Two central limit theorems and their application to the estimation of both parameters in the binomial distribution
by Willis John Alberda

A thesis submitted to the Graduate Faculty in partial fulfillment of the requirements for the degree of
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Montana State University
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Abstract:
While investigating experimentally the dynamics of a host-pathogen system, the statistical problem of estimating and finding confidence intervals for the probability of mutation from avirulence to virulence of the pathogen was encountered. Assuming the probability of mutation is constant during any experimental procedure, this problem may be considered as that of estimating the parameter \( p \) in the Binomial Distribution function \( B(z; n,p) \). Because of the nature of the pathogen, however, to obtain this estimator it was also necessary to estimate the total number of observations.

In the binomial setting this is equivalent to also estimating and finding confidence intervals for the parameter \( n \). With this experimental situation as background, two central limit theorems which give a solution to these problems are proved. These theorems are proved under various assumptions which appear feasible in the experimental situation. Other than the sampling without replacement scheme, the techniques are distribution free in so far as no specific underlying distribution function is assumed. These theorems, then, are an approach to estimating and finding confidence intervals for both parameters in the Binomial Distribution.

A solution to the problem of finding the rate of convergence in each case is also given. This solution is obtained using the same assumptions used in establishing the central limit theorems.

The techniques suggested by these two theorems and the rates of convergence for each case are then applied to the experimental data obtained.
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BINOMIAL DISTRIBUTION

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The author, Willis John Alberda, was born in Bozeman, Montana, February 7, 1936, to Mr. and Mrs. Peter W. Alberda of Manhattan, Montana. He received his secondary education at the Manhattan Christian High School, Manhattan, Montana, for two years, and graduated from Western Christian High School, Hull, Iowa. In 1959 he received a Bachelor of Arts degree in education with a mathematics major from Calvin College, Grand Rapids, Michigan. In 1963 he received a Master of Science degree in Mathematics from Montana State College, Bozeman, Montana.
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ABSTRACT

While investigating experimentally the dynamics of a host-pathogen system, the statistical problem of estimating and finding confidence intervals for the probability of mutation from avirulence to virulence of the pathogen was encountered. Assuming the probability of mutation is constant during any experimental procedure, this problem may be considered as that of estimating the parameter $p$ in the Binomial Distribution function $B(z; n, p)$. Because of the nature of the pathogen, however, to obtain this estimator it was also necessary to estimate the total number of observations. In the binomial setting this is equivalent to also estimating and finding confidence intervals for the parameter $n$. With this experimental situation as background, two central limit theorems which give a solution to these problems are proved. These theorems are proved under various assumptions which appear feasible in the experimental situation. Other than the sampling without replacement scheme, the techniques are distribution free in so far as no specific underlying distribution function is assumed. These theorems, then, are an approach to estimating and finding confidence intervals for both parameters in the Binomial Distribution.

A solution to the problem of finding the rate of convergence in each case is also given. This solution is obtained using the same assumptions used in establishing the central limit theorems.

The techniques suggested by these two theorems and the rates of convergence for each case are then applied to the experimental data obtained.
CHAPTER I
INTRODUCTION

Experimental Setting

The statistical problems considered in this dissertation arose in an experimental investigation of the dynamics of a biological host-pathogen system. The solutions to these problems, not necessarily the only possible solutions, were obtained under conditions which appeared most feasible in this experimental situation.

In this experimental investigation, the barley mildew fungus was treated with a mutagenic agent, inoculated on eight resistant varieties of barley, and then screened for mutants. One of the main objectives of this experimental investigation was the estimation of the probability of mutation from avirulence to virulence at eight loci of this fungus.

The principal statistical problem arising from this work was that of finding an estimator and confidence intervals for the probability of mutation at each locus. The difficulties in finding this estimator and confidence intervals, however, arise from the fact that under ordinary conditions the fungus does not grow on the resistant varieties of barley. Moreover, when a pustule appears on a resistant variety it is considered a mutant. The estimator of the probability of mutation at each locus of this fungus, quite naturally, will be a ratio of the total number of mutants observed on some specific resistant variety of barley to the total number of spores germinated on this variety of barley. Therefore, since it is impossible to count the total number of spores germinated on a set of resistant varieties, it is necessary to estimate this total number of
spores germinated for each resistant variety. The statistical problems are then to find estimators and confidence intervals for the probability of mutation at each locus and for the total number of spores germinated on each resistant variety of barley.

The experimental procedure for estimating the total number of spores germinated on a set of resistant varieties may be described as follows. Whenever a set of pots of resistant varieties of barley was inoculated with mildew spores, a set of pots of seedlings of a susceptible variety was also inoculated. Let $X_i$ represent the total number of spores germinated on leaf $i$ of a resistant variety of barley. $X_1, X_2, \ldots, X_N$ is then the population of the number of spores germinated on $N$ leaves of the resistant variety of barley, where $N$ is a known positive integer. The spores germinated on each resistant variety of barley could be represented in this way. As soon as pustules on the susceptible variety were visible, a count of the number of pustules on $n$ leaves was made. Let $x_i$ represent the number of pustules counted on leaf $i$ of the susceptible variety. The sample $x_1, x_2, \ldots, x_n$ is the number of pustules which appeared and were counted on $n$ leaves of the susceptible variety of barley, where $n$ is also known and $n < N$. The numbers $x_1, x_2, \ldots, x_n$ will be considered a random sample of size $n < N$ taken without replacement from a population identical to the finite population $X_1, X_2, \ldots, X_N$ of size $N$. If $\bar{x}$ is the average number of pustules per leaf on the susceptible leaves, then $N \bar{x}$ was used as an estimate of the total number of spores germinated on the resistant variety of barley or the total number of observations.
This procedure could be repeated indefinitely, say up to q stages, so that if \( \hat{N}_k \) represents the estimate of the total number of observations at the k-th stage, then

\[
\hat{S}_q = \sum_{k=1}^{q} \hat{N}_k \hat{x}_k
\]

provided an estimate of the total number of observations over q stages.

If \( z_q \) represents the total number of mutant pustules observed over q stages, then

\[
\hat{p}_q = \frac{z_q}{\hat{S}_q}
\]

provided an estimate of the probability of mutation.

The theoretical problem consists of finding confidence intervals for the total number of observations, \( S_q \), and the probability of mutation, \( p \).

Having considered the experimental situation in this setting, however, before proceeding to the discussion of the theoretical problems it is appropriate at this point to mention several results from sampling without replacement theory as found in Wilks (1962). These results and relations will serve to motivate certain concepts and symbols used in the discussion of the theoretical problems.

**Preliminary Results From Sampling Theory**

For \( k = 1, 2, 3, \ldots \), where \( k \) designates the k-th stage in this experimental procedure, let \( X_{k1}, X_{k2}, \ldots, X_{KN_k} \) be a finite population of size \( N_k \) with mean \( \mu_k \) and variance \( \sigma_k^2 \), where
\[ \mu_k = \frac{1}{N_k} \sum_{i=1}^{N_k} x_{ki}, \]

and

\[ \sigma_k^2 = \frac{1}{N_k-1} \sum_{i=1}^{N_k} (x_{ki} - \bar{x}_k)^2. \]

Let \( x_{k1}, x_{k2}, \ldots, x_{kn_k} \) be a sample of size \( n_k \) taken without replacement from this population with mean \( \bar{x}_k \) and variance \( \sigma_k^2 \), where

\[ \bar{x}_k = \frac{1}{n_k} \sum_{i=1}^{n_k} x_{ki}, \]

and

\[ \sigma_k^2 = \frac{1}{n_k-1} \sum_{i=1}^{n_k} (x_{ki} - \bar{x}_k)^2. \]

With these definitions, it is shown in the reference of Wilks cited above that

\[ E(\bar{x}_k) = \mu_k, \]

\[ \text{Var}(\bar{x}_k) = \left( \frac{1}{n_k} - \frac{1}{N_k} \right) \sigma_k^2, \]

and

\[ E(\sigma_k^2) = \sigma_k^2. \]

From these results it follows immediately that

\[ E(\bar{x}_k) = \mu_k, \]

\[ \text{Var}(\bar{x}_k) = \left( \frac{1}{n_k} - \frac{1}{N_k} \right) \sigma_k^2, \]

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From these results it follows immediately that

\[ E(\bar{x}_k) = \mu_k, \]

\[ \text{Var}(\bar{x}_k) = \left( \frac{1}{n_k} - \frac{1}{N_k} \right) \sigma_k^2, \]

and

\[ E(\sigma_k^2) = \sigma_k^2. \]
and \[ \text{Var} \left( \frac{N_k \overline{x}_k}{\hat{N}_k} \right) = N_k^2 \left( \frac{1}{N_k} - \frac{1}{\hat{N}_k} \right) \sigma_k^2. \]

Also it is obvious that \( E(\hat{S}_q) = S_q \), where
\[
\hat{S}_q = \sum_{k=1}^{q} N_k \overline{x}_k.
\]

and
\[
S_q = \sum_{k=1}^{q} N_k \overline{x}_k.
\]

and that \( E(\hat{s}_q^2) = s_q^2 \), where
\[
\hat{s}_q^2 = \sum_{k=1}^{q} N_k^2 \left( \frac{1}{N_k} - \frac{1}{\hat{N}_k} \right) \sigma_k^2,
\]

and
\[
s_q^2 = \sum_{k=1}^{q} N_k^2 \left( \frac{1}{N_k} - \frac{1}{\hat{N}_k} \right) \sigma_k^2.
\]

Furthermore, if the assumption of independence between stages is imposed, then the following theorem of some importance in the sequel is also true.

Theorem 1.1: If \( s_q^2, \hat{S}_q, \text{ and } S_q \) are defined as before and the \( N_k \overline{x}_k \) form a sequence of independent random variables, then
\[
\text{Var}(\hat{S}_q) = E(\hat{S}_q - S_q)^2 = s_q^2.
\]

Proof: Since \( E(\hat{S}_q) = S_q \),
\[
\text{Var}(\hat{S}_q) = E(\hat{S}_q - S_q)^2.
\]
\[
E(S_q^2 - s_q^2)^2 = E \left[ \sum_{k=1}^{q} \frac{N_k \mu_k^2 - \mu_k^2}{N_k} \right]^2,
\]

\[
= \sum_{k=1}^{q} \frac{N_k \sigma_k^2}{N_k}, \text{ by the assumption of independence,}
\]

\[
= \sum_{k=1}^{q} \frac{1}{N_k} \left( \frac{1}{n_k} - \frac{1}{N_k} \right) \sigma_k^2,
\]

\[
= \frac{s_q^2}{q}.
\]

With these preliminary results, the problems as stated in the first section can now be described more precisely in mathematical terms.

Theoretical Setting

In order to find confidence intervals for the total number of observations, \( S_q \), and for the probability of mutation, \( \pi \), it is necessary to determine the distribution functions of the random variables used to estimate these parameters. In many cases, as for example in this situation, the exact distribution functions may be difficult to determine and not amenable to tabulation. When these situations arise, a solution can be obtained by determining a limiting distribution which is amenable to tabulation. Approximate confidence intervals can then be constructed from this limiting distribution. This is the approach used to obtain a solution to the problems presented here.

Under fairly general assumptions it can be shown that the limiting
distribution of the random variable

\[ \frac{\hat{S}_q - S_q}{\hat{S}_q} \]

is Normal with mean zero and variance one. Since in many cases it is possible to substitute the estimator of the variance and still obtain the same limiting distribution, the problem of finding confidence intervals for \( S_q \), the total number of observations, appears quite logically to be that of determining the limiting distribution of the random variable

\[ \frac{\hat{S}_q - S_q}{\hat{S}_q} \]

Since \( s_q \) is assumed unknown, some estimator must be substituted. The choice of \( \hat{s}_q \) seems natural from the unbiasedness of \( \hat{s}_q^2 \) and will indeed plan an important role in the solution of the problem.

