'
[6]  X1←⎕
[7]  'ENTER THE INCREMENT SIZE DELTA:'
[8]  DEL←⎕
[9]  'ENTER THE NUMBER OF DEATHS IN EACH SAMPLE:'
[10] ND←⎕
[11] 'ENTER THE NUMBER OF SAMPLES IN THE SIMULATION:'
[12] NS←⎕
[13] 'ENTER THE RANDOM NUMBER GENERATING SEED:'
[14] ⎕RL←⎕
[15] S←SS←E←5⍴ZC←CNT←0
[16] P←10000×+\GEN X1,DEL
[17] R←⊛ 1 3 19 99
[18] AGAIN:XN←X1-DEL×+/(?ND⍴10000)∘.>P
[19] ZC←ZC+ERR←0=VAR←((+/XN×XN)÷ND-1)-((AV←(+/XN)÷ND)*2)×N
                                                  D÷ND-1
[20] →ERR/AGAIN
[21] B←(○1)÷(6×VAR)*0.5
[22] S←S+E←B,AV+(÷B)×R+¯0.577216+⊛¯1+*B×DEL
[23] SS←SS+E×E
[24] →(NS>CNT←CNT+1)/AGAIN
[25] '⍵'
[26] 'QUANTITY ESTIMATED     BETA     THETA      LD75      LD
                                                95      LD99'
[27] 'ACTUAL VALUE       ', 9 3 ⍕1,P
[28] 'MEAN OF ESTIMATES  ', 9 3 ⍕S÷NS
[29] 'VAR OF ESTIMATES   ', 9 3 ⍕(SS÷NS-1)-(S×S)÷NS×NS-1
[30] 'ALSO THERE WERE ',(⍕ZC),' SAMPLES WITH NO SOLUTION.'
[31] 'THE CPU TIME REQUIRED WAS ',⍕0.001×⎕AI[2]-T
```

```
[0]  FIN;P;X;K;N;NS;X2;T;NC;B;TH;NB;NTH;A;C;D;E;DEN;F;FF;X
                                        FF;G;H;ERR;S;SS;CNT;R;I
[1]  'THIS PROGRAM USES FINNEYS METHOD TO ESTIMATE'
[2]  'BETA, THETA, LD75, LD95, AND LD99. A FIXED'
[3]  'NUMBER OF SAMPLES OF THE SAME SIZE ARE TAKEN'
[4]  'AND THE NUMBER OF DEATHS IN EACH SAMPLE ARE'
[5]  'USED TO FIND THE MAX LIK SOLUTIONS.'
[6]  'ENTER THE PERCENTILES AT WHICH SAMPLES ARE TAKEN:'
[7]  P←0.01×(⍳0),⍞
[8]  'ENTER THE SAMPLE SIZE:'
[9]  K←⍞
[10] 'ENTER THE NUMBER OF SAMPLES IN THE SIMULATION:'
[11] NS←⍞
[12] 'ENTER THE RANDOM NUMBER SEED:'
[13] ⎕RL←⍞
[14] X2←X×X←⊕P÷1-P
[15] R←⊕ 1 3 19 99
[16] S←SS←5⍴NC←CNT←⎕IO←0×T←⎕AI[2]
[17] P←⌊+\10000×(P∘.*⍳K)×((1-P)∘.*K-⍳K)×((⍴P),K)⍴(⍳K)!K
[18] ⎕IO←1
[19] MAINLOOP:N←+/((K,⍴X)⍴?(⍴X)⍴10000)>P
[20]  I←B←1+TH←0
[21] AGAIN:A←+/FF←F×1-F←1÷1+*-B×X-TH
[22]  ERR←0.0001>|DEN←K×B×(A×D←+/X×XFF)-(C←+/XFF←X×FF)*2
[23]  NC←NC+ERR←ERR∨10<I←I+1
[24]  →ERR/MAINLOOP
[25]  NTH←TH+(÷DEN)×((G←+/N-K×F)×-D-TH×C)+(H←+/X×N-K×F)×C-T
                                        H×A
[26]  NB←B+(÷DEN)×B×(H×A)-G×C
[27]  NC←NC+ERR←(NB<0.1)∨(NB>10)∨25<|NTH
[28]  →ERR/MAINLOOP
[29]  →((0.01<|(B←NB)-B)∨(0.01<|(TH←NTH)-TH))/AGAIN
[30]  S←S+E←B,TH+R÷B
[31]  SS←SS+E×E
[32]  →(NS>CNT←CNT+1)⍴MAINLOOP
[33]  ' '
[34]  'QUANTITY ESTIMATED      BETA     THETA      LD75      LD
                                        95      LD99'
[35]  'ACTUAL VALUE       ', 9 3 ⍕1,R
[36]  ' '
[37]  'MEAN OF ESTIMATES ', 9 3 ⍕S÷NS
[38]  'VAR OF ESTIMATES  ', 9 3 ⍕(SS÷NS-1)-(S×S)÷NS×NS-1
[39]  ' '
[40]  'THE EXPECTED NUMBER OF DEATHS IS ',⍕K×+/1-÷1+*-X
[41]  'ALSO THERE WERE ',(⍕NC),' SAMPLES WHICH DID NOT CONV
                                        ERGE.'
[42]  ' '
[43]  'THE CPU TIME REQUIRED WAS ',⍕0.001×⎕AI[2]-T
```

