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ON TESTING FOR INDEPENDENCE OF UNBIASED COIN TOSSES LUMPED IN GROUPS TOO SMALL TO USE χ^2

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In genetics research and perhaps in other fields also, if we encounter data classified into two categories known to be equally likely, we may suspect that the individual observations are not independent and hence do not observe the binomial distribution, and we may wish to find out whether this suspicion is correct. If the groups (families, e.g.) into which the observations are lumped are sufficiently large, we may use the χ^2 test to test for independence; but if the group sizes are too small, an alternative test is needed. Such an alternative test is developed in this paper.

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ON TESTING FOR INDEPENDENCE OF UNBIASED COIN TOSSES LUMPED IN GROUPS TOO SMALL TO USE χ^2

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SUMMARY; ORIGIN OF THE PROBLEM

The problem treated in this paper manifested itself in genetics research, although it is of a general enough nature that it could arise in many other areas also. In genetics one sometimes encounters a situation where two phenotypes are known to occur in a 1:1 ratio; where data are available from (say) N families, the i-th family ($i = 1, 2, \ldots, N$) producing x_i offspring observed to be of one phenotype and $(n_i - x_i)$ offspring of the other phenotype; and where it is suspected that some factor (such as gonial crossing-over, e.g.) may be operating to cause the random variables x_i to have greater dispersion than they would under the model of n_i independent tosses of an unbiased coin. If the factor (gonial crossing-over, e.g.) is not present, then each x_i will behave as a binomial variate with parameters n_i and $\frac{1}{2}$; if the factor is present, then it is presumed that the two phenotypes will still occur in a 1:1 expected ratio and that the distribution of x_i will still be symmetric, but that the distribution of x_i will be heavier in the tails and lighter in the middle than the binomial

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distribution. To test the null hypothesis that the factor is absent against the alternative hypothesis that the factor is present, it is appropriate to use χ^2 with N degrees of freedom (and reject the null hypothesis for large χ^2 values), provided that the n_i's (the family or group sizes) are of sufficient magnitude for the χ^2 test. If the n_i's are too small to allow us to use χ^2, however, we need to have a test available in place of χ^2. Such a test is developed in this paper, and a numerical example based on some genetics data is presented.

Essentially the same basic (statistical) problem which gave rise to this paper has been recognized and considered before, by Grüneberg and Haldane (1937). The test employed by those authors, however, is evidently usable only when N is of a magnitude somewhat greater than that required for our test.

Although our test was developed specifically for the purpose of handling a situation where the n_i's are too small to use χ^2, we should mention that there is no reason why our test cannot also be used, if desired, even in the case where the n_i's are large enough for χ^2.

1. INTRODUCTION

We suppose that we have random variables z_{ij} ($j = 1, 2, \ldots, n_i$; $i = 1, 2, \ldots, N$) such that the <u>marginal</u> distribution for each z_{ij} corresponds to the model for the toss of an unbiased coin, i.e.,

$$(1.1) \qquad P\left\{z_{ij} = 0\right\} = \frac{1}{2}, \qquad P\left\{z_{ij} = 1\right\} = \frac{1}{2}$$

for all (i, j). The z_{ij}'s, however, are unobservable: we assume that it is possible to observe only the quantities

$$x_i = \sum_{j=1}^{n_i} z_{ij}$$

(1.2) and

$$x_i' = \sum_{j=1}^{n_i} (1 - z_{ij}) = n_i - x_i$$

for $i = 1, 2, \ldots, N$. Under either the null hypothesis or the alternative hypothesis, we assume that the vector random variables z_i [where $z_i(n_i \times 1) = (z_{i1}, z_{i2}, \ldots, z_{in_i})'$] are mutually independent (thereby implying that the x_i's are mutually independent), and that (1.1) holds.

We consider a null hypothesis H_o which specifies that, for each i, the elements of z_i are mutually independent. Hence, under H_o, the density function of x_i is

$$(1.3) \qquad \phi_{n_i}(x_i) = 2^{-n_i} \binom{n_i}{x_i} \quad .$$

We will consider alternative hypotheses H_1 which specify that the elements of z_i are <u>not</u> mutually independent. More specifically, we will be primarily concerned with alternative hypotheses under which (roughly speaking) either (a) the larger values of $|x_i - \frac{1}{2} n_i|$ generally occur with greater frequency than under H_o (1.3), and the smaller values with lesser frequency; or (b) the larger values of $|x_i - \frac{1}{2} n_i|$ generally occur with lesser frequency than under H_o (1.3), and the smaller values with greater frequency. We will refer to these two situations as alternative hypotheses of the forms H_{1a} and H_{1b} respectively. Thus, under an alternative hypothesis of the form H_{1a}, the distribution of x_i spreads out more into the tails than does (1.3) (roughly speaking); under an alternative hypothesis of the form H_{1b}, the distribution of x_i is bunched in the center more than (1.3).

In the particular problem which motivated this paper, the alternative hypothesis was (as already indicated) of the form H_{1a}. Because of this, our emphasis in this paper, particularly in Section 3, will be slightly more on the H_{1a} situation than the H_{1b}. However, the general approach we develop in Section 2 will be just as applicable to H_{1b} as to H_{1a}.

We will assume that, for any alternative hypothesis we consider, the distribution of z_i will be determined solely by n_i. In other words, for any (i, I)

such that $n_i = n_I$, the distribution of z_i will be the same as the distribution of z_I (under any permissible alternative hypothesis).

If the n_i's (the group sizes) are sufficiently large, the statistic

$$(1.4) \qquad \chi^2 = \sum_{i=1}^{N} (x_i - \tfrac{1}{2} n_i)^2/(\tfrac{1}{4} n_i)$$

will follow approximately the χ^2 distribution with N degrees of freedom if H_o [see (1.3)] is true. To test H_o against an alternative of the form H_{1a}, we reject H_o at the α-level if χ^2 (1.4) exceeds the $(1-\alpha)$ fractile of the χ^2_N distribution; to test H_o against an alternative of the form H_{1b}, we reject H_o at the α-level if χ^2 (1.4) falls short of the α fractile of the χ^2_N distribution.

This χ^2 test cannot be used, however, if the n_i's do not satisfy certain minimum requirements. A traditional rule-of-thumb for using χ^2 is that the expected frequency in every cell should be ≥ 5 (which, in our case, would be equivalent to requiring that every n_i be ≥ 10). More recently, some authors [see Cochran (1952), e.g.] have maintained that this rule-of-thumb can be liberalized to a certain extent, and that some of the expected cell frequencies can be permitted to drop below 5 under certain conditions. Regardless of what rule is accepted, though, experimental situations can clearly arise in which the rule says that the n_i's are not large enough for the χ^2 test to be satisfactorily accurate.

In such situations, where χ^2 cannot be used, it is desirable to have available another test which can be used instead. This paper presents a method of constructing such an alternative test.

The test statistic we present will be approximately normally distributed under H_o rather than approximately χ^2 - distributed. Furthermore, as $N \to \infty$

(with an upper bound assumed for the n_i's), the distribution of our test statistic under H_o will tend exactly to normality in the limit; note that an analogous property is not generally true for X^2 (1.4) [i.e., if we increase N, this need not improve the approximation of the distribution of X^2 (1.4) to the X^2 distribution if the n_i's remain small].