Furthermore, under fairly general assumptions the limiting distribution of the random variable

\[ \frac{z_q - S_q}{\sqrt{S_q \pi(1-\pi)}} \]

is Normal with mean zero and variance one. Since \( \hat{S}_q \) is an unbiased estimator of \( S_q \), the natural extension in this case is, if possible, to determine the limiting distribution of the random variable

\[ \frac{z_q - \hat{S}_q}{\sqrt{\hat{S}_q \pi(1-\pi)}} \]
From this it is possible to construct approximate confidence intervals for \( \pi \), the probability of mutation.

Once the limiting distribution of these two random variables have been established and are amenable to tabulation, it is possible for a fixed \( q \) to construct approximate confidence intervals for \( S_q \), the total number of observations, and \( \pi \), the probability of mutation, respectively. The final problem then is to find a rate of convergence to the limiting distribution in each case.

Before proceeding to the solution of these problems it is necessary to make some assumptions under which it is possible to solve the problems stated above and to exhibit the existence of a probability space on which the random variables with these imposed conditions are defined. The existence of this probability space is necessary in order to give meaning to phrases or symbols such as almost sure convergence (\( ^{\text{a.s.}} \)) of sequences of random variables, convergence in probability (\( ^{P} \)) of sequences of random variables, convergence in distribution (\( ^{L} (X) \rightarrow ^{L} (X) \)), and events \( \left( \left[ X_n \leq x \right] \right) \) as they appear in the sequel. (The symbol \( X_n \leq x \) means the set of \( \omega \) such that the random variable satisfies the condition stated, as for example, \( X_n(\omega') \leq x \).)

Basic Assumptions and an Existence Theorem

The problems as described in the previous section are solved under the following assumptions.

1. For \( q = 1, 2, 3, \ldots \), the population \( (X_{q1}, X_{q2}, \ldots, X_{qN_q}) \) is a finite population of distinct, positive integers with mean \( \mu_q \) and
variance $\sigma_q^2$, both unknown. The distinctness implies that for $q = 1, 2, 3, \ldots$, $\sigma_q^2 \geq d_1 > 0$ and also the sample variance $\hat{\sigma}_q^2 \geq d_2 > 0$.

2. For $q = 1, 2, 3, \ldots$, and $i = 1, 2, \ldots, N_q$, $0 < m \leq x_{qi} \leq M < \infty$, with $M - m > 0$.

3. The $N_q$ and $n_q$ are known, positive, integers such that for $q = 1, 2, 3, \ldots$, $2 < N_q \leq N < \infty$ and $2 \leq n_q \leq N_q - 1$.

4. $N_q x_q$, $q = 1, 2, 3, \ldots$, is a sequence of independent not necessarily identically distributed random variables.

5. For $q = 1, 2, 3, \ldots$, $z_{N_q} = \sum_{k=1}^{S_{N_q}} y_k$, the total number of mutants at stage $q$, and $N_q x_q$, the estimator of the total number of observations at stage $q$, are independent random variables. $S_{N_q}$ as defined before is the total number of observations at stage $q$. The random variables $y_k$ defined by

$$y_k = \begin{cases} 1 \text{ if mutation occurs,} \\ 0 \text{ otherwise,} \end{cases}$$

with $P[y_k = 1] = \pi$, for all $k$, are independent.

The following remarks and theorem exhibit the existence of a probability space on which the random variables satisfying these assumptions are defined.

For each $q$, the probability function of $N_q x_q$ and the range, $I_{1q}$, of this random variable are determined by the sampling without replacement scheme. For $q = 1, 2, 3, \ldots$, set
\[ P\left[N_q X_q = i_{1q}\right] = p_{1q}(i_{1q}), \]

where \( i_{1q} \) is some element of \( I_{1q} \), some finite set of real numbers.

As stated, \( p_{1q}(i_{1q}) \) for all \( i_{1q} \in I_{1q} \) is determined by the sampling without replacement probability function, but for use in the sequel need not be calculated. Similarly, for each \( q \), by the definition of the \( z_{Nq} \) and the \( y_k \) in assumption 5, the probability function of \( z_{Nq} \) is given by

\[ P\left[z_{Nq} = i_{2q}\right] = \binom{S_{Nq}}{i_{2q}} \cdot \frac{S_{Nq} - i_{2q}}{i_{2q}!(1-\pi)} = p_{2q}(i_{2q}), \]

where \( i_{2q} \) is an element of \( I_{2q} \), the range space of \( z_{Nq} \), which is some finite set of integers 0, 1, 2, ..., \( S_{Nq} \).

If \( X_q = (N_q, z_{Nq}) \), then the range space of the vector random variable \( X_q \) is some product space \( I_q = I_{1q} \times I_{2q} \), and by assumption 5, the probability function of the vector random variable \( X_q \) is

\[ P\left[X_q = i_q\right] = p_{1q}(i_{1q}) p_{2q}(i_{2q}) = p_q(i_q), \]

where \( i_q = (i_{1q}, i_{2q}) \) is an element of \( I_q \). With these remarks it is now possible to prove the following.

Theorem 1.2: (Existence Theorem) There exists a probability space \((\Omega, \mathcal{F}, P)\) with the sequence of independent vector random variables \( X_q \) defined on it and such that for each \( q \) the two elements of \( X_q \) are also independent.

Proof: In order to prove this theorem, it is sufficient to characterize
the space \( \mathcal{L} \), determine the \( \sigma \)-field \( \mathcal{G} \), and define a set function \( P \) on the \( \sigma \)-field \( \mathcal{G} \). Toward this end then, let \( \mathcal{L} \) be the set of all sequences of the form \((i_1, i_2, i_3, \ldots)\) where \( i_k \in I_k \). Define a cylinder \( C(i_1, i_2, \ldots, i_N) \) for some fixed \( N \) to be the set of all sequences in \( \mathcal{L} \) such that the fixed elements \( i_1, i_2, \ldots, i_N \) appear in the first \( N \) places. Varying \( N \) over all positive integers and \( i_k \) over all elements of \( I_k \), yields a class \( \mathcal{G} \) of all such cylinders \( C(i_1, i_2, \ldots, i_N) \). Then \( \mathcal{G} \) is taken to be the minimal \( \sigma \)-field over the class \( \mathcal{G} \). Now define the set function \( P \) on the class \( \mathcal{G} \) as follows. For each \( C(i_1, i_2, \ldots, i_N) \) assign the probability

\[
P_C(i_1, i_2, \ldots, i_N) = \prod_{t=1}^{N} p_t(i_t).
\]

The probabilities defined in this way are consistent. Hence, by various theorems, for example Theorem A, Pg. 137 Loève (1960), the set function on the class \( \mathcal{G} \) may be extended to a probability measure on \( \mathcal{G} \). Hence, it is possible to construct a probability space \((\mathcal{L}, \mathcal{G}, P)\). To define the random variables \( X_q \) on this probability space proceed as follows. If \( \omega \) is the sequence \((i_q)\), then set \( X_q(\omega) = i_q \) for \( q = 1, 2, 3, \ldots \). In this manner the vector random variables \( X_q \) are defined on this probability space and the assignment of the set function \( P \) makes them independent.

The assignment of \( p_q \) makes the elements of the vector independent. These assignments determine all distribution functions on this space and the theorem is proved.

From this theorem then, since \( z_q \) and \( S_q \) are sums of independent
random variables defined on this space, they too are defined on this probability space. Their joint distribution function is determined by the sampling without replacement scheme and the binomial distribution of the $y_k$.

In the sequel all events $[X_n \leq x]$ will be elements of the $\sigma$-field $\mathscr{A}$ and a.s. convergence and convergence in probability of sequences of random variables will be convergence with respect to this probability space.

Boundedness and divergence of sequences of random variables, though not designated as such in various places in the context, is a.s. boundedness and a.s. divergence with respect to this probability space. In these cases, however, the sets of unboundedness and of convergence are empty sets.

With this introduction and these preliminary theorems it is possible to proceed with the solution of the problems presented in the previous section.
CHAPTER II

THE LIMITING DISTRIBUTION OF $(\hat{S}_q - S_q)/\hat{s}_q$.

Using the assumptions made in the Introduction and the notation found there, the procedure used in finding the limiting distribution of the random variable $(\hat{S}_q - S_q)/\hat{s}_q$ is the following: first establish that

$$L \left( \frac{\hat{S}_q - S_q}{\hat{s}_q} \right) \rightarrow N(0,1),$$

second show that

$$P \left[ \frac{\hat{S}_q - S_q}{\hat{s}_q} - \frac{\hat{S}_q - S_q}{\hat{s}_q} \right] \rightarrow 0.$$ 

These two results are then sufficient to prove that

$$L \left( \frac{\hat{S}_q - S_q}{\hat{s}_q} \right) \rightarrow N(0,1),$$

from which approximate confidence intervals for $S_q$ can be constructed.

The first statement is shown by the following:

Theorem 2.1: If

$$Y_{qk} = \frac{\bar{x}_kk - S_q}{s_q},$$

then

$$\sum_{k=1}^{q} Y_{qk} = \frac{\hat{S}_q - S_q}{\hat{s}_q}.$$
and 
\[ L \left( \frac{S_k - S_q}{s_q} \right) \rightarrow N(0,1). \]

Proof: Obviously
\[
\sum_{k=1}^{q} Y_{qk} = \frac{\hat{S} - S_q}{s_q}
\]
by the definition of the \( Y_{qk} \). To prove this theorem it is possible to use the "Bounded Case" Theorem, Pg. 277 Loève (1960). It is then necessary to verify that

(i) \( |Y_{qk}| \) is uniformly bounded for all \( k \),

(ii) \( s_q \rightarrow \infty \) as \( q \rightarrow \infty \).

By the assumption of independence of the \( N_k \hat{X}_k \), the \( Y_{qk} \) are also independent random variables, and since \( E(\hat{X}_k) = \mu_k \) the \( Y_{qk} \) are centered at expectations so that the other conditions necessary to employ the "Bounded Case" Theorem are satisfied.

(i) Since \( s_q^2 > 0 \) and \( s_q^2 = N_k \mu_k \), \( |Y_{qk}| \) is bounded for all \( k \) if \( |N_k \hat{X}_k - N_k \mu_k| \) is bounded for all \( k \). But

\[
N_k |\hat{X}_k - \mu_k| \leq N_k (M-m) \text{ by assumption 2,}
\]

\[
\leq N(M-m) \text{ by assumption 3,}
\]
hence, \( |Y_{qk}| \) is uniformly bounded for all \( k \).
and since by assumption 1 \( \sigma_k^2 \geq d_1 > 0 \) for all \( k \) and by assumption 3 
\[ 2 \leq n_k < N_k < N, \]

\[ \frac{1}{N_k} \left( \frac{1}{n_k} - \frac{1}{N_k} \right) \sigma_k^2 \geq 0 \]

as \( k \to \infty \). Hence,

\[ \sum_{k=1}^{q} \frac{1}{N_k} \left( \frac{1}{n_k} - \frac{1}{N_k} \right) \sigma_k^2 \to \infty \]

as \( q \to \infty \) and therefore \( s_q \to \infty \) as \( q \to \infty \) and the theorem is proved.

The following relations are necessary to prove the next theorem and are also required in later theorems; hence, are given here as a lemma.