```
[0]  R←GEN PAR;X1;DELTA;NUM;PSUM;R;Q;N;P;PI
[1]  ⍝ THIS FUNCTION GENERATES THE PROBABILITIES FOR
[2]  ⍝ THE FIRST ZERO DISTRIBUTION. THETA AND BETA
[3]  ⍝ ARE ASSUMED TO BE 0 AND 1 RESPECTIVELY
[4]  X1←PAR[1]
[5]  DELTA←PAR[2]
[6]  NUM←PAR[⍴PAR]+500×(⍴PAR)<3
[7]  PSUM←R←1-Q←1÷1+*-X1
[8]  N←1
[9]  LOOP:P←Q×PI←1-1÷1+*-X1-DELTA×N
[10] PSUM←PSUM+P
[11] R←R,P
[12] Q←Q×1-PI
[13] N←N+1
[14] →((N<NUM)∧PSUM<0.9999)/LOOP
```

```
[0]  R←GENOR PAR;X1;DELTA;NUM;PSUM;R;Q;N;P;PI
[1] ⍝ THIS FUNCTION GENERATES THE PROBABILITIES FOR
[2] ⍝ THE FIRST ZERO DISTRIBUTION WHEN THE
[3] ⍝ UNDERLYING DISTRIBUTION IS NORMAL(0,1)
[4]  X1←PAR[1]
[5]  DELTA←PAR[2]
[6]  NUM←PAR[⍴PAR]+500×(⍴PAR)<3
[7]  PSUM←R←1-Q←NORMAL X1
[8]  N←1
[9] LOOP:P←Q×PI←1-NORMAL X1-DELTA×N
[10]  PSUM←PSUM+P
[11]  R←R,P
[12]  Q←Q×1-PI
[13]  N←N+1
[14]  →((N<NUM)∧PSUM<0.999)/LOOP
```

```
[0]  X1 NOREV DEL;XN;P;NS;ND;R;S;SS;E;VAR;AV;T;CNT;ZC;B;ER
                                                        R
[1]  ' '
[2]  'THIS PROGRAM CALCULATES THE ESTIMATES OF BETA, THETA
                                                    , LD75,'
[3]  'LD95, AND LD99 USING THE MOMENT ESTIMATES FROM THE E
                                                   XTREME'
[4]  'VALUE DISTRIBUTION WHEN THE ACTUAL DISTRIBUTION IS N
                                                   ORMAL'
[5]  'WITH MEAN 0 AND VARIANCE PI*2/6.'
[6]  T←⎕AI[2]
[7]  'SPECIFICATIONS:'
[8]  '     X1     DELTA    SAMPLE SIZE     SIMULATION SIZE
                                                   SEED'
[9]  7 3 7 2 13 0 17 0 18 0 ▼X1,DEL,NUMDEATHS,SIMSIZE,⎕RL
[10] ND←NUMDEATHS
[11] NS←SIMSIZE
[12] S←SS←E←5⍴ZC←CNT←0
[13] P←1000×+\GENOR(X1,DEL)×(6×0.5)÷○1
[14] R←⊕ 1 3 19 99
[15] AGAIN:XN←X1-DEL×+/(?ND⍴1000)∘.>P
[16] ZC←ZC+ERR←0=VAR←((+/XN×XN)÷ND-1)-((AV←(+/XN)÷ND)*2)×N
                                                   D÷ND-1
[17] →ERR/AGAIN
[18] B←(○1)÷(6×VAR)*0.5
[19] S←S+E←B,AV+(÷B)×R+¯0.577216+⊕¯1+*B×DEL
[20] SS←SS+E×E
[21] →(NS>CNT←CNT+1)/AGAIN
[22] 'QUANTITY ESTIMATED      BETA     THETA      LD75      LD
                                                  95      LD99'
[23] 'ACTUAL VALUE                    ', 9 3 ▼E←0,N75,N95,N99
[24] 'BIAS OF ESTIMATES ', 9 3 ▼(S÷NS)-1,E
[25] 'VAR OF ESTIMATES  ', 9 3 ▼(SS÷NS-1)-(S×S)÷NS×NS-1
[26] (▼ZC),' SAMPLES GAVE NO SOLUTION. CPU TIME ',(▼0.001×
                                                  ⎕AI[2]-T)
[27] ' '
[28] ' '
```