The test used by Grüneberg and Haldane (1937) employs X^2 (1.4), but not in the usual way. The exact value of $\mathrm{var}(X^2|H_o)$ (which will be $< 2N$) is calculated, and is required for the denominator of the statistic

$$\frac{X^2 - N}{[\mathrm{var}(X^2 \mid H_o)]^{\frac{1}{2}}} \qquad (1.5)$$

Under H_o, (1.5) will be approximately $N(0,1)$ for sufficiently large N [Cochran (1952) seems to feel that N should be ≥ 60]. Thus, in the test of Grüneberg and Haldane (1937) which uses (1.5), X^2 is taken to be approximately normal under H_o rather than approximately χ^2_N - distributed (which it is not for small n_i's). However, the distribution of X^2 (1.4), like that of χ^2_N, is evidently rather slow to approach normality with increasing N; for this reason, a somewhat larger N seems to be required for the test using (1.5) than for our test.

When the n_i's are too small to use X^2, it is evident that a possible test of H_o could be obtained by pooling certain of the groups so that the sizes of the pooled groups would be sufficiently large to calculate a X^2 based on the pooled groups. However, such a X^2 test, in addition to forcing arbitrary decisions as to how the pooling would be done, would apparently have the more serious disadvantage of adversely affecting the power of the test at least against certain alternatives. Thus it looks as though we should, if possible, avoid this kind of test of H_o.

Our proposed technique of testing H_o will be introduced in Section 2; also in Section 2 it will be demonstrated that our test statistic exhibits the desired behavior under the null hypothesis. Section 3 deals with the role of the alternative hypothesis. Section 4, which is intended to suit the needs of the non-mathematical reader, treats a numerical example based on data from a genetics experiment.

2. THE TEST STATISTIC, AND ITS BEHAVIOR UNDER H_o

We will start by constructing some new random variables which are functions of the x_i's (1.2). In this section and the next section, we will sometimes drop the subscript i on x_i and n_i, and write simply x and n respectively. Suppose we let

$$(2.1) \qquad r_i = \min(x_i, n_i - x_i) \text{ or simply } r = \min(x, n-x) \quad .$$

We remark that we can obtain from (1.3) the distribution of $r(2.1)$ under the null hypothesis: using f_{nr} to denote the density function of r under H_o, we can write, if n is odd $(n = 2m + 1, \text{ say})$,

$$(2.2a) \qquad f_{nr} = 2^{1-n} \binom{n}{r} \quad (\text{for } r = 0, 1, 2, \ldots, m) \quad ,$$

and if n is even $(n = 2M, \text{ say})$,

$$(2.2b) \qquad \begin{aligned} f_{nr} &= 2^{1-n} \binom{n}{r} \quad (\text{for } r = 0, 1, 2, \ldots, M-1) \\ &= 2^{-n} \binom{n}{r} \quad (\text{for } r = M) \end{aligned} \quad .$$

We will define random variables

$$(2.3a) \qquad y = y_{nr} = 2^{-n} \left[2 \sum_{k=0}^{r-1} \binom{n}{k} + \binom{n}{r} \right] \quad (\text{for } r = 0,1,2,\ldots,m)$$

for n odd $(n = 2m + 1)$, and

$$\text{(2.3b)} \qquad y = y_{nr} = 2^{-n} \left[2 \sum_{k=0}^{r-1} \binom{n}{k} + \binom{n}{r} \right] \quad (\text{for } r = 0, 1, 2, \ldots, M-1)$$

$$= 2^{-n} \left[2 \sum_{k=0}^{r-1} \binom{n}{k} + \frac{1}{2} \binom{n}{r} \right] \text{ (for } r=M\text{), i.e., } y_{nM} = 1-2^{-n-1}\binom{n}{M}$$

for n even ($n = 2M$). We also define $y_i = y_{n_i r_i}$. In the notation (2.3), remember that n is a constant and r is a random variable.

Our proposed technique for testing the null hypothesis H_o against an alternative of the form H_{1a} or H_{1b} will be based on a test statistic of the form

$$\text{(2.4)} \qquad u = \sum_{i=1}^{N} w_i \; y_i \qquad ,$$

which is a weighted linear combination of the y's (2.3). The special desirable property possessed by these y's (2.3) has to do with their expectations: we will show that

$$\text{(2.5)} \qquad E(y_{nr}) = \frac{1}{2} \quad (\text{for all } n) \quad \text{under } H_o \quad ,$$

whereas it appears that $E(y_{nr})$ should generally be $< \frac{1}{2}$ or $> \frac{1}{2}$ under the respective (as yet somewhat imprecisely defined) alternative hypotheses H_{1a} or H_{1b} [in fact, see (3.1 - 3.2)].

At the end of this section we will prove that, under H_o, the distribution of

$$\text{(2.6)} \qquad Z = \frac{u - E(u \mid H_o)}{\left[\text{var}(u \mid H_o)\right]^{\frac{1}{2}}}$$

approaches the $N(0,1)$ distribution as $N \to \infty$. Thus we will be able to conclude that, in order to test H_o against H_{1a} at (approximately) the α-level, we can use a test with critical region

$$\text{(2.7a)} \qquad Z < -z_\alpha \qquad ,$$

where z_α is the $(1-\alpha)$ fractile of the $N(0,1)$ distribution; and that, in order to test H_o against H_{1b}, we can use the critical region

$$(2.7b) \qquad Z > z_\alpha \quad .$$

The consistency of the tests (2.7) will be discussed in Section 3.

The weights w_i in (2.4) are constants whose selection must of course not be influenced by knowledge of the y_i's (or r_i's). It seems appropriate to try to choose the w_i's in such a way as to maximize the power of the test against the alternative hypothesis, and this line of approach will be explored more fully in Section 3. Beacuse of our assumption, indicated in Section 1, to the effect that the distribution of z_i is determined solely by n_i (for any alternative hypothesis), it would seem logical to stipulate that w_i should also be determined solely by n_i:

$$(2.8) \qquad w_i = w(n_i) \quad .$$

Except for this restriction (2.8), however, our development in this section will be in terms of general w_i's, and will be valid for any appropriate weight function $w(n)$ which might be chosen.

<u>Expectation of y under H_o.</u> We now prove (2.5). First note that, if n is odd $(n = 2m + 1)$, then

$$(2.9) \quad \sum_{r=0}^{m} \binom{n}{r}\left[2\sum_{k=0}^{r-1}\binom{n}{k} + \binom{n}{r}\right] = 2\sum_{0 \le k < r \le m}\binom{n}{k}\binom{n}{r} + \sum_{r=0}^{m}\binom{n}{r}^2$$

$$= \left[\sum_{r=0}^{m}\binom{n}{r}\right]^2 = \left[\frac{1}{2}\cdot 2^n\right]^2 = 2^{2n-2} ,$$

and if n is even $(n = 2M)$, then

$$(2.10)\quad \sum_{r=0}^{M-1} \binom{n}{r} \left[2 \sum_{k=0}^{r-1} \binom{n}{k} + \binom{n}{r} \right] = \left[\sum_{r=0}^{M-1} \binom{n}{r} \right]^2 = \left[\frac{1}{2} \left\{ 2^n - \binom{n}{M} \right\} \right]^2$$

$$= 2^{2n-2} - 2^{n-1} \binom{n}{M} + \frac{1}{4} \binom{n}{M}^2 .$$

From (2.2a), (2.3a), and (2.9) we obtain

$$(2.11)\quad E(y_{nr} | H_o) = \sum_{r=0}^{m} f_{nr}\, y_{nr} = 2^{1-n} \cdot 2^{-n} \cdot 2^{2n-2} = \frac{1}{2} \text{ (for odd } n\text{)};$$

from (2.2b), (2.3b), and (2.10) we obtain

$$(2.12)\quad E(y_{nr} | H_o) = \sum_{r=0}^{M-1} f_{nr}\, y_{nr} + f_{nM}\, y_{nM}$$

$$= 2^{1-2n} \left[2^{2n-2} - 2^{n-1} \binom{n}{M} + \frac{1}{4} \binom{n}{M}^2 \right] + 2^{-n} \binom{n}{M} \left[1 - 2^{-n-1} \binom{n}{M} \right] = \frac{1}{2}$$

(for even n) .

