

# **Essay on Cumulants of Fisher's Scores in Estimation of Linkage**

## **Publication/Creation**

c.1946

## **Persistent URL**

<https://wellcomecollection.org/works/ecapqqpu>

## **License and attribution**

You have permission to make copies of this work under a Creative Commons, Attribution, Non-commercial license.

Non-commercial use includes private study, academic research, teaching, and other activities that are not primarily intended for, or directed towards, commercial advantage or private monetary compensation. See the Legal Code for further information.

Image source should be attributed as specified in the full catalogue record. If no source is given the image should be attributed to Wellcome Collection.



Wellcome Collection  
183 Euston Road  
London NW1 2BE UK  
T +44 (0)20 7611 8722  
E [library@wellcomecollection.org](mailto:library@wellcomecollection.org)  
<https://wellcomecollection.org>

The cumulants of the distributions of Fisher's <sup>" $u_1$ " and " $u_2$ "</sup> ~~" $u_1$ " and " $u_2$ "~~ scores used in the detection and estimation of ~~partial sex~~ linkage in man.

By J. B. S. Haldane, F. R. S.

The detection of linkage <sup>between</sup> ~~in man~~ other than complete sex-linkage <sup>or linkage of sex-linked genes</sup> in man, almost invariably involves statistical methods which have been gradually developed since the pioneer work of Bernstein <sup>(1931)</sup>. Wherever one of the genes concerned is an autosomal or partially sex-linked recessive, Fisher's " $u$ " score is the method of choice, and by far the most important is the  $u_1$  score. For example this is invariably used in the case of partial sex-linkage, and in the case of an autosomal recessive Finney <sup>(1940)</sup> used  $u_1$  <sup>43 out of 55 of</sup> in all the families analysed for linkage with the ~~sex~~ blood-group genes, and <sup>38 out of 40</sup> ~~all but one~~ of those tested for linkage with M and N. As the data on partial sex linkage are at present more extensive and much more significant of linkage than those on autosomal linkage we shall be mainly concerned with them. It will be ~~demonstrated~~ <sup>demonstrated</sup> that a ~~previous~~ <sup>new</sup> step in the precision of the method shows that the evidence for partial sex linkage is somewhat less decisive than appeared, but still cogent. However in <sup>one</sup> ~~some~~ other cases the significance of the evidence for <sup>an autosomal</sup> linkage becomes doubtful.

Fisher's (1935-a, 1935-b) original methods for the detection and estimation of linkage assumed, either that the probability of recording a family containing recessives was independent of the number of recessives in it, or that it was proportional to that number. In either case he used a score

$$u_1 = (a - 3b - c + 3d)^2 - (a + 9b + c + 9d).$$

where (in the case of suspected partial sex-linkage) a sibship consists of  $a$  normal males,  $b$  affected males,  $c$  normal females, and  $d$  affected females. However in the data on which Haldane (1936) inferred the existence of

partial sex-linkage, neither of ~~these~~ the above conditions was fulfilled. Fisher<sup>(1936)</sup> therefore considered the case where a sibship consisted of  $s_1$  normals and  $s_2$  abnormals. In what follows I shall use  $N$  to denote  $s_1$ , and  $n$  to denote  $s_2$ , since in my experience suffixes render algebra hard for the average biologist to follow.

Fisher did not consider any moments of the distribution of  $\bar{u}$  beyond the second, and assumed that a positive value of  $\bar{S}(\bar{u})$  for a group of sibships is to be regarded as significant according to the ratio which it bears to ~~its standard error~~ <sup>its sampling error</sup> in the absence of linkage; in fact that the <sup>sampling</sup> distribution of  $\bar{S}(\bar{u})$  may be taken as normal. We shall see that this is far from being the case for <sup>some of</sup> the groups of sibships on which the evidence for linkage is based. Of course when more data accumulate, the distribution will become more nearly normal, but at the same time the need for critical tests of significance will be lessened. It is unfortunately just where the data are on the borderline of significance that the present criterion are least satisfactory. Hence, just as in the case of the coefficient of correlation, a device for approx transformation which will approximately normalize the distribution of  $\bar{S}(\bar{u})$  is much to be desired.