Lemma 2.1: If (i) \( s_q^2, s_q^2, \sigma_q^2, \sigma_k^2 \) are defined as before,

(ii) \( \sigma_k^2 \geq d_1 > 0 \) and \( \sigma_k^2 \geq d_2 > 0 \) (assumption 1),

(iii) \( 2 \leq n_k \leq N_k - 1 \) (assumption 3),

then

(1) \( 0 < d_1 \leq \sigma_k^2 \leq 2(M-m)^2 \) for all \( k \),

(2) \( 0 < d_2 \leq \sigma_k^2 \leq 2(M-m)^2 \) for all \( k \),
(3) \( 0 < q d_1 \leq \sigma^2_k \leq 2qN^2(M-m)^2, \)

(4) \( 0 < q d_2 \leq \sigma^2_k \leq 2qN^2(M-m)^2. \)

Proof: (1) By (ii) \( \sigma^2_k \geq d_1 > 0 \) and

\[
\sigma^2_k = \frac{1}{N_k - 1} \sum_{i=1}^{N_k} (x_{ki} - \mu_k)^2 \leq \frac{1}{N_k - 1} \sum_{i=1}^{N_k} (M-m)^2 \text{ by assumption 2,}
\]

\[= \frac{N_k}{N_k - 1} (M-m)^2, \]

\[\leq 2(M-m)^2, \]

since by assumption 3, \( 2 < N_k. \)

(2) By (ii) \( \sigma^2_k \geq d_2 > 0 \) and by the same reasoning as in (1),

\[
\sigma^2_k = \frac{1}{n_k - 1} \sum_{i=1}^{n_k} (x_{ki} - \bar{x}_k)^2 \leq \frac{n_k}{n_k - 1} (M-m)^2 \leq 2(M-m)^2,
\]

since by assumption 3 also, \( 2 \leq n_k. \)

(3) \( s^2_q = \sum_{k=1}^{q} N_k \left(\frac{1}{n_k} - \frac{1}{N_k}\right) \sigma^2_k \geq d_1 \sum_{k=1}^{q} N_k \left(\frac{1}{n_k} - \frac{1}{N_k}\right) \text{ by (1),}
\]

\[\geq q d_1, \text{ since by (iii) and assumption 3 } N_k \left(\frac{1}{n_k} - \frac{1}{N_k}\right) \geq 1. \]
Also

\[ s^2_q \leq \sum_{k=1}^{q} 2N_k^2 \left( \frac{1}{n_k} - \frac{1}{N_k} \right) (M-m) \text{ by (2)}, \]

\[ \leq 2 qN^2 (M-m)^2 \text{ since by (iii) and assumption 3} \]

\[ N_k^2 \left( \frac{1}{n_k} - \frac{1}{N_k} \right) \leq N^2. \]

(4) Replacing \( \sigma^2_k \) by \( \sigma^2_k \) and \( d_1 \) by \( d_2 \) in the proof of (3), it follows immediately that

\[ qd_2 \leq s^2_q \leq 2qN^2 (M-m)^2, \]

and the lemma is proved.

These relations are useful in the next theorem which in turn gives the key to establishing the second statement in the introduction of this chapter.

Theorem 2.2: \textit{If} \( s^2_q \text{ and } \hat{s}^2_q \text{ are defined as before, then}

\[ \frac{s^2_q - \hat{s}^2_q}{q} \text{ a.s. } 0. \]

Proof: Using Kolmogorov's Convergence Criterion, Loève (1960); Pg. 238, on the random variables

\[ Y_k = N_k^2 \left( \frac{1}{n_k} - \frac{1}{N_k} \right) (\sigma^2_k - \sigma^2_k), \]

it must be shown that

(i) \( E(Y_k) = 0 \) which then also proves that the \( Y_k \) are integrable,

(ii) \( \text{the } Y_k \text{ are independent}, \)

(iii) \( \sum_{k=1}^{\infty} \frac{\text{Var}(Y_k)}{k^2} < \infty. \)
(i) \( \mathbb{E}(Y_k) = 0 \) since \( \mathbb{E}(\frac{\sigma_k^2}{k}) = \sigma_k^2 \).

(ii) The \( Y_k \) are independent by assumption 4.

(iii) \[
\sum_{k=1}^{\infty} \frac{\text{Var}(X_k)}{k^2} = \sum_{k=1}^{\infty} \frac{\mathbb{E}(Y_k^2)}{k^2} = \sum_{k=1}^{\infty} \frac{N_k \left( \frac{1}{n_k} - \frac{1}{N_k} \right)^2}{k^2} \mathbb{E}(\sigma_k^2 - \sigma_k^2)^2
\]

\[
= \sum_{k=1}^{\infty} \frac{N_k \left( \frac{1}{n_k} - \frac{1}{N_k} \right)^2}{k^2} \left( \mathbb{E} \sigma_k^4 - \sigma_k^4 \right),
\]

\[
< \sum_{k=1}^{\infty} \frac{N_k (M-m) \left( \frac{1}{n_k} - \frac{1}{N_k} \right)^2}{k^2} \mathbb{E} \sigma_k^4,
\]

\[
\leq \frac{4N_k (M-m)^2}{k^2} \sum_{k=1}^{\infty} \frac{1}{q} < \infty,
\]

since \( \sum_{k=1}^{\infty} \frac{1}{q} < \infty \) and \( N \) and \( M-m \) are finite. This proves the theorem.

This result gives the key to proving the following

Theorem 2.3: If \( \hat{S}_q, \overline{S}_q, \hat{s}_q \) and \( \overline{s}_q \) are defined as before, then

\[
\frac{\hat{S}_q - \overline{S}_q}{\overline{s}_q} - \frac{\hat{s}_q - \overline{s}_q}{\overline{s}_q} \xrightarrow{P} 0.
\]
Proof:

By Markov's Inequality

$$P \left[ \frac{1}{s_q} \left| \hat{s}^2 - s_q \right| \geq \frac{1}{s_q} \left| \hat{s}^2 - s_q \right| \geq \varepsilon \right] \leq \frac{1}{s_q} \left| \hat{s}^2 - s_q \right| \geq \frac{1}{s_q} \left| \hat{s}^2 - s_q \right| / \varepsilon.$$ 

for all \( \varepsilon > 0 \) and by Schwarz's Inequality

$$\frac{1}{s_q} \left| \hat{s}^2 - s_q \right| \leq \sqrt{E \left( \frac{1}{s_q} \left| \hat{s}^2 - s_q \right|^2 \right) \cdot E \left( \frac{1}{s_q} \left| \hat{s}^2 - s_q \right|^2 \right)}$$

But \( E \left( \frac{1}{s_q} \left| \hat{s}^2 - s_q \right|^2 \right) = \frac{s^2}{s_q} \) by Theorem 1.1 and

$$E \left( \frac{1}{s_q} \left| \hat{s}^2 - s_q \right|^2 \right) = E \left( \frac{1}{s_q} \left| \hat{s}^2 - s_q \right|^2 \right) = \frac{1}{s_q} \left| \hat{s}^2 - s_q \right|^2.$$ 

Moreover,

$$E \left( \frac{1}{s_q} \left| \hat{s}^2 - s_q \right|^2 \right) = E \left[ \left| \hat{s}^2 - s_q \right|^2 \right],$$

$$= \frac{1}{s_q^2} \left| \hat{s}^2 - s_q \right|^2,$$

$$\leq \frac{1}{s_q^2} \left| \hat{s}^2 - s_q \right|^2 \leq \frac{1}{s_q^2} \left| \hat{s}^2 - s_q \right|^2 \leq \frac{1}{s_q} \left| \hat{s}^2 - s_q \right|^2 \leq \frac{1}{s_q} \left| \hat{s}^2 - s_q \right|^2 \leq \frac{1}{s_q} \left| \hat{s}^2 - s_q \right|^2 \text{ by Lemma 2.1.}$$
Thus
\[ E\left(\hat{s}_q^2 - s_q^2\right)^2 \leq E\left(\frac{1}{s_q} - \frac{1}{\hat{s}_q}\right)^2 \leq \frac{1}{q^2} E\left|\hat{s}_q^2 - s_q^2\right| \] .

But \( |\hat{s}_q^2 - s_q^2| < \frac{s_q^2 + s_q^2}{q} < 4N^2q(M-m)^2 \) by Lemma 2.1 so that
\[ \frac{s_q^2 - s_q^2}{q} < 4N^2(M-m)^2 < \infty . \]

Hence, the random variables \( \frac{s_q^2 - s_q^2}{q} \) are integrable. Also by Theorem 2.2 this sequence of random variables converges almost surely to 0, hence, the sequence converges in probability to 0 and by the Dominated Convergence Theorem, Loève (1960); Pg. 152,
\[ E\left[\frac{s_q^2 - s_q^2}{q}\right] \to 0 \]
as \( q \to \infty \) and the theorem is proved.

In order to prove the final theorem of this chapter, it is necessary at this point to employ a theorem of Loève (1960); Pg. 168.

The following theorem stated in an equivalent manner as that in Loève is given without proof for the general case.

**Theorem 2.4:** If
\[ (i) \quad L(x_n) \to L(y), \]
\[ (ii) \quad x_n - y_n \overset{P}{\to} 0, \]
then
\[ L(x_n) \to L(y). \]
Note: If \( X_n - Y_n \overset{a.s.}{\to} 0 \), the theorem also holds.

The Central Limit Theorem of interest in this chapter then follows immediately as shown by

Theorem 2.5: If \( S_q, \hat{S}_q \) and \( \hat{S}_q \) are defined as before, then

\[
\mathcal{L} \left( \frac{\hat{S}_q - S_q}{\hat{S}_q} \right) \to N(0,1).
\]

Proof: By Theorem 2.1

\[
\mathcal{L} \left( \frac{\hat{A}_q - S_q}{\hat{S}_q} \right) \to N(0,1),
\]

and by Theorem 2.3

\[
\frac{\hat{S}_q - S_q}{\hat{S}_q} \to S_q - S_q \overset{P}{\to} 0,
\]

thus by applying Theorem 2.4 the result follows.

From this theorem then it follows that

\[
\lim_{q} P \left[ \frac{\hat{S}_q - S_q}{\hat{S}_q} \leq z \right] = \frac{1}{\sqrt{2\pi}} \int_{-z}^{z} e^{-t^2/2} \, dt \text{ for } z > 0
\]

so that for \( q \) "sufficiently" large an approximate confidence interval for \( S_q \) is given by

\[
P \left[ \hat{S}_q - z \sqrt{\hat{S}_q} \leq S_q \leq \hat{S}_q + z \sqrt{\hat{S}_q} \right] \approx 1 - \alpha.
\]
CHAPTER III

THE LIMITING DISTRIBUTION OF \( \frac{z_q - \hat{S}_q \pi}{\sqrt{\hat{S}_q \pi(1-\pi)}} \).

The Central Limit Theorem

In establishing the limiting distribution of \( \frac{(z_q - \hat{S}_q \pi)}{\sqrt{\hat{S}_q \pi(1-\pi)}} \), it is necessary to employ methods differing from those in Chapter II. After having shown that

\[
L \left( \frac{z_q - S_q \pi}{\sqrt{S_q \pi(1-\pi)}} \right) \to N(0,1),
\]

attempts to show that

\[
\frac{z_q - S_q \pi}{\sqrt{S_q \pi(1-\pi)}} - \frac{z_q - \hat{S}_q \pi}{\sqrt{\hat{S}_q \pi(1-\pi)}} \to 0.
\]

The theorem, however, is proved by showing that for all \( z \in R \), \( R \) the set of real numbers,

\[
\left| P \left[ \frac{z_q - S_q \pi}{\sqrt{S_q \pi(1-\pi)}} < z \right] - P \left[ \frac{z_q - \hat{S}_q \pi}{\sqrt{\hat{S}_q \pi(1-\pi)}} < z \right] \right| \to 0.
\]

In order to justify the use of the pivotal quantity

\[
\frac{z_q - \hat{S}_q \pi}{\sqrt{\hat{S}_q \pi(1-\pi)}}
\]

as the expression from which to work for confidence intervals for the probability of mutation \( \pi > 0 \), which is assumed to be constant over all stages, consider the following. If as in assumption 5 the \( y_i \) are defined
as

\[ y_i = 1 \text{ if mutation occurs} \]
\[ y_i = 0 \text{ otherwise} \]

where \( P[y_i = 1] = \pi \), then the probability function of \( y_i \) is

\[ h(y_i) = \pi^y (1-\pi)^{1-y_i} \]

If, as before, \( z_q = \sum_{i=1}^{s_q} y_i \) is the total number of mutations over \( q \) stages

where the \( y_i \) are independent indicators as defined above, then the following two theorems are well known and are given without proof.