Thus (2.11) and (2.12) together prove (2.5).

Note that (2.4) and (2.5) give us

$$(2.13)\quad E(u \mid H_o) = \frac{1}{2} \sum_{i=1}^{N} w_i .$$

<u>Variance of y under H_o.</u> Observe from (2.4) that

$$(2.14)\quad \operatorname{var}(u \mid H_o) = \sum_{i=1}^{N} w_i^2\, v(n_i) ,$$

where we define

$$(2.15)\quad v(n) = \operatorname{var}(y_{nr} \mid H_o) .$$

Thus, in order to be able to calculate the denominator of (2.6), we will need to have available the values of $v(n)$ (2.15) .

We proceed to develop formulas for these variances. First we establish two combinatorial identities. For odd n, we get

$$(2.16)\quad \sum_{r=0}^{m}\binom{n}{r}\left[2\sum_{k=0}^{r-1}\binom{n}{k}+\binom{n}{r}\right]^2=\sum_{r=0}^{m}\binom{n}{r}\left[8\sum_{0\le k<\ell\le r-1}\binom{n}{k}\binom{n}{\ell}+4\sum_{k=0}^{r-1}\binom{n}{k}^2\right.$$

$$\left.+\;4\sum_{k=0}^{r-1}\binom{n}{k}\binom{n}{r}+\binom{n}{r}^2\right]$$

$$=(4/3)\left[6\sum_{0\le k<\ell<r\le m}\binom{n}{k}\binom{n}{\ell}\binom{n}{r}+3\sum_{0\le k<r\le m}\binom{n}{k}^2\binom{n}{r}\right.$$

$$\left.+\;3\sum_{0\le k<r\le m}\binom{n}{k}\binom{n}{r}^2+\sum_{r=0}^{m}\binom{n}{r}^3\right]-(1/3)\sum_{r=0}^{m}\binom{n}{r}^3$$

$$=(4/3)\left[\sum_{r=0}^{m}\binom{n}{r}\right]^3-(1/3)\sum_{r=0}^{m}\binom{n}{r}^3$$

$$=(4/3)\left[\tfrac{1}{2}\cdot 2^n\right]^3-(1/3)\sum_{r=0}^{m}\binom{n}{r}^3$$

$$=(1/3)\,2^{3n-1}-(1/6)\,S_n\qquad ,$$

where we define

$$(2.17)\qquad S_n=\sum_{r=0}^{n}\binom{n}{r}^3 \qquad .$$

In a similar manner, we obtain for even n the identity

$$(2.18)\quad \sum_{r=0}^{M-1}\binom{n}{r}\left[2\sum_{k=0}^{r-1}\binom{n}{k}+\binom{n}{r}\right]^2=(4/3)\left[\sum_{r=0}^{M-1}\binom{n}{r}\right]^3-(1/3)\sum_{r=0}^{M-1}\binom{n}{r}^3$$

$$=(4/3)\left[\tfrac{1}{2}\left\{2^n-\binom{n}{M}\right\}\right]^3-(1/3)\sum_{r=0}^{M-1}\binom{n}{r}^3$$

$$=(1/3)\,2^{3n-1}-2^{2n-1}\binom{n}{M}+2^{n-1}\binom{n}{M}^2-(1/6)S_n\quad ,$$

S_n again being defined by (2.17) .

We now use (2.2a), (2.3a), and (2.16) to get

$$(2.19a)\quad v(n) = \sum_{r=0}^{m} f_{nr}\, y_{nr}^2 - \frac{1}{4}$$

$$= (1/12) - (1/3)\, 2^{-3n}\, S_n \qquad (\text{for odd } n) \quad .$$

From (2.2b), (2.3b) and (2.18) we obtain

$$(2.19b)\quad v(n) = \sum_{r=0}^{M-1} f_{nr}\, y_{nr}^2 + f_{nM}\, y_{nM}^2 - \frac{1}{4}$$

$$= (1/12) - (1/3)\, 2^{-3n}\, S_n + 2^{-3n-2}\binom{n}{M}^3 \qquad (\text{ for even } n) \quad .$$

The values of $v(n)$, as calculated by the formulas (2.19), are exhibited in Table 2.1 for $n = 1, 2, \ldots, 20$. Table 2.1 also presents (as a matter of information) the values of S_n (2.17), which were obtained via the recursion formula

$$(2.20)\qquad n^2 S_n = (7n^2 - 7n + 2)\, S_{n-1} + 8(n-1)^2\, S_{n-2} \quad .$$

This formula (2.20) was derived by Franel (1894), and is listed by Gould (1959) [see p. 69, formula (X.13)].

TABLE 2.1. Values of S_n (2.17) and $v(n)$ (2.19) .

n	S_n	v(n)
1	2	.000000
2	10	.062500
3	56	.046875
4	346	.068359
5	2,252	.060425
6	15,184	.071655
7	104,960	.066650
8	739,162	.073759
9	5,280,932	.070218
10	38,165,260	.075211
11	278,415,920	.072529
12	2,046,924,400	.076274
13	15,148,345,760	.074148
14	112,738,423,360	.077087
15	843,126,957,056	.075346
16	6,332,299,624,282	.077728
17	47,737,325,577,620	.076267
18	361,077,477,684,436	.078247
19	2,739,270,870,994,736	.076997
20	20,836,827,035,351,596	.078677

Observe that, if we substitute (2.4), (2.13), and (2.14) into (2.6), we obtain a computing formula for Z:

$$(2.21) \qquad Z = \frac{\sum_{i=1}^{N} w_i y_i - \frac{1}{2} \sum_{i=1}^{N} w_i}{\left[\sum_{i=1}^{N} w_i^2 \; v(n_i) \right]^{\frac{1}{2}}} .$$

We now show that Z has the limiting distribution which was previously indicated.

Asymptotic normality of Z under H_o. To prove that Z (2.6, 2.21) is asymptotically $N(0,1)$ under H_o, we will utilize Liapounoff's version of the central limit theorem. In order to simplify our argument, we will assume an upper bound on the n_i's: we specify that there exists an integer n_o such that

$$(2.22) \qquad n_i \leq n_o \qquad \text{for all } i .$$

We also assume that there are no groups with $n_i = 1$ (such groups could contribute nothing to testing the hypothesis anyway). Our proof will be valid for any weight function $w(n)$ [see (2.8)], provided that $w(n) > 0$ for all $n \geq 2$.