To study the deviation from normality we must calculate one or more of the cumulants, beyond the second, of the distribution of  $\bar{u}$ . Fisher gives an operational method of calculating them. However in the case of  $N$  normals and  $n$  ~~recessives~~ abnormals a more elementary method is available, although it is less generally applicable. For  $\bar{a}$  and  $\bar{c}$  are derived by simple sampling in a sample of  $N$ ,  $\bar{b}$  and  $\bar{d}$  in a sample of  $n$ . Let  $\bar{a} - \bar{c} = x$ ,  $\bar{b} - \bar{d} = y$ . Then  $u_{31} = (x - 3y)^2 - (N + 4n)$ .

The distribution of  $x$  and that of  $y$  for any linkage value are given by a binomial expansion. Hence their cumulants can be calculated. Further  $x$  and  $y$  are uncorrelated, provided the intensity of linkage does not vary from one family to another. Hence the cumulants of  $x - 3y$  can be written down, and those of  $(x - 3y)^2$  derived from them.

The distribution of  $u_3$ , in the absence of linkage.

First consider the case of partial sex-linkage, where it is ~~known~~ assumed that every sibship, even if it consists of one sex only, is potentially segregating for ~~sex~~ the sexes with equal frequency. The fact that the sex ratio is not unity introduces a slight error. If the true sex-ratio is  $\frac{1}{2}(1+k)$  <sup>in the absence of linkage</sup>,  $\frac{1}{2}(1+k) \sigma^1 : \frac{1}{2}(1-k) \sigma^2$ ,  $E(u) = k^2 [(N+3n)^2 - (N+qn)]$ . Thus the estimate of linkage for an autosomal gene on a sufficiently vast sample would be  $\chi = \frac{1}{2} - \frac{3k \sum [(N+3n)^2 - (N+qn)]}{2 \sum [(N+qn)^2 - (N+qn)]}$ , that is to say the apparent recombination

frequency would be less than <sup>50%</sup> by a value probably slightly greater than  $\frac{k}{2}$ , or 0.4%. This correction will be neglected. <sup>\*</sup>The correction where a  $\delta$  dominant test factor takes the place of sex will be considered later.

$x = 2u - N$ , and the distribution of  $u$  is given by the symmetrical binomial  $2^{-N}(1+\theta)^N$ . The cumulant-generating function is  $N \log \cosh t$ . Odd cumulants vanish, and the even cumulants (Haldane 1940) are: —

$$K_2 = N, K_4 = -2N, K_6 = 2^4 N, K_8 = -2^4 \cdot 17 N, K_{10} = 2^8 \cdot 31 N, K_{12} = -2^8 \cdot 691 N, \text{ etc.}$$

$$K_{2r} = (-1)^{r-1} r^{-1} B_r \cdot 2^{2r-1} (2^{2r}-1) N.$$

\* though it should be made to calculated cross-over values.



Similarly the cumulants of  $3y$  are: -

$$K_2 = qn, K_4 = -2 \cdot q^3 n, K_6 = 2^4 \cdot q^3 n, K_8 = -2^4 \cdot 14 \cdot q^4 n, K_{10} = 2^8 \cdot 31 \cdot q^5 n, K_{12} = -2^9 \cdot 691 \cdot q^6 n.$$

So the cumulants of  $2x - 3y$  are:

$$K_2 = N + qn, K_4 = -2(N + q^3 n), K_6 = 2^4(N + q^3 n), K_8 = -2^4 \cdot 14(N + q^4 n),$$

$$K_{10} = 2^8 \cdot 31(N + q^5 n), K_{12} = -2^9 \cdot 691(N + q^6 n), \text{ etc.}$$