Note: \( S_q \) and the random variable \( z_q \) are non-negative integers and \( z_q \leq S_q \).

Theorem 3.1: If the \( y_i \)'s are as defined above and

(i) \( \pi = P[y_i = 1] \),

(ii) \( z_q = \sum_{i=1}^{s_q} y_i \),

then the probability function of \( z_q \) is

\[ h(z_q) = \binom{S_q}{z_q} \pi^z (1-\pi)^{S_q - z_q} \]

Theorem 3.2: If the probability function of \( z_q \) is \( h(z_q) \) defined above, then the maximum likelihood estimator of \( \pi \) is \( \hat{\pi}_q = z_q / S_q \) and
(i) \( E(\pi_q) = \pi \),
(ii) \( \text{Var}(\pi_q) = \frac{\pi(1-\pi)}{S_q} \).

Now since

\[
\frac{\pi_q - \pi}{\sqrt{\frac{\pi(1-\pi)}{S_q}}} - \frac{Z_q - S_q\pi}{\sqrt{S_q\pi(1-\pi)}}
\]

it is possible to find confidence intervals for \( \pi \) if the limiting distribution of the random variable formed by replacing \( S_q \) by \( \hat{S}_q \) can be shown to be \( N(0,1) \).

Before proceeding to the theorems, the following lemma will be required in the proofs of these theorems.

Lemma 3.1: If \( S_q \) and \( \hat{S}_q \) are defined as before, then

(i) \( S_q \to \infty \) as \( q \to \infty \),
(ii) \( \hat{S}_q \to \infty \) as \( q \to \infty \),

(iii) \( 0 < \frac{m}{M} \leq \frac{\hat{S}_q}{S_q} \leq \frac{M}{m} < \infty \).

Proof:

(i) \( S_q = \sum_{k=1}^{q} \sum_{k=1}^{N_k} N_k \pi_k \geq \sum_{k=1}^{q} \sum_{k=1}^{N_k} N_k \pi_k \to \infty \) as \( q \to \infty \) by assumptions 2 and 3.

(ii) Similarly \( \hat{S}_q = \sum_{k=1}^{q} \sum_{k=1}^{\hat{N}_k} \hat{N}_k \hat{\pi}_k \geq \sum_{k=1}^{q} \sum_{k=1}^{\hat{N}_k} \hat{N}_k \hat{\pi}_k \to \infty \) as \( q \to \infty \).

(iii) \( \frac{\hat{S}_q}{S_q} = \frac{\sum_{k=1}^{q} \sum_{k=1}^{\hat{N}_k} \hat{N}_k \hat{\pi}_k}{\sum_{k=1}^{q} \sum_{k=1}^{N_k} N_k \pi_k} \leq \frac{\sum_{k=1}^{q} \sum_{k=1}^{\hat{N}_k} \hat{N}_k \hat{\pi}_k}{\sum_{k=1}^{q} \sum_{k=1}^{N_k} N_k \pi_k} = \frac{M}{m} < \infty \) by assumption 2.
also,

\[
\frac{\sum_{k=1}^{q} N_k m}{\sum_{k=1}^{q} N_k M_k} = \frac{m}{M} > 0.
\]

Thus,

\[
0 < \frac{m}{M} \leq \frac{S_q}{S_q} < \frac{M}{m} < \infty.
\]

These results are useful in proving the following central limit theorem.

**Theorem 3.3**: If \( z_q, S_q, S_{N_k}, \) and \( \bar{z}_{N_k} \) are defined as before and

\[
\bar{z}_{N_k} = \frac{z_{N_k} - S_{N_k}}{\sqrt{S_q \pi(1-\pi)}},
\]

then

\[
\sum_{k=1}^{q} z_{qk} = \frac{z_q - S_q}{\sqrt{S_q \pi(1-\pi)}}
\]

and

\[
\mathcal{L} \left( \frac{z_q - S_q}{\sqrt{S_q \pi(1-\pi)}} \right) \to \mathcal{N}(0,1).
\]

**Proof**: Obviously

\[
\sum_{k=1}^{q} z_{qk} = \frac{z_q - S_q}{\sqrt{S_q \pi(1-\pi)}}
\]

by the definition of \( z_{qk} \). Also \( E(\bar{z}_{N_k}) = S_{N_k} \pi \), hence, the random variables \( z_{qk} \) are centered at expectations. Again using the "Bounded Case" Theorem,
Loe's (1960); Pg. 277, it is apparent from the definition of the $z_{N_k}$ that the $Z_{qk}$ are independent random variables and since $|z_{N_k} - S_{N_k}| < N(M) < \infty$, the $Z_{qk}$ are uniformly bounded. By Lemma 3.1 $S_q(1-\pi) \to \infty$ as $q \to \infty$ so all conditions of the "Bounded Case" Theorem are satisfied and the theorem is proved.

Now in order to determine the limiting distribution of the random variable formed by replacing $S_q$ by $\hat{S}_q$ it is necessary to introduce a random variable which can be utilized because of (iii) Lemma 3.1.

Definition 3.1: Let $\theta_q = \frac{\hat{S}_q}{M_m}$, where $S_q$, $\hat{S}_q$, $M$ and $m$ are defined as before.

This random variable introduced for the sake of convenience of notation gives the key to the proof of the principal central limit theorem of this chapter. From Lemma 3.1 it is obvious that

$0 < (m/M)^2 \leq \theta_q \leq 1$. The following is also a true theorem.

Theorem 3.4: If $\theta_q$ is as defined above, then

(i) $E(\theta_q) = m/M$,

(ii) $\theta_q \overset{a.s.}{\to} m/M$.

Proof:

(i) $E(\theta_q) = E\left(\frac{\hat{S}_q}{M_m}\right) = \frac{mE(\hat{S}_q)}{M_m} = m/M$.

(ii) By Tchebichev's Inequality, for all $\epsilon > 0$

$$P\left[|\theta_q - m/M| \geq \epsilon\right] \leq \frac{E(\theta_q - m/M)^2}{\epsilon^2}.$$
But $E(\theta_q - m/M)^2 = E\theta_q^2 - (m/M)^2 = (m/M)^2 \frac{1}{s_{q}^2} E(s_q^2) - (m/M)^2 = (m/M)^2 s_q^2/s_q^2$

since by Theorem 1.1 $E(s_q^2) = s_q^2 + S_q^2$.

Thus by Lemmas 2.1 and 3.1

$E(\theta_q - m/M)^2 \leq (m/M)^2 \frac{2N^2 (M-m)^2}{q^4 m^2} = \frac{K}{q}$ where $K = \frac{N^2 (M-m)^2}{2m^2}$

therefore $K/q \to 0$ as $q \to \infty$ and thus $\theta_q \approx m/M$. Moreover since

$0 < (m/M)^2 \leq \theta_q \leq 1$,

$|\theta_{q+r} - \theta_q| = \theta_q \frac{\theta_{q+r} - 1}{\theta_q} \leq \frac{\theta_{q+r} - 1}{\theta_q} = \frac{\theta_{q+r} - 1}{\theta_q} \leq \frac{s_{q+r}}{s_q s_{q+r}}$.

Now let $\hat{s}_r = \sum_{k=q+1}^{q+r} N_k \hat{x}_k$ and $\hat{s}_r = \sum_{k=q+1}^{q+r} N_k \hat{u}_k$ then

$|\theta_{q+r} - \theta_q| \leq \left| \frac{s_{q} \hat{s}_q + \hat{s}_r}{s_{q} \hat{s}_q + \hat{s}_r} \right| \leq \left| \frac{s_{q+r} \hat{s}_q - s_{q+r} \hat{s}_r}{s_{q+r} \hat{s}_q} \right|$

$\leq \frac{s_{q+r}}{s_{q}} \frac{\hat{s}_r}{s_{q+r}} \frac{s_{q+r}}{s_{q}}$ since $\phi \leq s_r$,

$= \left| \frac{s_r}{s_q} - \frac{s_{q+r}}{s_q} \right| \to 0$ as $q \to \infty$,

since $s_r$ and $\hat{s}_r$ are bounded and $s_{q}$ and $\hat{s}_q$ diverge as $q \to \infty$ by Lemma 3.1.

Thus the $\theta_q$ satisfy the Cauchy a.s. convergence criterion so that

$\theta_q \text{ a.s.} \to \theta$ for some $\theta$. However, since $\theta_q \approx m/M$, there exists a subsequence
such that \( \theta_q, q \rightarrow \frac{m}{M} \), but since the sequence itself also converges a.s. they must converge to the same limit \( \frac{m}{M} \). Thus \( \theta_q \rightarrow \frac{m}{M} \) and the theorem is proved.

Note: Since \( 0 < (\frac{m}{M})^2 \leq \theta_q \leq 1, \frac{1}{\theta_q} \frac{m}{M} \) for

\[
|\theta_q - \frac{m}{M}| = \left(\frac{m}{M}\right) \theta_q |\frac{M}{m} - \frac{1}{\theta_q}| \geq \left(\frac{m}{M}\right)^3 |\frac{M}{m} - \frac{1}{\theta_q}|
\]

With this result the central limit theorem follows from the following observation.

Theorem 3.5: For all \( z \in \mathbb{R}, \mathbb{R} \) the set of real numbers, and \( \pi > 0 \),

\[
|P \left[ \frac{z - \frac{S_q\pi}{\sqrt{S_q(1-\pi)}}}{\sqrt{S_q\pi(1-\pi)}} < z \right] - P \left[ \frac{\hat{\pi} - \frac{S_q\pi}{\sqrt{S_q(1-\pi)}}}{\sqrt{S_q\pi(1-\pi)}} < z \right] | \leq P \left[ \theta_q \neq \frac{m}{M} \right]
\]

Proof:

\[
P \left[ \frac{z - \frac{S_q\pi}{\sqrt{S_q(1-\pi)}}}{\sqrt{S_q\pi(1-\pi)}} < z \right] = P \left[ \frac{\frac{\pi q - \pi}{\sqrt{\pi(1-\pi)}}}{\sqrt{S_q}} < z \right]
\]

and

\[
P \left[ \frac{z - \frac{S_q\pi}{\sqrt{S_q(1-\pi)}}}{\sqrt{S_q\pi(1-\pi)}} < z \right] = P \left[ \frac{\hat{\pi} - \frac{\pi}{\sqrt{\pi(1-\pi)}}}{\sqrt{S_q}} < z \right]
\]

where \( \pi_q = z/S_q \) and \( \hat{\pi} = z/S_q \). Also, by the definition of \( \theta_q \),

\[
\frac{\pi_q - \pi}{\sqrt{\pi(1-\pi)} \sqrt{\pi_q(1-\pi)}} = \sqrt{m}\frac{\pi_q}{\pi} \left( \frac{\frac{m}{M} \pi_q}{\pi} - \pi \right) \sqrt{\frac{M}{M} \pi_q \pi - \pi}
\]
Thus,

\[ P\left[ \frac{z_q - \pi_q}{\sqrt{\frac{\pi_q(1-\pi_q)}{m}}} < z \right] = P\left[ \pi_q - \pi < z^* \right], \]

and,

\[ P\left[ \frac{z - \frac{\pi}{\sqrt{\frac{\pi(1-\pi)}{m}}} q}{\sqrt{\frac{\pi_q(1-\pi)}{m}}} < z \right] = P\left[ \sqrt{\frac{M\pi}{m}} \left( \frac{m}{M\pi} \pi_q - \pi \right) < z^* \right], \]

where \( z^* = z \sqrt{\frac{\pi(1-\pi)}{S_q}} \).