Let us define

$$(2.23) \qquad \begin{aligned} K_1 &= \min \left[w(2), w(3), \ldots, w(n_o) \right] \\ K_2 &= \max \left[w(2), w(3), \ldots, w(n_o) \right] \end{aligned}$$

and

$$(2.24) \qquad K_3 = \min \left[v(2), v(3), \ldots, v(n_o) \right] .$$

Now K_1 is > 0 by assumption. Hence it follows from (2.8), (2.22), and (2.23) that

$$(2.25) \qquad 0 < K_1 \leq w_i \leq K_2 \qquad \text{for all } i .$$

It is easily shown [via an induction proof based on formula (2.20), e.g.] that $v(n) > 0$ for all $n \geq 2$. Hence K_3 is > 0, and it follows from (2.22) and (2.24) that

(2.26) $$0 < K_3 \leq v(n_i) \qquad \text{for all } i \quad .$$

We are now in a position to show that the independent but non-identically distributed random variables

(2.27) $$u_i = w_i \; y_i$$

satisfy the Liapounoff condition under H_o. Let ρ_i^3 be the third absolute central moment of u_i (2.27) under H_o. From (2.3) we know that $0 \leq y \leq 1$. Hence

(2.28) $$\rho_i^3 = w_i^3 \; E(|y_i - \tfrac{1}{2}|^3) \leq w_i^3 \quad .$$

If we let σ_i^2 be the variance of u_i (2.27) under H_o, then

(2.29) $$\sigma_i^2 = w_i^2 \, v(n_i) \quad .$$

Using (2.28), (2.29), (2.26), and (2.25), we find that

$$\frac{\left[\sum_{i=1}^{N} \rho_i^3\right]^{\frac{1}{3}}}{\left[\sum_{i=1}^{N} \sigma_i^2\right]^{\frac{1}{2}}} \leq \frac{\left[\sum_{i=1}^{N} w_i^3\right]^{\frac{1}{3}}}{\left[K_3 \sum_{i=1}^{N} w_i^2\right]^{\frac{1}{2}}} \leq \frac{\left[N \, K_2^3\right]^{\frac{1}{3}}}{\left[K_3 \, N \, K_1^2\right]^{\frac{1}{2}}} = \frac{K_2}{K_1 \, K_3^{\frac{1}{2}}} \, N^{-\frac{1}{6}} \quad ,$$

which $\longrightarrow 0$ as $N \longrightarrow \infty$. Hence the Liapounoff condition is established for the u_i's (2.27) under H_o, and (since $u = \sum_{i=1}^{N} u_i$) it follows immediately that Z(2.6, 2.21) has the $N(0,1)$ limiting distribution.

We have not made any very detailed attempts to investigate how rapidly the distribution of Z approaches normality, or how large N needs to be in order for the normal approximation to be sufficiently accurate. However, we might simply point out that, for $n = 2$ and 3, y_{nr} (2.3) is essentially a binomial variate; and that, as n becomes large, it looks as though the distribution of y_{nr} tends to the uniform (rectangular) distribution on the interval $[0, 1]$. Since the distribution of a sum of binomial variates and the distribution of a sum of rectangular variates both approach normality rather rapidly, we might be justified in suspecting that the distribution of Z converges to normality with roughly the same order of rapidity. The numerical example which we give in Section 4 has $N = 11$.

3. THE ROLE OF THE ALTERNATIVE HYPOTHESIS

In Section 1, alternative hypotheses of the forms H_{1a} and H_{1b} were "defined" heuristically in language which was mathematically somewhat vague. Now that we have defined the y's (2.3), however, we are in a position to set up bona fide definitions for H_{1a} and H_{1b}, definitions which may seem to be less meaningful but which will be mathematically precise:

We say that an alternative hypothesis is of the form H_{1a} if

$$(3.1) \qquad E(y_{nr} \mid H_{1a}) < \frac{1}{2} \qquad \text{for all } n \geq 2 \quad .$$

Similarly, we say that an alternative hypothesis is of the form H_{1b} if

$$(3.2) \qquad E(y_{nr} \mid H_{1b}) > \frac{1}{2} \qquad \text{for all } n \geq 2 \ .$$

Our "definitions" of H_{1a} and H_{1b} given in Section 1 were based on intuitive notions. The definitions (3.1 - 3.2) represent an attempt to translate these intuitive notions into precise terms, the y's (2.3) having been constructed explicitly for the purpose of discriminating between H_o and H_{1a} or H_{1b}.

<u>Consistency of the tests (2.7).</u> In establishing consistency, we will make the same assumptions as in the asymptotic normality proof: no n_i's equal to 1, $w(n) > 0$ for all $n \geq 2$, and the assumption (2.22). Under these assumptions, the test (2.7a) is consistent against all alternatives of the form H_{1a} (3.1), and the test (2.7b) is consistent against all alternatives of the form H_{1b} (3.2). We need prove only the first of these two statements, since the proof for H_{1b} is analogous to that for H_{1a}.

Let us define

$$(3.3) \qquad d_n = \frac{1}{2} - E(y_{nr} \mid H_{1a})$$

and

$$(3.4) \qquad D = \min(d_2, d_3, \ldots, d_{n_o}) \quad .$$

From (3.1) it follows that $D > 0$. We also define

$$(3.5) \qquad W_i = w_i / (\sum_{I=1}^{N} w_I) \quad .$$

Applying (2.25) to (3.5), we find that

$$(3.6) \qquad W_i \leq K_2 / N K_1 \quad .$$

Now, since $0 \leq y_i \leq 1$, var (y_i) will be ≤ 1 under either H_o or H_{1a}. Hence we conclude from (3.6) that

$$(3.7) \quad \text{var}(\sum_{i=1}^{N} W_i y_i) \leq K_2^2 / N K_1^2 \qquad \text{(under either } H_o \text{ or } H_{1a}) \quad .$$

Having established these preliminaries, we use (2.7a), (2.21), (3.5), (3.3), and (3.4) to write

$$\begin{aligned}(3.8) \quad P\left\{\text{rejecting } H_o\right\} &= P\left\{Z < -z_\alpha\right\} = P\left\{\Sigma\, w_i(y_i - \tfrac{1}{2}) < - z_\alpha [\text{var}(\Sigma\, w_i y_i | H_o)]^{1/2}\right\} \\ &= P\left\{\Sigma\, W_i y_i - E(\Sigma\, W_i y_i | H_{1a}) < - z_\alpha [\text{var}(\Sigma\, W_i y_i | H_o)]^{\frac{1}{2}} + \Sigma\, W_i\, d_{n_i}\right\} \\ &\geq P\left\{\Sigma\, W_i y_i - E(\Sigma\, W_i y_i | H_{1a}) < D - z_\alpha [\text{var}(\Sigma\, W_i y_i | H_o)]^{\frac{1}{2}}\right\} .\end{aligned}$$

From (3.7) it follows that the expression on the right of the $<$ sign in the last line of (3.8) will become positive for sufficiently large N. Hence, for large enough N, we may apply Tchebycheff's inequality to (3.8) to obtain

$$(3.9)\qquad P\left\{\text{rejecting } H_o \mid H_{1a}\right\} \geq 1 - \frac{\operatorname{var}(\Sigma W_i y_i \mid H_{1a})}{\left\{D - z_\alpha \left[\operatorname{var}(\Sigma W_i y_i \mid H_o)\right]^{\frac{1}{2}}\right\}^2} .$$

Again utilizing (3.7), we see that the right-hand side of (3.9) $\rightarrow 1$ as $N \rightarrow \infty$. This completes the consistency proof.