```
[0]  R←NORMAL X;XSQ;P;REM;N;ERR;SIGN;L;H
[1]  ⍝ THIS FUNCTION RETURNS A NORMAL(0,1)
[2]  ⍝ DISTRIBUTION FUNCTION VALUE
[3]  ⍝ THE ACCURACY IS TO 4 DECIMAL PLACES
[4]  L←X>¯4
[5]  H←X<4
[6]  X←X×L×H
[7]  SIGN←X<0
[8]  XSQ←X×X←|X
[9]  P←(*¯0.5×XSQ)×(○2)*¯0.5
[10] ERR←0.0001÷P
[11] R←REM←X
[12] N←1
[13] LOOP:N←N+2
[14] REM←REM×XSQ÷N
[15] R←R+REM
[16] →(∨/REM>ERR)/LOOP
[17] R←SIGN+(1-2×SIGN)×0.5+P×R
[18] R←(R×L)+0.5×~H
```

```
[0]  X1 NORSIM DEL;T;R;K;N;P;NS;D;B;NOSOL;TH;E;SUM;SSQ;ERR
[1]  ' '
[2]  'THIS FUNCTION CALCULATES THE EXPONENTIAL ESTIMATES'
[3]  'WHEN THE ACTUAL UNDERLYING DISTRIBUTION IS NORMAL.'
[4]  T←⎕AI[2]
[5]  R←⊛ 1 3 19 99
[6]  'SPECIFICATIONS:'
[7]  '   X1   DELTA    SAMPLE SIZE    SIMULATION SIZE
                                                SEED'
[8]  6 3 6 2 11 0 18 0 18 0 ▼X1,DEL,NUMDEATHS,SIMSIZE,⎕RL
[9]  K←NUMDEATHS
[10] N←SIMSIZE
[11] P←1000×+\GENOR(X1,DEL)÷(○1)×6*-0.5
[12] SUM←SSQ←5⍴NS←NOSOL←0
[13] MAINLOOP:D←DEL×0.5++/(?K⍴1000)∘.>P
[14] B←BEXPML D
[15] NOSOL←NOSOL+ERR←(B>10)∨B<0.1
[16] →ERR/MAINLOOP
[17] TH←X1+(÷B)×⊛K×(¯1+*B×DEL)÷+/¯1+*B×D
[18] E←B,TH+R÷B
[19] SUM←SUM+E
[20] SSQ←SSQ+E*2
[21] →(N>NS←NS+1)/MAINLOOP
[22] 'QUANTITY ESTIMATED     BETA    THETA      LD75      LD
                                              95      LD99'
[23] 'ACTUAL VALUE                ', 9 3 ▼E←0,N75,N95,N99
[24] 'MEAN BIAS°          ', 9 3 ▼(SUM÷N)-1,E
[25] 'VAR OF ESTIMATES    ', 9 3 ▼(SSQ÷N-1)-(SUM*2)÷N×N-1
[26] (▼NOSOL),' SAMPLES GAVE NO SOLUTION. CPU TIME ',▼0.00
                                              1×⎕AI[2]-T
[27] ' '
[28] ' '
```