Now let

\[ A_q = \left[ \pi_q - \pi < z^* \right], \]

\[ B_q = \left[ \frac{M\pi}{m} \left( \frac{m}{M\pi} \pi_q - \pi \right) < z^* \right], \]

\[ C_q = \left[ \theta_q = \frac{m}{M} \right], \]

and \( A_q^c, B_q^c \) and \( C_q^c \) be the complements of each of these events. Clearly if \( \omega \in A_q^c \), then \( \omega \notin B_q^c \), thus \( A_q^c \cup B_q^c \subseteq A_q \cup C_q \) so that

\[ PB_q \leq P(A_q \cup C_q^c) \leq PA_q + PC_q. \]

Thus \( PB_q - PA_q \leq PC_q \) and \( -PC_q \leq PA_q - PB_q \).

Moreover, if \( \omega \in B_q^c \), then \( \omega \notin A_q^c \), so that \( B_q^c \subseteq A_q^c \) and \( A_q \subseteq B_q \cup C_q^c \).

Thus, \( PA_q \leq P(B_q \cup C_q^c) \leq PB_q + PC_q \) and \( PA_q - PB_q \leq PC_q \) which coupled with the previous result gives \( |PA_q - PB_q| \leq PC_q \). This, when converted to the original notation, proves the theorem.

This bound on the difference of the probabilities of these two random variables for all \( z \) belonging to \( R \) together with the previous theorems of this chapter gives the following central limit theorem.
Theorem 3.6: If \( z, q, \hat{s}_q, m, \pi > 0 \), are defined as before, then

\[
\mathcal{L} \left( \frac{z - \hat{s}_q \pi}{\sqrt{\hat{s}_q \pi (1-\pi)}} \right) \rightarrow N(0,1).
\]

Proof: Let

\[
F_q(z) = P \left[ \frac{z - \hat{s}_q \pi}{\sqrt{\hat{s}_q \pi (1-\pi)}} < z \right],
\]

\[
H_q(z) = P \left[ \frac{z - \hat{s}_q \pi}{\sqrt{\hat{s}_q \pi (1-\pi)}} < z \right],
\]

and,

\[
G(z) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{z} e^{-t^2/2} \, dt, \text{ here } \pi = 3.1416\ldots.
\]

The theorem is proved if it can be shown that for all \( z \in \mathbb{R} \)

\[
|F_q(z) - G(z)| \rightarrow 0. \quad \text{However, } |F_q(z) - G(z)| \leq |F_q(z) - H_q(z)| + |H_q(z) - G(z)| \quad \text{and by Theorem 3.5, } |H_q(z) - G(z)| \rightarrow 0. \quad \text{From Theorem 3.5}
\]

\[
|F_q(z) - H_q(z)| \leq P \left[ \theta_q \neq m/M \right]
\]

which approaches zero as \( q \to \infty \) since by Theorem 3.4 \( \theta_q \xrightarrow{a.s.} m/M \), and the theorem is proved.

From this theorem it follows that for \( z > 0 \):

\[
\lim_{q} P \left[ \frac{z - \hat{s}_q \pi}{\sqrt{\hat{s}_q \pi (1-\pi)}} < z \right] = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{z} e^{-t^2/2} \, dt
\]
from which approximate confidence intervals for \( \pi \), the probability of mutation, can be constructed. In the next section a discussion is given concerning the construction of these confidence intervals and some of their properties.

**Properties of the Approximate Confidence Intervals for \( \pi \).**

It is of interest to investigate the properties of the confidence intervals for \( \pi \) derived from the previous theorem. In order to do this the following concept is of some importance.

**Definition 3.2:** An estimator \( \hat{\theta}_n \) is said to be an almost sure (a.s.) estimator of \( \theta \) if, and only if, \( \hat{\theta}_n \) converges almost surely to \( \theta \).

**Note:** Almost sure estimators are consistent estimators and in fact the convergence is point wise convergence.

**Theorem 3.7:** If

(i) \[ \pi_q = z_q/S_q, \]

(ii) \[ \hat{\pi}_q = z_q/\hat{S}_q \text{ with } z_q \leq \hat{S}_q, \]

then \( \hat{\pi}_q \) is an a.s. estimator of \( \pi \). \( \pi_q \xrightarrow{a.s.} \pi \) and \( \hat{\pi}_q \) is an asymptotically unbiased estimator of \( \pi \).

**Proof:** By the definition of the \( z_{N_q} \), they are independent and integrable and \( \text{Var}(z_{N_q}) = S_{N_q}^2 \pi(1-\pi) \) so that

\[
\sum_{q=1}^{\infty} \frac{\text{Var}(z_{N_q})}{S_q^2} \leq \frac{\text{Var}(z_{N_q})}{m^2} \sum_{q=1}^{\infty} \frac{1}{q^2} < \infty.
\]
Thus, by Kolmogorov's a.s. convergence criterion Pg. 238 Loève (1960)

$$\pi_q = \sum_{k=1}^{q} \frac{z_k}{S_q} $$

$$|\hat{\pi}_q - \pi| = |\pi_q - \pi_q + \pi - \pi| \leq |\pi_q - \pi_q| + |\pi_q - \pi|.$$ 

By the first part of the proof $|\pi_q - \pi| \overset{a.s.}{\to} 0$ and

$$|\pi_q - \pi| = \frac{|z_q - S_q|}{S_q} = \frac{z_q}{S_q} \frac{m}{M} - 1 \overset{a.s.}{\to} 0$$

since $\frac{z_q}{S_q} \overset{a.s.}{\to} \pi$ and $\frac{z_q}{S_q} \overset{a.s.}{\to} m/M$. Thus $\hat{\pi}_q$ is an a.s. estimator of $\pi$.

Also, since $\hat{\pi}_q$ is a.s. bounded, it follows by the Dominated Convergence Theorem Pg. 152 Loève (1960), that $E(\hat{\pi}_q) \to \pi$, and the theorem is proved.

The following lemmas are useful in establishing properties of the confidence intervals for $\pi$.

**Lemma 3.2:** In the equation with real coefficients $ax^2 + bx + c = 0$
if

(i) $a > 0$, $b < 0$, $c > 0$,

(ii) $2a + b > 0$, $b^2 - 4ac > 0$,

(iii) $a + b \geq -c$,

then the roots,

$$x_1 = -\frac{b - \sqrt{b^2 - 4ac}}{2a} \quad \text{and} \quad x_2 = -\frac{b + \sqrt{b^2 - 4ac}}{2a}.$$
have the following characteristics:

\[ 0 \leq x_1 \leq x_2 \leq 1. \]

Proof: Since \( b^2 - 4ac \geq 0 \), the roots are real, and since \( a > 0 \), \( b < 0 \), then \(-b/2a > 0\) so that

\[
\begin{align*}
\frac{-b - \sqrt{b^2 - 4ac}}{2a} &< \frac{-b + \sqrt{b^2 - 4ac}}{2a} = x_2, \\
x_1 &> 0 \text{ if } -b - \sqrt{b^2 - 4ac} \geq 0 \text{ since } a > 0. \quad \text{But } ac \geq 0 \text{ since } a > 0 \text{ and } c \geq 0, \text{ so } -4ac \leq 0 \text{ and } b^2 - 4ac \leq b^2. \quad \text{Thus } \sqrt{b^2 - 4ac} \leq -b \text{ since } -b > 0 \text{ and therefore, } x_1 \geq 0. \quad \text{If } -c \leq a + b, \text{ then } -4ac \leq 4a^2 + 4ab \text{ and } b^2 - 4ac \leq 4a^2 + 4ab + b^2 = (2a + b)^2, \text{ so that } \\
\sqrt{b^2 - 4ac} &\leq 2a + b \text{ since } 2a + b > 0. \\
\text{Thus, } \\
-b + \sqrt{b^2 - 4ac} &\leq 2a, \\
or \\
x_2 &= \frac{-b + \sqrt{b^2 - 4ac}}{2a} \leq 1 \text{ since } a > 0, \\
\text{and the lemma is proved.}
\]

Lemma 3.3: If \( y \) is any real number and \( x \) is a non-negative real number, then \( |y| \leq x \) if, and only if, \( y^2 \leq x^2 \).

Proof: If \( |y| \leq x \), then \( |y| \leq |y| |x| \leq x^2 \) or \( y^2 \leq x^2 \). If \( y^2 \leq x^2 \), then \( y^2 - x^2 \leq 0 \) or \( (y - x)(y + x) \leq 0 \), which implies

(i) \( (y - x) \leq 0 \) and \( (y + x) \geq 0 \), or

(ii) \( (y - x) \geq 0 \) and \( (y + x) \leq 0 \).
But,

(i) implies \( y \leq x \) and \( y \geq -x \) or \(|y| \leq x\), and

(ii) implies \( y \geq x > 0 \) and \( y < 0 \) since \( x > 0 \).

This is impossible, hence, the only possible conclusion is that \(|y| \leq x\).

The following theorem shows the equivalence between the pivotal quantity

\[
\frac{|z_q - \hat{\pi}_q|}{\sqrt{\hat{\pi}_q(1-\pi)}} \leq z
\]

and the fact that the end points of the confidence interval for \( \pi \) are roots of an appropriate quadratic equation and that they also satisfy certain conditions.

**Theorem 3.8:** For \( 0 < z < \infty \)

(i) \[
\frac{|z_q - \hat{\pi}_q|}{\sqrt{\hat{\pi}_q(1-\pi)}} \leq z
\]

if, and only if, \( a_q \pi^2 + b_q \pi + c_q \leq 0 \) where

\[
a_q = \hat{\pi}_q(\hat{\pi}_q + z^2),
\]

\[
b_q = -\hat{\pi}_q(2z_q + z^2),
\]

\[
c_q = z_q^2,
\]

(ii) the roots of the equation \( a_q \pi^2 + b_q \pi + c_q = 0 \) are

\[
\pi_{1q} = \frac{-b_q - \sqrt{b_q^2 - 4a_qc_q}}{2a_q}, \quad \pi_{2q} = \frac{-b_q + \sqrt{b_q^2 - 4a_qc_q}}{2a_q}
\]
and if $S_q \Rightarrow a.s.$, $z_q$ satisfy

(iii) $0 \leq \pi_{1q} \leq \pi_{2q} \leq 1$,

(iv) $\pi_{1q} - \pi_{2q} \Rightarrow a.s. 0$,

(v) If $z_q = 0$, then $\pi_{1q} = 0$.

Proof: (i) From Lemma 3.5

$$\frac{|z_q - \hat{S}_q \pi|}{\sqrt{\hat{S}_q \pi (1-\pi)}} \leq z$$

if, and only if,

$$\left(\frac{z_q - \hat{S}_q \pi}{\hat{S}_q \pi (1-\pi)}\right)^2 \leq z^2$$

or, equivalently, if, and only if,

$$z_q^2 - 2z_q \hat{S}_q \pi + \hat{S}_q^2 \pi \leq z^2 \hat{S}_q \pi (1-\pi),$$

or,

$$\hat{S}_q (\hat{S}_q + z^2) \pi^2 - \hat{S}_q (2z_q + z^2) \pi + z_q^2 \leq 0,$$

which proves (i).