Selection of the weight function $w(n)$. In Section 2 we indicated that it would be sensible to try to choose the weight function $w(n)$ in such a way as to maximize the power of the test against the alternative hypothesis. The remainder of Section 3 will be concerned with this problem. Our approach will be to try to find some sort of rational basis for choosing $w(n)$ rather than to attempt a more rigorous (and more complicated) development aimed at finding a more exact solution to a problem of maximizing the power. In other words, our line of argument will be heuristic to a certain extent, since there will be a few steps which will represent approximations or which we will not justify rigorously. This lack of rigor at this stage of the game will not be particularly disadvantageous, however, in the sense that all of the results which we have already proved are valid for any choice of $w(n)$ [so long as $w(n) > 0$ for all $n \geq 2$]; thus, in this sense, it does not matter how $w(n)$ is obtained. In the remainder of the paper, we will consider in detail only alternative hypotheses of the form H_{1a}, since (as indicated previously) the problem motivating this paper was concerned with an alternative hypothesis of the form H_{1a} rather than H_{1b}.

For the test (2.7a), we can use (2.6, 2.21) and (3.3) to write

$$(3.10)\qquad P\left\{\text{rejecting } H_o\right\} = P\left\{Z < -z_\alpha\right\} = P\left\{\frac{u - E(u \mid H_{1a})}{\left[\operatorname{var}(u \mid H_{1a})\right]^{\frac{1}{2}}} < \frac{-z_\alpha \left[\operatorname{var}(u \mid H_o)\right]^{\frac{1}{2}} + \sum_{i=1}^{N} w_i d_{n_i}}{\left[\operatorname{var}(u \mid H_{1a})\right]^{\frac{1}{2}}}\right\}.$$

If u (2.4) is approximately normally distributed under an alternative hypothesis of the form H_{1a}, then we can conclude from (3.10) that the power of the test (2.7a) against H_{1a} is approximately

$$(3.11)\qquad \Phi\left(\frac{[\mathrm{var}(u|H_o)]^{\frac{1}{2}}}{[\mathrm{var}(u|H_{1a})]^{\frac{1}{2}}}\left\{-z_\alpha+\frac{\sum_{i=1}^{N} w_i\, d_{n_i}}{[\sum_{i=1}^{N} w_i^2\, v(n_i)]^{\frac{1}{2}}}\right\}\right)\qquad,$$

where $\Phi(\cdot)$ is the $N(0,1)$ c.d.f. To maximize (3.11) (with respect to the w_i's), it of course suffices to maximize the argument of Φ. Instead of maximizing the entire argument in (3.11), however, we will attack the much more tractable task of maximizing only that portion of the argument between the curly brackets, and will hope that the w_i's thus obtained will result in producing approximately the maximum possible value of the entire argument. It would seem plausible that the expression $[\mathrm{var}(u|H_o)]^{1/2}/[\mathrm{var}(u|H_{1a})]^{1/2}$ may not vary too much under different choices of $w(n)$; if such be the case, then our approximation (which ignores this expression in front of the curly brackets in order to circumvent certain other problems) should not hurt us noticeably.

Maximizing the expression within the curly brackets in (3.11) is equivalent to maximizing the quantity

$$(3.12)\qquad (\Sigma\, w_i\, d_{n_i})^2/(\Sigma\, w_i^2\, v_i)\qquad,$$

where v_i denotes $v(n_i)$. First we use Cauchy's inequality to write

$$(3.13)\qquad [\Sigma(w_i v_i^{\frac{1}{2}})(d_{n_i}\, v_i^{-\frac{1}{2}})]^2 \le [\Sigma\, w_i^2\, v_i][\Sigma\, d_{n_i}^2/v_i]\quad.$$

Since (3.13) tells us that (3.12) cannot exceed $\Sigma\, d_{n_i}^2/v_i$ for any choice of the w_i's, it follows that (3.12) achieves its maximum value ($= \Sigma\, d_{n_i}^2/v_i$) with respect to the w_i's if we put $w_i = d_{n_i}/v_i$, i.e., if we use

$$(3.14) \qquad w(n) = d_n/v(n)$$

as the weight function. Thus, it appears that the weight function (3.14) approximately maximizes the power of the test (2.7a) against an alternative of the form H_{1a} (3.1).

Although the denominator of (3.14) will clearly be the same for all alternative hypotheses, the numerator will be different. The imagination can concoct a number of alternative hypotheses seeming to be of the form H_{1a}, each with its own d_n's (3.3). Here, however, it will suffice for us to explore two such hypotheses, to be designated as H_{1aA} and H_{1aB}. For both of these, we will evaluate the d_n's when the H_{1a} is "close" to H_o, and the two sets of d_n's will turn out to be markedly different from each other.

Alternative hypothesis H_{1aA}. In the first of our two alternative hypotheses, we suppose that the z_{ij}'s are determined as follows. Let z_{i1} be determined according to (1.1). For $j > 1$, we suppose that, with probability $(1-\delta)$, z_{ij} is determined by a coin toss [as in (1.1)], but that the remaining δ of the time z_{ij} automatically assumes the same value as $z_{i,j-1}$; in other words,

$$(3.15) \qquad P\left\{z_{ij} = z_{i,j-1}\right\} = \frac{1}{2}(1-\delta) + \delta = \frac{1+\delta}{2} \qquad (j > 1)$$

$$P\left\{z_{ij} \neq z_{i,j-1}\right\} = \frac{1-\delta}{2} \qquad (j > 1) ,$$

where the statement "$z_{ij} \neq z_{i,j-1}$" means that $z_{ij} = 1$ if $z_{i,j-1} = 0$ and vice versa.

If $\phi^*_{n_i}(x_i)$ denotes the density function of x_i under H_{1a}, then we can deduce from (3.15) that

$$(3.16)\quad \phi_n^*(x) = \sum_{R=1}^{n} \left[\binom{n}{x} g_{nx}(R)\right] \left[\frac{1}{2}\left(\frac{1+\delta}{2}\right)^{n-R} \left(\frac{1-\delta}{2}\right)^{R-1}\right] ,$$

where R represents the number of runs in a sequence of x 1's and $(n-x)$ 0's, and where $\left[\binom{n}{x} g_{nx}(R)\right]$ is the total possible number of such sequences containing exactly R runs. That is, $g_{nx}(R)$ can be thought of as the probability of obtaining R runs in a randomly arranged sequence of x 1's and $(n-x)$ 0's, assuming all $\binom{n}{x}$ possible sequences to be equally likely; the formula for $g_{nx}(R)$ is given (e.g.) by Feller (1950) [see p. 57, formulas (4.1 - 4.2)]. Re-writing (3.16) [and remembering that $g_{nx}(R)$ can be thought of as a density function], we obtain

$$(3.17)\quad \phi_n^*(x) = 2^{-n}\binom{n}{x}\left\{\sum_{R=1}^{n} g_{nx}(R) + \delta \sum_{R=1}^{n}(n-2R+1)\, g_{nx}(R)\right\} + 0(\delta^2)$$

$$= \phi_n(x) + 2^{-n}\binom{n}{x}\left[(n+1) - 2\sum_{R=1}^{n} R\, g_{nx}(R)\right]\delta + 0(\delta^2) ,$$

where $\phi_n(x)$ is defined by (1.3). Now we may interpret $\Sigma R\, g_{nx}(R)$ as being simply the expectation of R, the formula for which is well-known [see Dixon and Massey (1957), p. 289 or 422, or utilize Feller (1950), Chapter 9, Problem 12, pp. 188 and 406]:

$$(3.18)\quad \sum_{R=1}^{n} R\, g_{nx}(R) = \frac{2x(n-x)}{n} + 1 .$$

Substituting (3.18) into (3.17), we end up with

$$(3.19)\quad \phi_n^*(x) = \phi_n(x) + 2^{-n}(n-1)\left[\binom{n}{x} - 4\binom{n-2}{x-1}\right]\delta + 0(\delta^2) .$$