```
[0]  X1 SINKEV DELTA;P;D;DROP;ADD;V
[1]  ⍝ GET BASIC PROBABILITIES
[2]   P←+\⍎GEN X1,DELTA
[3]   D←(⊛¯1+⍟DELTA)+⍎X1+DELTA×1-⍳⍴P
[4]  ⍝ TRIM BELOW
[5]   DROP←+/D<¯3
[6]   P←DROP↓P
[7]   D←DROP↓D
[8]  ⍝ TRIM ABOVE
[9]   DROP←+/D>4.5
[10]  D←(-DROP)↓D
[11]  D←¯2↓,D,(0.5×D+1⍎D),[1.5] 1⍎D
[12]  P←(-DROP)↓P
[13]  P←¯2↓,P,P,[1.5] P
[14] ⍝ CALCULATE THE TRUNCATED PROBABILITIES
[15]  Y3←⍟-⍟-D
[16]  Y3←Y3÷¯1↑Y3
[17] ⍝ FILL OUT THE VECTORS TO 4.5
[18]  V←¯3.1+0.2×⍳38
[19]  ADD←+/D[⍴D]≥V
[20]  D←D,ADD↓V
[21]  P←P,ADD↓38⍴1
[22]  Y3←Y3,ADD↓38⍴1
[23] ⍝ PUT INTO DISCRETE FORM IE STEPS
[24]  X←D
[25]  Y1←P
[26]  Y2←⍟-⍟-X
[27]  (⍕⍴X),',  3,'
[28]  ((⍴X),56)⍴(((4×⍴X),13)⍴ 13 4 ⍕X,Y1,Y2,[1.5] Y3),','
```

```
[0]  X1 SINKEXP DEL;DROP
[1]  P←+\GEN X1,DEL
[2]  D←((*-X1)÷¯1+*DEL)×¯1+*DEL×¯1+⍳ρP
[3]  DROP←+/D≥5
[4]  D←((-DROP)↓D),5
[5]  D←¯2↓,D,(0.5×D+1⌽D),[1.5] 1⌽D
[6]  P←(1-DROP)↓P
[7]  P←¯2↓,P,P,[1.5] P
[8]  E←1-*-D
[9]  (⍕ρD),',  2,'
[10] ((ρD),42)ρ(((3×ρD),13)ρ 13 4 ⍕D,E,[1.5] P),','
```

```
[0]  THETA←PAR;X1;DEL;XI;WI;TH;NTH;E;G;GP;ND;NS;CNT;T;P;S;
                                        SS;WEX;N;EX;D;TOT;TO;A;B
[1]  'THIS PROGRAM CALCULATES THE EXACT, EXPONENTIAL, AND
                                        EXTREME VALUE'
[2]  'ESTIMATES OF THETA AND THEIR DIFFERENCE WHEN BETA IS
                                        KNOWN TO BE 1.'
[3]  X1←PAR[1]
[4]  DEL←PAR[2]
[5]  ND←PAR[3]
[6]  NS←SIMSIZE
[7]  'SPECIFICATIONS'
[8]  '        X1        DELTA      DEATHS    SAMPLES     SEED'
[9]  10 3 10 2 10 0 10 0 14 0 ▼X1,DEL,ND,NS,⎕RL
[10] T←⎕AI[2]
[11] P←10000×+\GEN X1,DEL
[12] S←SS←8ρTOT←CNT←0
[13] A←-0.57721567-⍟¯1+⍳DEL
[14] B←(⍟ND)-PSI ND
[15] MAINLOOP:N←1++/(?NDρ10000)∘.>P
[16] →(=/N)/MAINLOOP
[17] E←TH←X1+⍟(ND×¯1+⍳DEL)÷+/¯1+⍳DEL×N-1
[18] WI←+/(ι⌈/N)∘.≤N
[19] WEX←WI×EX←⍳-XI←X1+DEL×1-ιρWI
[20] THLOOP:G←(-ND)++/WEX×D←÷EX+⍳TH
[21] GP←(⍳TH)×+/WEX×D×D
[22] NTH←TH+G÷GP
[23] →(25<|NTH)/MAINLOOP
[24] →(0.01<|(TH←NTH)-TH)/THLOOP
[25] NTH←A+X1+DEL×1-TO←(+/N)÷ND
[26] TOT←TOT+TO
[27] S←S+E←TH,(TH-E),E,B,(E-B),(E-B+NTH),NTH,NTH-TH
[28] SS←SS+E×E
[29] →(NS>CNT←CNT+1)/MAINLOOP
[30] ' '
[31] 'TYPE OF  EXACT                          EXPONENTIAL
                                        EXT VAL'
[32] 'ESTIMATE  MLE                          MLE                UMVUE
                                        MOMENT'
[33] 'BIAS', 9 3 ▼S÷NS
[34] 'VAR ', 9 3 ▼(SS÷NS-1)-(S×S)÷NS×NS-1
[35] 'CPU TIME ',(▼0.001×⎕AI[2]-T),'   OBS/DEATH', 6 2 ▼TO
                                        T÷NS
[36] ⎕←⎕←⎕←' '
```