(ii) Clearly the roots of the equation

$$a_q \pi^2 + b_q \pi + c_q = 0$$

where

$$a_q = \hat{S}_q (\hat{S}_q + z^2),$$

$$b_q = -\hat{S}_q (2z_q + z^2),$$

$$c_q = -\hat{S}_q z^2.$$
\[ c_q = z_q^2 \]

are

\[ \pi_{1q} = \frac{-b_q - \sqrt{b_q^2 - 4a_q c_q}}{2a_q} \quad \text{and} \quad \pi_{2q} = \frac{-b_q + \sqrt{b_q^2 - 4a_q c_q}}{2a_q}. \]

(iii) Since it is assumed that \( \hat{S}_q \geq z_q \) and by definition \( \hat{S}_q > 0 \) and \( z_q^2 > 0 \) and \( z^2 > 0 \), it is evident that \( a_q > 0 \), \( b_q < 0 \), and \( c_q > 0 \). Since

\[ \hat{S}_q \overset{a.s.}{\geq} z_q \]

\[ a_q + b_q = \hat{S}_q \left( \hat{S}_q - 2z_q \right) \overset{a.s.}{\geq} z_q (z_q - 2z_q) = -z_q^2 = -c_q. \]

\[ b_q^2 - 4a_q c_q = z_q^2(4z_q^2 + 4z_q z^2 + z^4) - 4z_q^2 \hat{S}_q (\hat{S}_q + z^2) \]

\[ = 4z_q \hat{S}_q z(\hat{S}_q - z_q) + z^4 \hat{S}_q^2 \overset{a.s.}{> 0}. \]

\[ 2a_q + b_q = 2\hat{S}_q (\hat{S}_q - z_q) + \hat{S}_q^2 \overset{a.s.}{> 0}. \]

Thus by Lemma 3.2, \( 0 \leq \pi_{1q} \leq \pi_{2q} \leq 1. \)

(iv)

\[ \sqrt{b_q^2 - 4a_q c_q} \]

\[ \pi_{2q} - \pi_{1q} = \frac{-b_q - \sqrt{b_q^2 - 4a_q c_q}}{a_q} \]

\[ = \frac{\sqrt{4z_q \hat{S}_q^2 z^2(\hat{S}_q - z_q) + z_q^2 \hat{S}_q^2}}{\hat{S}_q (\hat{S}_q + z^2)} \overset{a.s.}{\leq} \sqrt{\frac{4z^3}{\hat{S}_q} z^2 + \frac{4z^3}{\hat{S}_q} \hat{S}_q^2}, \]

since \( \hat{S}_q \overset{a.s.}{\geq} z_q \) and...
\[ \hat{S}_q \geq 1 \text{ for } q \text{ large.} \]

Therefore,

\[ \pi_{2q} - \pi_{1q} \overset{a.s.}{\to} \frac{1}{\sqrt{\hat{S}_q}} \frac{\sqrt{4z^2 + z^4}}{1 + z_q^2/\hat{S}_q} \to 0, \]

as \( q \to \infty \) since \( \hat{S}_q \to \infty \) as \( q \to \infty \) and \( \sqrt{4z^2 + z^4} \) is finite for \( z \) finite.

Thus, \( \pi_{2q} - \pi_{1q} \overset{a.s.}{\to} 0. \)

(v) If \( z_q = 0 \), then \( c_q = 0 \) and

\[ \pi_{1q} = \frac{-b_q - \sqrt{b_q^2}}{2a_q} = \frac{-b_q - (-b_q)}{2a_q} = 0 \text{ since } b_q < 0, \]

and the theorem is proved.

These results prove that

\[ P \left( \frac{|z_q - \hat{S}_q\pi|}{\sqrt{\hat{S}_q\pi(1-\pi)}} \leq z \right) = P \left[ \pi_{1q} \leq \pi \leq \pi_{2q} \right], \]

so that

\[ \lim_{q} P \left[ \pi_{1q} \leq \pi \leq \pi_{2q} \right] = \frac{1}{2\pi} \int_{-\infty}^{\infty} e^{-t^2/2} dt, \]

where \( z > 0 \) and \( \pi_{1q} \) and \( \pi_{2q} \) have the characteristics given in the theorem above.

Furthermore for all \( \pi \)

\[ \left[ \pi_{1q} \pi_{2q} \right], \]

\[ \frac{|z_q - \hat{S}_q\pi|}{\sqrt{\hat{S}_q\pi(1-\pi)}} \leq z \]
for all $z > 0$, and conversely. This is true since the function

$$y_q = a_q \pi^2 + b_q \pi + c_q$$

is a quadratic function in $\pi$ and $a_q > 0$ implies the graph of the function is a parabola opening upward with $\pi$-intercepts at $\pi_{1q}$ and $\pi_{2q}$.
CHAPTER IV

RATES OF CONVERGENCE

In this chapter an attempt is made to determine just how good the approximate confidence intervals in the preceding two chapters are or alternatively to determine the rate in terms of $q$ at which each of these distribution functions approach the Normal Distribution with mean zero and variance one.

In Theorem 2.1 it was shown that

$$
\mathcal{L} \left( \frac{S_q - S^q}{s_q} \right) \rightarrow N(0,1),
$$

and in Theorem 3.3 it was shown that

$$
\mathcal{L} \left( \frac{z_q - S^q \pi}{\sqrt{S_q \pi(1-\pi)}} \right) \rightarrow N(0,1).
$$

Both of these random variables were shown to be sums of independent random variables centered at expectations and by the bounded assumption the third absolute moment is finite. They thus satisfy the conditions necessary to employ the theorem of Gramm (1937), Pg. 77, for determining their rates of convergence to $N(0,1)$.

In Theorem 3.5 it was shown that

$$
|P \left[ \frac{z_q - S^q \pi}{\sqrt{S_q \pi(1-\pi)}} < z \right] - P \left[ \frac{z_q - S^q \pi}{\sqrt{S_q \pi(1-\pi)}} < \frac{\hat{\theta}_q - m/M}{\sqrt{S_q \pi(1-\pi)}} \right] | \leq P \left[ \theta_q \neq m/M \right]
$$

for all $z \in \mathbb{R}$, $\mathbb{R}$ the set of real numbers. But since
\[ \theta_q = \frac{S^q / S_q}{M/m}, \]
\[ P\left[ \theta_q = m/M \right] = P\left[ S^q / S_q = 1 \right] = P\left[ \frac{S - S^q}{S_q} = 0 \right], \]

where by Theorem 3.4
\[ \frac{S - S_q}{S_q} \text{ a.s.}, \]
\[ \frac{S}{S_q} \rightarrow 0. \]

A similar result holds for
\[ \left| P \left[ \frac{S^q - S_q}{s_q} < z \right] - P \left[ \frac{S^q - S_q}{S^q} < z \right] \right| \]

for all \( z \in \mathbb{R} \), as is shown by the following

Theorem 4.1. If \( S_q, \hat{S}_q, s_q \) and \( \hat{s}_q \) are defined as before, then
\[ \left| P \left[ \frac{\hat{S}_q - S_q}{s_q} < z \right] - P \left[ \frac{\hat{S}_q - S_q}{\hat{s}_q} < z \right] \right| \leq P \left[ \frac{s^2 - s^2}{s_q^2} \neq 0 \right], \]

for all real \( z \).

Proof: Using the same procedure as employed in Theorem 3.5, set
\[ A_q = \left[ \frac{\hat{S}_q - S_q}{s_q} < z \right], \]
\[ B_q = \left[ \frac{s_q(\hat{S}_q - S_q)}{\hat{s}_q s_q} < z \right]. \]
\[ C_q = \left[ \frac{s_q}{s_q^c} = 1 \right] , \]

with \( A_q^c, B_q^c, \) and \( C_q^c \) the complements of each of these events. If \( \omega \notin \overline{\overline{A_q}} \),

then \( \omega \in B_q^c \) and by complementation \( B_q \subset A_q \cup \overline{C_q} \) so that

\[ PB_q \leq PA_q + PC_q. \]

Moreover, if \( \omega \notin B_q^c \), then \( \omega \notin A_q^c \), thus \( B_q^c \subset \overline{A_q} \) so that

\[ PA_q \leq PB_q + PC_q^c. \]

Combining these results gives

\[ |P \left[ \frac{S^q - S_q}{\overline{A_q}} < z \right] - P \left[ \frac{S^q - S_q}{\overline{C_q}} < z \right]| \leq P \left[ s_q / s_q^c \neq 1 \right]. \]

But

\[ \left[ s_q^2 / s_q^2 \neq 1 \right] = \left[ \frac{s_q^2 - s_q}{s_q^2} \neq 0 \right] = \left[ \frac{(s_q - s_q)(s_q + s_q)}{s_q} \neq 0 \right] . \]

However, since for all \( q \)

\[ 0 < \frac{s_q + s_q}{s_q} < \infty , \]

\[ \left[ \frac{s_q^2}{s_q^2} \neq 1 \right] = \left[ \frac{s_q - s_q}{s_q^2} \neq 0 \right] = \left[ \frac{s_q}{s_q} \neq 1 \right] . \]

Also \( s_q / s_q = 1 \) if, and only if \( s_q / s_q^c = 1 \), thus \( \left[ s_q / s_q^c \neq 1 \right] = \left[ s_q / s_q^c \neq 1 \right] . \)

and the theorem is proved.

Moreover, the following is also true.

Theorem 4.2: If \( s_q \) and \( \overline{s_q} \) are defined as before then,
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\[ \frac{A^2 - S^2}{\alpha^2 q} \xrightarrow{a.s.} 0. \]

Proof: By Theorem 2.2

\[ \frac{S^2 - s^2}{q} \xrightarrow{a.s.} 0, \]

and from Lemma 2.1

\[ s_q^2 \geq q d_l \]

where \( 0 < d_l < \infty \).

Thus

\[ \left| \frac{S^2 - s^2}{q} \right| \leq \frac{1}{d_l} \left| \frac{s^2 - s_q^2}{q} \right| \xrightarrow{a.s.} 0, \]

and the theorem is proved.

From these remarks and theorems it is then apparent that the rates of convergence in both cases can be examined with the same method. Toward this end it is convenient to introduce the following general notation. Let

\[ Y_q = \frac{S_q - s_q}{\sqrt{S_q \pi(1-\pi)}}, \quad \frac{z_q - S_q \pi}{\sqrt{S_q \pi(1-\pi)}}, \]

\[ Y_q = \frac{S^2 - s^2}{q} \]

or

\[ \frac{z^2 - S^2 \pi}{q}, \quad \sqrt{S_q \pi(1-\pi)} \]
according as
\[ x_q = \frac{\sum q - s^2}{s^2} \quad \text{or} \quad \frac{\sum q - S_q}{S_q}, \]

and let
\[ F_q(z) = P\left[ \sum Y_q < z \right], \]
\[ H_q(z) = P\left[ Y_q < z \right], \]

and
\[ G(z) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{z} e^{-t^2/2} \, dt. \]

Implied in these definitions is the convention that \( \sum Y_q, Y_q \) and \( X_q \) are simultaneously the first random variable or the second, since these are the combinations of interest in the context.

Using this notation the problem in each case is to bound
\[ |F_q(z) - G(z)| \]
for all \( z \in \mathbb{R} \). This is done by considering
\[ |F_q(z) - G(z)| \leq |F_q(z) - H_q(z)| + |H_q(z) - G(z)|, \]
where by Theorems 3.5 and 4.1.
\[ |F_q(z) - H_q(z)| \leq P[X_q \neq 0] \]
and
\[ |H_q(z) - G(z)| < c_1 q \log q / \sqrt{q} \]
by the theorem of Cramer mentioned above, where \( c_1 \) is an absolute constant which can be taken to be 3 according to H. Cramer (1928),
so that the second difference is bounded.