If f_{nr}^* denotes the density function for r under H_{1a}, then for H_{1aA} (and also for H_{1aB}, it will turn out) we can write the formulas

$$(3.20a)\quad f_{nr}^* = 2\,\phi_n^*(r) \qquad (\text{for } r = 0, 1, 2, \ldots, m)$$

for odd $n (n = 2m + 1)$, and

$$(3.20b)\qquad f^*_{nr} = 2\,\phi^*_n(r) \qquad (\text{for } r = 0, 1, 2, \ldots, M-1)$$
$$= \phi^*_n(r) \qquad (\text{for } r = M)$$

for even $n (n = 2M)$. Before we proceed to use (3.19 - 3.20) to evaluate d_n (3.3), however, we will first need to establish some combinatorial identities.

First note that

$$(3.21)\quad 2\sum_{k=0}^{s}\binom{n}{k} + \binom{n}{s+1} = 2\sum_{k=0}^{s}\left[\binom{n-2}{k-2} + 2\binom{n-2}{k-1} + \binom{n-2}{k}\right] + \left[\binom{n-2}{s-1} + 2\binom{n-2}{s} + \binom{n-2}{s+1}\right]$$

$$= 4\left[2\sum_{k=0}^{s-1}\binom{n-2}{k} + \binom{n-2}{s}\right] + \binom{n-2}{s+1} - \binom{n-2}{s-1} \quad .$$

If n is odd $(n = 2m + 1)$, we can use (3.21) and (2.9) to write

$$(3.22)\quad \sum_{r=0}^{m}\binom{n-2}{r-1}\left[2\sum_{k=0}^{r-1}\binom{n}{k} + \binom{n}{r}\right] = \sum_{s=0}^{m-1}\binom{n-2}{s}\left[2\sum_{k=0}^{s}\binom{n}{k} + \binom{n}{s+1}\right]$$

$$= 4\cdot 2^{2(n-2)-2} + \sum_{s=0}^{m-1}\binom{n-2}{s}\left[\binom{n-2}{s+1} - \binom{n-2}{s-1}\right]$$

$$= 2^{2n-4} + \frac{1}{4}\binom{2m}{m}^2 \quad .$$

Similarly, for even $n (n = 2M)$, we use (3.21) and (2.10) to obtain

$$(3.23)\quad \sum_{r=0}^{M-1}\binom{n-2}{r-1}\left[2\sum_{k=0}^{r-1}\binom{n}{k} + \binom{n}{r}\right] = \sum_{s=0}^{M-2}\binom{n-2}{s}\left[2\sum_{k=0}^{s}\binom{n}{k} + \binom{n}{s+1}\right]$$

$$= 4\left[2^{2n-6} - 2^{n-3}\binom{n-2}{M-1} + \frac{1}{4}\binom{n-2}{M-1}^2\right] + \binom{n-2}{M-2}\binom{n-2}{M-1}$$

$$= 2^{2n-4} - 2^{n-3}\,\frac{n}{n-1}\binom{n}{M} + 2^{-3}\,\frac{n}{n-1}\binom{n}{M}^2 \quad .$$

From (2.9) and (3.22) we obtain for odd n the formula

$$(3.24)\quad \sum_{r=0}^{m} \left[\binom{n}{r} - 4\binom{n-2}{r-1}\right]\left[2\sum_{k=0}^{r-1}\binom{n}{k} + \binom{n}{r}\right] = -\binom{2m}{m}^2 .$$

For even n, we can apply (2.10) and (3.23) and write the formula

$$(3.25)\quad \sum_{r=0}^{M-1}\left[\binom{n}{r}-4\binom{n-2}{r-1}\right]\left[2\sum_{k=0}^{r-1}\binom{n}{k}+\binom{n}{r}\right]+\frac{1}{2}\left[\binom{n}{M}-4\binom{n-2}{M-1}\right]\left[2\sum_{k=0}^{M-1}\binom{n}{k}+\frac{1}{2}\binom{n}{M}\right]$$

$$= \left\{2^{n-1}\frac{1}{n-1}\binom{n}{M} - \frac{1}{4}\frac{n+1}{n-1}\binom{n}{M}^2\right\} + \left\{\frac{1}{2}\left[-\frac{1}{n-1}\binom{n}{M}\right]\left[2^{n}-\frac{1}{2}\binom{n}{M}\right]\right\}$$

$$= -\frac{1}{4}\frac{n}{n-1}\binom{n}{M}^2 .$$

Now that we have (3.24) and (3.25), we can evaluate d_n. Using (3.3), (3.20a), (3.19), (2.11), (2.3a), and (3.24), we get

$$(3.26)\quad d_n = \frac{1}{2} - \sum_{r=0}^{m} f^*_{nr}\, y_{nr} = 2\cdot 2^{-n}(n-1)\cdot 2^{-n}\binom{2m}{m}^2 \delta + O(\delta^2)$$

$$= 2^{-4m}\, m \binom{2m}{m}^2 \delta + O(\delta^2) \qquad \text{(for odd } n,\ n = 2m+1) .$$

By using (3.3), (3.20b), (3.19), (2.12), (2.3b), and (3.25), we obtain

$$(3.27)\quad d_n = 2\cdot 2^{-n}(n-1)\cdot 2^{-n}\left[\frac{1}{4}\frac{n}{n-1}\binom{n}{M}^2\right]\delta + O(\delta^2)$$

$$= 2^{-4M}\, M\binom{2M}{M}^2 \delta + O(\delta^2) \qquad \text{(for even } n,\ n = 2M) .$$

Thus, if δ is near 0 (i.e., if H_{1aA} is "close" to H_o), it would seem appropriate to use the weight function

$$(3.28)\quad w_A(n) = 2^{-4m}\, m\binom{2m}{m}^2 / v(n) \qquad (\text{for } n = 2m+1)$$

$$= 2^{-4M}\, M\binom{2M}{M}^2 / v(n) \qquad (\text{for } n = 2M) .$$

[There of course is no effect on Z (2.21) if $w(n)$ is multiplied by a constant, such as $1/\delta$.] If we utilize Stirling's formula, we find that

$$(3.29)\qquad 2^{-4m}\, m\binom{2m}{m}^2 \cong 1/\pi ,$$

which indicates that d_n is about the same for all n. Because of (3.29), one might consider using the weight function

$$(3.30) \qquad w_{A'}(n) = 1/v(n)$$

in place of (3.28) .

Our second alternative hypothesis will result in a weight function which is radically different from (3.28) or (3.30).