To bound \( P[X_q \neq 0] = 1 - P[X_q = 0] \), it is necessary only to consider the rate at which \( P[X_q = 0] \) approaches one. By a theorem Pg. 168 Loève (1960), since \( X_q \xrightarrow{a.s.} 0 \), the distribution function of \( X_q \), \( F_{X_q}(x) \to 0 \) or 1 according as \( x < 0 \) or \( x > 0 \), which is equivalent to saying \( P[X_q = 0] \to 1 \).

Thus the problem reduces to finding the rate of convergence of the sequence of random variables \( X_q \) in law to a distribution degenerate at zero.

Since \( \mathcal{L}(X_q) \to \mathcal{L}(0) \), the characteristic function \( f_q(u) \to 1 = f(u) \), the characteristic function of the degenerate law. Also by theorem Pg. 199, Loève (1960),

\[
f_q(u) = 1 + \frac{2^{1-\delta}}{1+\delta} \theta_q u^{1+\delta} E X_q^{1+\delta}
\]

for \( 0 < \delta \leq 1 \) and \( \theta_q \) is a complex valued quantity with \( |\theta_q| \leq 1 \).

Taking \( \delta = 1 \) gives

\[
f_q(u) = 1 + \frac{1}{2} \theta_q u^2 E X_q^2
\]

From this expansion of \( f_q(u) \)
\begin{equation}
\theta_q(u) = \frac{2(f_q(u) - 1)}{u^2 \text{Ex}_q^2}
\end{equation}

is a function of \( u \). From this it follows that

\[-R \theta_q(u) \leq \frac{4}{u^2 \text{Ex}_q^2}\]

since \( R f_q(u) - 1 \leq 0 \) and \( |f_q(u) - 1| \leq 2 \). (Here \( R \) denotes the real part of the complex function.)

Using these observations it is then possible to prove

Theorem 4.3. For all \( q \) and real \( u \),

\[-R \theta_q(u) \leq \frac{1}{u^2}\]

where \(-R \theta_q(u)\) is defined as above.

Proof: The result is trivial for \(-1 \leq u \leq 1\) since \( |\theta_q'(u)| \leq 1 \) for all \( u \). Thus the result must be proved for the case \( |u| > 1 \). From the

Increments Inequality Pg. 195, Loewy (1960); which states that for any real \( u \) and \( h \)

\[|f_q(u) - f_q(u + h)|^2 \leq 2f_q(0) \left(f_q(0) - Rf_q(h)\right),\]

it follows since \( f_q(0) = 1 \) that

\[2\left(1 - Rf_q(h)\right) \geq |f_q(u) - f_q(u+h)|^2,
\]

and since \( |1 - f_q(u)| \geq 1 - Rf_q(u)\),

\[2|f_q(h) - 1| \geq |f_q(u) - f_q(u+h)|^2.\]
But
\[ f_q(u) = 1 + \frac{1}{2} \theta_q(u) u^2 \]
and
\[ f_q(u+h) = 1 + \frac{1}{2} \theta_q(u+h) (u+h)^2 \]
Thus
\[ 2|f_q(h) - 1| \geq \frac{1}{4} (\frac{1}{EX_q^2}) |\theta_q(u)u^2 - \theta_q(u+h)(u+h)^2|^2 \]
\[ \geq \frac{1}{2} (\frac{1}{EX_q^2})^2 |R \theta_q(u)u^2 - R \theta_q(u+h)(u+h)^2|^2 . \]
Now assume that for \(|u| > 1\) and for all \(q\)
\[-R \theta_q(u) > \frac{1}{u^2} .\]
Coupled with the fact that
\[-R \theta_q(u) \leq \frac{h}{u^2 EX_q^2} ,\]
it follows that
\[ \frac{1}{4} (\frac{1}{EX_q^2})^2 |R \theta_q(u)u^2 - R \theta_q(u+h)(u+h)^2|^2 \geq \frac{1}{4} (\frac{1}{EX_q^2})^2 |\frac{1}{u^2} u^2 - \frac{h}{EX_q^2} (u+h)^2|^2 , \]
or for all \(h\)
\[ 2|f_q(h) - 1| > \frac{1}{4} |EX_q^2 - h|^2 . \]
However for \( h = 0 \), this implies

\[
0 > \frac{1}{4} \left| \text{EX}_q^2 - 4 \right|^2 > 0
\]

for all \( q \), a contradiction. Hence, \(-R \theta_q(u) \leq \frac{1}{u^2}\) for all \( q \) and all \( u \).

This result then gives the key to the following.

**Theorem 4.4**: If \( \mathcal{L}_q(X^2) \rightarrow \mathcal{L}(0) \), then

\[
P[X_q \neq 0] \leq 7 \text{EX}_q^2.
\]

**Proof**: By the second Truncation Inequality Pg. 196, Loève (1960); for all \( u > 0 \),

\[
\int_{|x| \geq 1/u} dF_{\mathcal{L}_q}(x) = \int_0^u \int_{|x| > 1/u} \left( f_q(0) - Rf_q(v) \right) dv
\]

\[
< \frac{7}{u} \int_0^u \left( -R \theta_q(v) \right) \text{EX}_q^2 v^2 dv
\]

\[
< \frac{7}{u} \int_0^u \text{EX}_q^2 dv \quad \text{since} \quad -R \theta_q(u) \leq \frac{1}{u^2}
\]

\[
= 7 \text{EX}_q^2.
\]

Since the bound is independent of \( u \), and the characteristic function is defined for \(-\infty < u < \infty\), taking the limit on \( u \) gives

\[
P[X_q \neq 0] = \int_{|x| > 0} dF_{\mathcal{L}_q} \leq 7 \text{EX}_q^2
\]

and the theorem is proved.
From this theorem and the previous remarks it follows that for all real $z$

\[
|p\left[\frac{S - q}{s_q} < z\right]| \leq \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{z} e^{-t^2/2} \, dt < \frac{\sum_{k=1}^{q} E|N_k - S_{N_k}|^3}{1} + \frac{3 \log q}{\sqrt{q}} \rho_{3q}
\]

where

\[
\rho_{3q} = \frac{1}{q} \frac{\sum_{k=1}^{q} E|N_k - S_{N_k}|^3}{\left(s_q^2\right)^{3/2}},
\]

and

\[
|p\left[\frac{z - \hat{S}/(s_q \sqrt{\pi(1-\pi)})}{s_q} < z\right]| \leq \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{z} e^{-t^2/2} \, dt < \frac{\sum_{k=1}^{q} E|z - S_{N_k}|^3}{1} + \frac{3 \log q}{\sqrt{q}} \rho_{3q}
\]

where

\[
\rho_{3q} = \frac{1}{q} \frac{\sum_{k=1}^{q} E|z - S_{N_k}|^3}{\left(s_q \sqrt{\pi(1-\pi)}\right)^{3/2}}.
\]

With these results it is possible to prove the following.

Theorem 4.5: If the constants $N, M, m$ are defined as before, then

\begin{align*}
(\text{i}) & \quad |p\left[\frac{S - q}{s_q} < z\right] - G(z)| < \frac{5q(M-m)N(M-2)}{s_q} + \frac{3 \log q \, N(M-m)}{\sqrt{q^2}} \rho_{3q}, \\
(\text{ii}) & \quad |p\left[\frac{z - S/\sqrt{s_q \pi(1-\pi)}}{s_q} < z\right] - G(z)| < \frac{s_q^2}{s_q^2} + \frac{3 \log q}{q} \sqrt{3NM + \frac{1}{\pi(1-\pi)}}
\end{align*}

for all real $z$, where $G(z)$ is the distribution function of the Normal Distribution with mean zero and variance one.
Proof: (i) By the independence assumption,

\[ E(\bar{s}_q^2 - s_q^2)^2 = \sum_{k=1}^{q} \left[ N_k^2 \left( \frac{1}{n_k} - \frac{1}{N_k} \right) E(\bar{\sigma}_k^2 - \sigma_k^2)^2 \right]. \]

By the sampling without replacement probability function,

\[ E(\bar{\sigma}_k^2 - \sigma_k^2)^2 = \frac{N_k - n_k}{(n_k-1)(N_k+1)} \left( \frac{N_k n_k - n_k N_k - 1}{n_k N_k (N_k-1)} \right) \sum_{i=1}^{M} (X_{ki} - \mu_k)^4 + 2 \sigma_k^4. \]

Thus by Lemma 2.1 and assumption 3,

\[ \sum_{k=1}^{q} \left[ N_k^2 \left( \frac{1}{n_k} - \frac{1}{N_k} \right) E(\bar{\sigma}_k^2 - \sigma_k^2)^2 \right] < 5(M-m)^4(N-2)^2, \]

so

\[ E(\bar{s}_q^2 - s_q^2)^2 < \frac{5q(M-m)^4(N-2)^2}{s_q^2}. \]

Using the boundedness of the \( N_k \) and the \( X_{ki} \), it follows that

\[ \sum_{k=1}^{q} E|N_k \bar{X}_k - S_N| \leq \sum_{k=1}^{q} E(N_k \bar{X}_k - S_N)^2 N(M-m) = s_q^2 N(M-m), \]

so that

\[ \rho_3q < \frac{N(M-m)}{s_q}, \]

which proves (i).

(ii) Since \( E(\bar{s}_q^2 - s_q^2)^2 = s_q^2 \).
and in this case, using Schwarz's Inequality,

\[
E\left(\frac{S_q - S_q^*}{S_q}\right)^2 \leq \frac{s_q^2}{s_q^2},
\]

so that

\[
E|z_{N_k} - S_{N_k}\pi|^3 \leq \sqrt{E(z_{N_k} - S_{N_k}\pi)^2 E(z_{N_k} - S_{N_k}\pi)^4},
\]

\[
< S_{N_k}\pi(1 - \pi) \sqrt{3NM(1 - \pi)} + 1,
\]

so that

\[
\rho_{3q} < \frac{1}{\sqrt{S_q}} \sqrt{3NM + \frac{1}{\pi(1 - \pi)}},
\]

and (ii) is proved.

From these results, together with the results proved earlier that

\[
s_q^4 > q_2^2, s_q^2 > h_q m^2 \quad \text{and} \quad s_q^2 < qN^2(M-m)^2,
\]

it follows that both of the differences, (i) and (ii), in Theorem 4.5 will be less than \( \epsilon > 0 \), if

\[
\frac{q}{\log q} \geq \max. \left[\frac{(M-m)N^2}{\sqrt{d_1}} \epsilon, \frac{2N^2M^2}{\min(1 - \pi)}\right].
\]

These results are obtained with the added assumptions that \( (M-m) \geq 1 \),

\( d_1 \geq 1 \) and \( \log q \geq 1 \). However, these are very conservative bounds.

If the sum of the two bounds in (i) or (ii) of Theorem 4.5 can be made less than some prescribed number, then the so-called \( 1-\delta \) per cent confidence intervals have a degree of confidence which can be determined.
For example, if the sum of the two bounds in (i) or (ii) of Theorem 4.5 is less than or equal to .05, then the constructed 95 per cent confidence intervals have at least an 85 per cent confidence.

Under the assumption that the $N_k \bar{x}_k$ are also identically distributed, the rate of convergence in each case is faster as can be seen from the following.

Theorem 4.6: If, in addition to the previous assumptions, the $N_k \bar{x}_k$ are identically distributed, then

\[(i) \quad |P \left[ \frac{M \bar{q} - S_q}{\sqrt{q} \pi (1-\pi)} < z \right] - G(z)| < \frac{\sqrt{3N}(M-m)(N-2)^2}{q(n(2/ \pi - 1)\sigma^2)} + \frac{c(M-m)}{q(n(2/ \pi - 1)\sigma^2)^{3/2}}
\]

\[(ii) \quad |P \left[ \frac{z - \bar{q} \pi}{\sqrt{q} \pi (1-\pi)} < z \right] - G(z)| < \frac{N^2(\frac{1}{n} - \frac{1}{N})\sigma^2}{qS_{N}^2} + \frac{c}{\sqrt{qs}_{N}} \sqrt{3NM + \frac{1}{\pi(1-\pi)}}
\]

for all real $z$ where $G(z)$ is the Normal Distribution with mean zero and variance one, and $S_{N} = N \mu$, $N,M$ and $m$ are as defined before and $c < 3$.

Proof: In the identically distributed case all the $N_k \bar{x}_k$ and $X_{ki}$ are the same for all $k$. In this case $\log q/\sqrt{q}$ becomes $1/\sqrt{q}$ according to Cramér (1937).

(i) In the identically distributed case

\[P_{3q} = \frac{E[N_k \bar{x}_k - S_q]^3}{(n^2(1/n - 1/N)\sigma^2)^{3/2}} < \frac{N(M-m)}{(N^2(1/n - 1/N)\sigma^2)^{1/2}} = (\frac{1}{n} - \frac{1}{N})^{1/2}\sigma.
\]
\[
E(s_q^2 - s_q^2)^2 = qN^2 \left(\frac{1}{n} - \frac{1}{N}\right) E(s_k^2 - \sigma^2)^2 < 5q(M-m)^4(N-2)^2
\]
so that
\[
E(\frac{s_q^2 - s_q^2}{s_q^2}) < \frac{5(M-m)^4(N-2)^2}{q(N^2 \left(\frac{1}{n} - \frac{1}{N}\right) \sigma^2)}
\]

\[(11)\]
\[
\rho_{3q} = \frac{E|z_{N_k} - S_N\pi|^3}{\left(S_N\pi(1-\pi)\right)^{3/2}} < \frac{1}{\sqrt{S_N}} \sqrt{3NM + \frac{1}{\pi(1-\pi)}}
\]
\[
E(\frac{s_q^2 - s_q^2}{s_q^2}) = s_q^2 = qN^2 \left(\frac{1}{n} - \frac{1}{N}\right) \sigma^2 = \frac{N^2 \left(\frac{1}{n} - \frac{1}{N}\right) \sigma^2}{qS_N^2}
\]

This proves the theorem.

In the identically distributed case the rate of convergence is faster, but this assumption also requires, as mentioned, that all the \(N_k\), \(n_k\), and \(X_{kl}\) are the same. This condition would be impractical in the experimental situation discussed here. However, if the experimental situation could be standardized so that this assumption is met, the rate of convergence would be faster.

These theorems do not necessarily solve the rates of convergence problem, since much sharper bounds may exist. The bounds derived in Theorems 4.5 and 4.6, however, do give some information as to how fast each of these distribution functions approaches the Normal Distribution with mean 0 and variance 1.
CHAPTER V
APPLICATIONS TO EXPERIMENTAL RESULTS

An experiment designed to estimate the probability of spontaneous mutation from avirulence to virulence at the Algerian locus of the fungus was performed with the following results. The estimate of $S_q$, the total number of spores germinated on the variety Algerian, was $\hat{S}_q = 4,587,088$, but no mutation was observed. Using the techniques suggested in the previous chapters, the approximate 95 per cent confidence interval for $S_q$ is $(4,440,541; 4,733,635)$. The point estimate of $\pi$ is zero and an approximate 95 per cent confidence interval for $\pi$, the probability of mutation, is $(0; 8.720 \times 10^{-7})$. The number $q$ in this experiment, the number of repetitions, was 59. The numbers $N$, $M$ and $m$ cannot be determined exactly from the experimental data, but from the data obtained it is known that $N \geq 1,181$, $M \geq 366$, $m \leq 6$ and $\hat{\sigma}_q^2 = 5,594,024,219$. Substituting these estimates in the bounds derived in Theorem 4.5, gives the following bounds; for (i) approximately $\hat{\pi}$ and for (ii) approximately $0.3$.

Experiments were also made to induce mutations from avirulence to virulence at the Algerian locus in the fungus using gamma radiation. In the experiments using gamma irradiation the following experimental technique was used. Plants of the susceptible variety Compana were inoculated with mildew spores when they were about seven days old. Two days after inoculation the Compana plants were treated with gamma irradiation continuously for 48 hours. During this period they received an estimated dosage of 4800r. In about seven days after the irradiation treatment, the mildew on the Compana plants began to sporulate. These spores were
then used to inoculate the resistant variety Algerian in order to screen for mutations from avirulence to virulence. This experiment produced no mutations and the final estimate of $S_q$, the total number of observations on the variety Algerian, was $\hat{S}_q = 431,931$. Using the same techniques as before gives the approximate 95 per cent confidence interval for $S_q$ as $(405,775; 458,077)$. The point estimate of $\pi$ is zero with approximate 95 per cent confidence interval for $\pi$ being $(0; 8.839 \times 10^{-6})$. In this case $q = 22$, $N \geq 309$, $M \geq 227$, $m = 1$ and $\hat{A}_q^2 = 178,086,341$. Substituting these estimates into the bounds obtained in Theorem 4.5 gives the approximate bounds for (i) and (ii), respectively, as 3 and .5. Moreover, in this experiment it was possible to consider each pot of Algerian plants a stage in the q-stage experimental procedure. When the data obtained is analyzed in this way, the estimate of the total number of observations is again $\hat{S}_q = 431,931$, but the approximate 95 per cent confidence interval for $S_q$ is $(420,547; 443,315)$. The point estimate and the approximate 95 per cent confidence interval for $\pi$ are again 0 and $(0; 8.835 \times 10^{-6})$, respectively. In this case, however, $q = 169$, $N \geq 67$, $M \geq 227$, $m = 1$ and $\hat{A}_q^2 = 33,730,972$. Using these estimates in the bounds derived in Theorem 4.5 gives approximate bounds for (i); 5.8 and for (ii); .3. It is interesting to note that what is gained in shorter confidence intervals for $S_q$, is lost in the approximate bound obtained in the rate of convergence problem.

Further experiments were made to induce mutations at all eight loci of the barley mildew fungus using diethyl sulfate. In the experiments
using diethyl sulfate, Compana barley plants were sprayed five times at
30 minute intervals with fresh 0.0076M solutions one to two days after
inoculation. When pustules appeared on the Compana plants, these were
then used to inoculate eight resistant varieties of barley. Each resistant
variety of barley carries a distinct gene for mildew resistance. After
an estimated 20,270 spores had been tested on the resistant variety Hana
m/n AB 62-4, a pustule appeared on this variety. This pustule, after
further screening, was considered a mutant. Applying the same technique
in this case gives $\hat{\lambda}_q = 20,270$ and approximate 95 per cent confidence
intervals for $S_q$ as $(18,630; 21,910)$. The point estimate of $\pi$ is
\[4.904 \times 10^{-5}\] with approximate 95 per cent confidence interval $(8.485 \times 10^{-6}; 2.875 \times 10^{-4})$. In this case $q = 15$. From the experimental data it is
known that $M \geq 54$, $N \geq 79$, $m \leq 10$ and that $a_q^2 = 672,389$. Using these
numbers to determine the bounds in Theorem 4.5 gives for (i) approximately
12 and for (ii) approximately 1.5.

From a purely intuitive point of view, the confidence intervals
obtained for the parameters $S_q$ and $\pi$ in these experiments appear quite
reasonable. The bounds obtained, however, are not very sharp. This is
not surprising, however, since the bounds obtained in Theorem 4.5 are very
conservative. It is possible that sharper bounds exist and that if these
could be found they would provide better bounds even if estimators were
substituted for parameters or constants which appear.
CHAPTER VI

SUMMARY AND REMARKS

The two central limit theorems, 2.5 and 3.6, as stated and proved in Chapters II and III when considered in a general setting, are an approach to estimating and finding confidence intervals for both parameters in the Binomial Distribution. The assumptions made to prove these theorems are general enough to make the theorems applicable to many more experimental situations than the one given in Chapter I. The methods of proof, too, may be applicable to other proofs of central limit theorems.

The first theorem,

\[ L\left(\frac{\hat{S}_q - S_q}{s_q}\right) \rightarrow N(0,1), \]

at first glance may not appear to be a new theorem. However, this theorem differs from others of this type in that the condition \( \hat{S}_q^2/s_q^2 \rightarrow l \) is less restrictive than that of requiring a consistent estimator or the assumption of the summands being identically distributed. In fact, the condition of the ratio of the estimator to the parameter converging almost surely to one is implied by the condition of a consistent estimator.

The second theorem,

\[ L\left(\frac{z_q - \hat{S}_q x}{\sqrt{S_q x(1-x)}}\right) \rightarrow N(0,1) \]

is typically binomial except for the fact that \( \hat{S}_q \) is also a random variable. In this sense, under the assumptions stated, the theorem is, to the author's knowledge, new. In this theorem, too, the ratio of the
estimator to the parameter, \( \hat{\theta} q / \theta q \), converging almost surely to one played an important role. This idea, having worked more than once, might be considered a device in proving other central limit theorems in other situations. This is particularly true when both estimator and parameter diverge.

The method of proof of these two theorems could have been the same, namely, showing the difference of two distribution functions converge to zero. However, it should be noted that a more "restrictive" condition could be shown in the first case and not in the second.

The rates of convergence theorem for the degenerate law is, to the author's knowledge, new. This, then, combined with the classical rates of convergence theorem of Cramer can be considered a new rates of convergence theorem for random variable of the type discussed in Chapter IV.

A clue to an approach to the rates of convergence for this setting became apparent in the proof of the second central limit theorem, namely, that it was possible to bound the difference of two distribution functions uniformly by the probability that an almost surely convergent random variable is not equal to its limit. This led to the consideration of the rate of convergence of a random variable to the degenerate law, \( \mathcal{L}(0) \). Various theorems from Loève (1960), on distribution and characteristic functions were of great importance in finding a solution to this problem. Even though the rates as they appeared in Chapter IV and in the experimental applications seem fairly reasonable, and in some instances very good, it should be kept in mind that in this situation \( \text{EX}_q^2 \) and \( \rho_{3q} \)
could not be evaluated exactly and could only be bounded. The rates are thus very conservative.

The concept of almost sure estimator, for example \( \hat{\pi}_q \), played an important role in establishing the pleasant properties of the confidence intervals for \( \pi \), the probability of mutation. Almost sure estimators, as noted, are always consistent and if bounded, asymptotically unbiased estimators. This concept is, in a sense, an extension of Kolmogorov's Strong Law of Large Numbers.

Further work could be done in investigating the possible truth of these theorems when the assumption of boundedness is dropped by working with truncated random variables. Also, it may be possible to derive sharper bounds by evaluating the second and fourth moments exactly, and rather than bounding these expressions, leave them in the expanded form. In the applications then, it would be possible to use Tukey's multiple-k statistics to possibly obtain sharper bounds.

Recognition should be made of two articles which appeared in Pub. Math. Inst. Hungarian Acad. Science written by Erdös P. and Ré'myi, A. (1959), and Hajek, J. (1960). These articles were not available for perusal at the time of this writing, but from the reference made to the articles in Chapter II of Sampling Techniques by Cochran; 2nd Edition, it was felt that the central limit theorems obtained in this paper were proved in an entirely different setting and are new results.


Alberda, W.J.
Two central limit theorems...