Alternative hypothesis H_{1aB}. Under H_{1aB} we suppose that, just before the z_{ij}'s are determined, a number c_i is obtained by a coin toss (so that this c_i has a 50°/o chance of being either 0 or 1). Then for any j we suppose that, with probability $(1-\delta)$, z_{ij} is determined by a coin toss [as in (1.1)], but that the remaining δ of the time z_{ij} automatically assumes the value c_i. Thus, given $c_i = 0$, the z_{ij}'s will be independent binomial variates with $P\left\{z_{ij} = 1\right\} = \frac{1}{2}(1-\delta)$; conditional on $c_i = 1$, the z_{ij}'s will be independent binomial variates with $P\left\{z_{ij} = 1\right\} = \frac{1}{2}(1+\delta)$. Hence

$$(3.31) \quad \phi_n^*(x) = \tfrac{1}{2}\binom{n}{x}\left[\tfrac{1}{2}(1-\delta)\right]^x \left[\tfrac{1}{2}(1+\delta)\right]^{n-x} + \tfrac{1}{2}\binom{n}{x}\left[\tfrac{1}{2}(1+\delta)\right]^x \left[\tfrac{1}{2}(1-\delta)\right]^{n-x}$$

for H_{1aB}. Re-writing (3.31), we have

$$(3.32) \quad \phi_n^*(x) = \frac{1}{2}\binom{n}{x} 2^{-n} (1-\delta^2)^x \left[(1+\delta)^{n-2x} + (1-\delta)^{n-2x}\right]$$

$$= \phi_n(x) + 2^{-n}\binom{n}{x}\left[-x + \binom{n-2x}{2}\right]\delta^2 + O(\delta^4)$$

$$= \phi_n(x) + 2^{-n}\binom{n}{2}\left[\binom{n}{x} - 4\binom{n-2}{x-1}\right]\delta^2 + O(\delta^4) \quad .$$

Except for the important matter of a factor of $(n/2)$, (3.32) is virtually identical with (3.19). Thanks to this similarity, all of our work in evaluating d_n for H_{1aB} has essentially already been done. We obtain

$$(3.33) \quad d_n = 2^{-4m-1}\, mn \binom{2m}{m}^2 \delta^2 + O(\delta^4) \qquad (\text{for } n = 2m+1)$$

$$= 2^{-4M-1}\, Mn \binom{2M}{M}^2 \delta^2 + O(\delta^4) \qquad (\text{for } n = 2M) \quad ,$$

corresponding to which we have the weight function

$$(3.34) \quad w_B(n) = 2^{-4m}\, mn \binom{2m}{m}^2 / v(n) \qquad (\text{for } n = 2m+1)$$

$$= 2^{-4M}\, Mn \binom{2M}{M}^2 / v(n) \qquad (\text{for } n = 2M)$$

if we consider δ^2 to be near 0 and disregard the term $O(\delta^4)$. If the numerators in (3.34) are replaced by their approximate values based on Stirling's formula, we can write the weight function

$$(3.35) \quad w_{B'}(n) = n/v(n) \quad .$$

Looking at (3.30) and (3.35), it appears possible that H_{1aA} and H_{1aB} may represent two rather extreme (and opposite) types of alternative hypotheses of the form H_{1a}. If this is so, then it might be reasonable to consider some sort of "minimax weight function", such as

$$(3.36) \quad w_{AB}(n) = 2^{-4m}\, mn^{\frac{1}{2}} \binom{2m}{m}^2 / v(n) \qquad (\text{for } n = 2m+1)$$

$$= 2^{-4M}\, Mn^{\frac{1}{2}} \binom{2M}{M}^2 / v(n) \qquad (\text{for } n = 2M)$$

or

$$(3.37) \qquad w_{A'B'}(n) = n^{\frac{1}{2}}/v(n) \quad ,$$

which lies "between" the weight functions for H_{1aA} and H_{1aB}. Such weight functions as (3.36) or (3.37) might be appropriate particularly when the exact nature of H_{1a} is only hazily envisioned.

We now make some final remarks relevant to our rather limited and somewhat heuristic investigation of the optimum weight function:

(i) The sharp difference between (3.30) and (3.35) might suggest that the use of a non-optimal weight function could have an emphatic adverse effect on the power. However, some rough calculations indicate that the power lost by using (3.30) when (3.35) should be used, or vice versa, may not be as great as one might suspect. Moreover, it appears that the maximum possible power loss which could result from use of a non-optimal weight function can be cut substantially by employing a "minimax" weight function such as (3.37) [or (3.36)].

(ii) Sometimes it might be most suitable to base the choice of $w(n)$ on experimental data. That is, the weight function to be used for a given experiment E (say) could be selected on the basis of data from a different (independent) experiment E_o (say). For example, the data from E_o could be utilized to estimate d_n by fitting a linear regression of the form $(\alpha + \beta n)$, and this E_o estimate of d_n (i.e., $\hat{\alpha} + \hat{\beta} n$) could then be used as the numerator of the weight function $w(n)$ (3.14) employed for experiment E.

(iii) A number of possible specific alternative hypotheses besides H_{1aA} and H_{1aB} can evidently be conceived of. For example, just by allowing δ to be a function of n [$\delta = \delta(n)$] in either H_{1aA} or H_{1aB}, and/or by taking weighted combinations of different H_{1a} density functions, we can obtain several new patterns for H_{1a}.

(iv) For both H_{1aA} and H_{1aB}, the formulas obtained for $w(n)$ were arrived at by assuming δ to be near 0. No attempt was made to determine whether larger values of δ would result in any important change in the suggested formulas for $w(n)$. [In fact, strictly speaking, we did not even prove (for either H_{1aA} or H_{1aB}) that (3.1) holds for larger δ; this relation (3.1) was formally proved only for δ near 0.]

(v) Although our discussion of the choice of $w(n)$ was directed only toward H_{1a}, part of our development is evidently applicable to H_{1b} also. Certainly a formula analogous to (3.14) can be obtained for H_{1b}, via an argument analogous to the one we used in getting (3.14). If, in H_{1aA}, we assume that δ is negative rather than positive in equations (3.15) ff. (which amounts to assuming that, δ of the time, z_{ij} automatically takes the value opposite from $z_{i,j-1}$, rather than the same value as $z_{i,j-1}$), then (for δ near 0) we will have an alternative hypothesis of the form H_{1b} and will end up with the weight functions $w_A(n)$ (3.28) and $w_{A'}(n)$ (3.30). There seems to be no way, however, of obtaining an alternative hypothesis of the form H_{1b} which is an analogue of H_{1aB} (3.31).

4. NUMERICAL ILLUSTRATION

For illustration we will use some data obtained by one of the authors (M.W.) in a pilot experiment which was concerned, among other things, with trying to detect gonial crossing-over [see Whittinghill (1950) for a more detailed discussion of this phenomenon] is non-irradiated *Drosophila melanogaster* females. The offspring of 12 females in this test-cross experiment were classified according to the characteristics purple eye color (pr) and straw bristle (stw), both of which are on the second chromosome. Thus each offspring belonged to one of the four categories + +, pr stw, pr +, or +stw. For purposes of the illustration here, we are not concerned with the data for the two non-cross-over classes (+ + and pr stw). The results of the classification for the two cross-over classes (pr + and + stw) are presented in the first four columns of Table 4.1. (E.g., the 6th female had $x=1$ pr + offspring and $x'=7$ +stw offspring, or a total of $n = 8$ cross-over offspring altogether.) On the average, pr + cross-overs and + stw cross-overs will occur equally often. Furthermore, if classical genetic theory holds strictly, the cross-overs for each of the 12 families should observe the binomial distribution (1.3). If some gonial crossing-over (which is not allowed for in classical theory) is present, however, the distribution will not be binomial, since the cross-overs will no longer all be independent events. Rather, in the presence of gonial crossing-over, it is expected that pr + and + stw cross-overs will still occur equally often in the long run, but that the more lop-sided ratios (lop-sided in either direction) of x to x'(pr + to + stw) will occur more frequently than in the binomial distribution (1.3). In order to determine whether the experimental data in Table 4.1 support the null hypothesis of no gonial crossing-over, we will calculate the statistic Z (2.21); we will use the one-tail test (2.7a) and reject the null hypothesis of no gonial crossing-over at the .05 level if $Z < -1.645$.

We may write the formula (2.21) more explicitly in the form

$$(4.1) \qquad Z = \frac{\sum_{i=1}^{N} w(n_i)\, y_{n_i r_i} - \frac{1}{2} \sum_{i=1}^{N} w(n_i)}{\sqrt{\sum_{i=1}^{N} [w(n_i)]^2\, v(n_i)}} ,$$

where $v(n_i)$ is obtained from Table 2.1, $y_{n_i r_i}$ is specified by (2.3), and $w(n_i)$ depends on our choice of weight function based on the suspected alternative hypothesis (see Section 3). Since it seems to be rather difficult in this case to formulate the alternative hypothesis (i.e., the hypothesis that there does exist some gonial crossing-over) in explicit mathematical terms, we will make what seems to be the relatively "safe" choice and use the "minimax" weight function (3.37) for purposes of our illustration:

$$(4.2) \qquad w(n_i) = \frac{\sqrt{n_i}}{v\,(n_i)} .$$

N in (4.1) is the number of families (females), and, in effect, is equal to 11 rather than 12 in our example, since we must discard the data for the 3rd family; any family having only one cross-over offspring ($n_i = 1$) can contribute nothing toward distinguishing between the null hypothesis and the alternative hypothesis, and is therefore discarded.

The last four columns of Table 4.1 represent the intermediate steps in the calculation of Z (4.1). The first of these four columns, r_i (2.1), is just the lesser of x_i and x_i'. The second column is obtained from Table 2.1, and the third column from formula (4.2). The final column is for $y_{n_i r_i}$ (2.3), which is a certain linear function of some binomial coefficients and is easily evaluated. For example, for $i = 1$ we have $n_1 = 5$ and $r_1 = 2$, so that [using (2.3a)] we get

$$(4.3) \quad y_{n_1 r_1} = y_{52} = 2^{-5} \left[2 \sum_{k=0}^{1} \binom{5}{k} + \binom{5}{2} \right]$$

$$= 2^{-5} \left[2(1+5) + 10 \right] = 22/32 = .6875 \quad .$$

Alternatively, we note that (2.3) may be re-written in the form

$$(4.4) \quad y_{nr} = \left[2^{-n} \sum_{k=0}^{r-1} \binom{n}{k} \right] + \left[2^{-n} \sum_{k=0}^{r} \binom{n}{k} \right] \qquad (\text{if } n \neq 2r)$$

$$= \frac{3}{2} \left[2^{-n} \sum_{k=0}^{r-1} \binom{n}{k} \right] + \frac{1}{2} \left[2^{-n} \sum_{k=0}^{r} \binom{n}{k} \right] \qquad (\text{if } n = 2r) ,$$

which tells us that y_{nr} may be obtained simply by using tables of the cumulative binomial distribution [see Owen (1962), p. 265, e.g.]; thus, if we use (4.4) to evaluate y_{52} (e.g.), we have

$$y_{52} = B(5,1,\tfrac{1}{2}) + B(5,2,\tfrac{1}{2}) = .1875 + .5000 = .6875 \quad ,$$

which is the same as (4.3). We should emphasize the difference in the formula for y_{nr} in the special case where $n = 2r$ [see (2.3b), second line, or (4.4), second line]: for $i = 12$, e.g., we have $n_{12} = 2$ and $r_{12} = 1$, so that

$$y_{n_{12}r_{12}} = y_{21} = 2^{-2}\left[2\binom{2}{0} + \frac{1}{2}\binom{2}{1}\right] = .75$$

$$\text{or} \qquad = 1 - 2^{-2-1}\binom{2}{1} = .75$$

$$\text{or} \qquad = \frac{3}{2}[.25] + \frac{1}{2}[.75] = .75 \qquad .$$

Using Table 4.1, we now calculate

$$(4.5) \quad \Sigma\, w(n_i)y_{n_ir_i} = (37.006)(.68750) + \ldots + (22.627)(.75000) = 171.3969$$

and

$$(4.6) \quad \Sigma[w(n_i)]^2\, v(n_i) = (37.006)^2\,(.060425) + \ldots + (22.627)^2(.062500) = 993.6335.$$

Plugging (4.5), (4.6), and the sum of the $w(n_i)$'s (see Table 4.1) into (4.1), we obtain

$$(4.7) \quad Z = \frac{171.3969 - \frac{1}{2}(393.597)}{\sqrt{993.6335}} = - \frac{25.4016}{31.5220} = - .806 \quad .$$

Since our computed Z-value (4.7) is not < -1.645, we donot have sufficient evidence to reject the null hypothesis (i.e., the hypothesis that there is no gonial crossing-over and that the data are binomially distributed). However, we might note that the sign of Z (4.7) is negative (as we would anticipate it to be if gonial crossing-over were present), and that the significance level corresponding to $Z = -.806$ is .21. Thus the results of the experiment are not conclusive and seem to suggest that additional investigation is needed in order to establish something definite about gonial crossing-over.

In order to get a rough idea of the sensitivity of our test for detecting gonial crossing-over, we used the artificial device of arbitrarily adding 1 to the larger of x_i and x_i' for each value of i (each family) in Table 4.1 (e.g., for $i = 8$, the data became $x = 1$, $x' = 6$, $n = 7$), and then Z (4.1) was re-computed using this artificial data. The resulting (artificial) Z turned out to be -2.80, which is highly significant (significance level = .0026). Thus this might seem to suggest that the test is rather sensitive for detecting certain departures from the null hypothesis.

In the example discussed in this section, there are both a priori and experimental reasons for believing that the two classes (pr + and + stw in this case) occur with equal likelihood (50°/o for each). Oftentimes, however, it may be desired to test the null hypothesis of independence within each set of n_i observations when it is known or suspected that the two classes do not occur with equal likelihood. In such situations, our test is of course not applicable; this problem provides a possible area for further investigation.

TABLE 4.1. Experimental data and intermediate calculations for the numerical illustration based on a genetics experiment with *Drosophila melanogaster*.

Experimental results				Calculations			
Family (Mother) i	Number of pr + offspring x_i	Number of +stw offspring x_i'	Total cross-over offspring n_i	r_i	$v(n_i)$	$w(n_i)$	$y_{n_i r_i}$
1	3	2	5	2	.060425	37.006	.68750
2	4	3	7	3	.066650	39.696	.72656
3	1	0	1				
4	6	0	6	0	.071655	34.184	.01562
5	5	1	6	1	.071655	34.184	.12500
6	1	7	8	1	.073759	38.347	.03906
7	1	2	3	1	.046875	36.950	.62500
8	1	5	6	1	.071655	34.184	.12500
9	1	2	3	1	.046875	36.950	.62500
10	11	9	20	9	.078677	56.842	.66362
11	0	2	2	0	.062500	22.627	.25000
12	1	1	2	1	.062500	22.627	.75000
Total	35	34	69			393.597	

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