Now the mean of  $u$  is zero. Its other cumulants are the same as those of  $(2x - 3y)^2$ . Halotane (1941) has given formulae<sup>(3)</sup> for the cumulants of the distribution of the square of a variate, in terms of the ~~dist~~ cumulants of the distribution of that variate. Thus if  $z$  is symmetrically distributed with cumulants  $K_2, K_4, \text{ etc.}$ , the fourth cumulant of the distribution of  $z^2$  is  $48K_2^4 + 144K_2^2 K_4 + 8(3K_2 K_6 + 4K_4^2) + K_8$ . Applying these formulae, we find for the cumulants of  $u_{31}$ : -

$$K_1 = 0.$$

$$K_2 = 2[(N + qn)^2 - (N + q^2 n)].$$

$$K_3 = 8[(N + qn)^3 - 3(N + qn)(N + q^2 n) + 2(N + q^3 n)].$$

$$K_4 = 16[3(N + qn)^4 - 18(N + qn)^2(N + q^2 n) + 8\{3(N + qn)(N + q^3 n) + (N + q^2 n)^2\} - 14(N + q^4 n)].$$

$$= 16[3(N + qn)^4 - 18(N + qn)^2(N + q^2 n) + 32(N^2 + 66 \cdot qNn + q^4 n^2) - 14(N + q^4 n)].$$

$$K_5 = 128[3(N + qn)^5 - 30(N + qn)^3(N + q^2 n) + 20\{3(N + qn)(N + q^3 n) + 2(N + q^2 n)^2\} - 5\{14(N + qn)(N + q^4 n) + 10(N + q^2 n)(N + q^3 n)\} + 62(N + q^5 n)].$$

$$= 128[3(N + qn)^5 - 30(N + qn)^3(N + q^2 n) + 20(5N^2 + 282 \cdot qNn + 5 \cdot q^4 n^2) - 5\{14(N + qn)(N + q^4 n) + 10(N + q^2 n)(N + q^3 n)\} + 62(N + q^5 n)].$$

$$\begin{aligned}
 N+q^1 &= a \\
 N+q^2 &= a+b \\
 N+q^3 &= a+10b \\
 N+q^4 &= a+91b \\
 N+q^5 &= a+820b \\
 N+q^6 &= a+7381b
 \end{aligned}$$

$$\frac{1}{24}(8581-4) = \frac{1}{2} \cdot 428$$

$$\begin{array}{r}
 1+10 \\
 1+2+1
 \end{array}$$

$$\begin{array}{r}
 491 \\
 120 \\
 \hline
 6561 \\
 7381
 \end{array}$$

$$7+21+42+84+126+168+210$$

$$f. 4 v$$

$$\begin{aligned}
 [E_6] &= \frac{1}{2} [15a^6 - 225a^4(a+b) + 600a^2\{a(a+10b) + (a+b)^2\} - 15\{85a^2(a+91b) + 100a(a+b)(a+10b) + 11(a+b)^3\} \\
 &\quad + 4\{465a(a+820b) + 255(a+b)(a+91b) + 113(a+10b)^2\} - 1382(a+7381b)] \\
 &= \frac{1}{2} [15a^6 - 225a^4(a+b) + 600a^2(2a^2 + 12ab + b^2) - 15(146a^3 + 8868a^2b + 1033ab^2 + 11b^3) \\
 &\quad + 4(833a^2 + 407020ab + 34505b^2) - 1382(a+7381b)] \\
 &= \frac{1}{2} [15a^6 - 225a^5 + 1200a^4 - 2440a^3 + 3332a^2 - 1382a] - \frac{1}{2} b [225a^4 - 7200a^3 + 754434a^2 \\
 &\quad - 4407020a + 13827381] \\
 &\quad + \frac{1}{2} b^2 [600a^2 - 154033a + 2464010] - \frac{15}{2} b^3 \\
 &= \frac{1}{2} a(a-1) [15a^4 - 210a^3 + 990a^2 - 1450a + 1382] - \frac{1}{2} b [225(a-8)^4 + 461620(a^2 - 25a + 200) \\
 &\quad + 1480a - 44958] \\
 &\quad + 10b^2 (30a^2 - 248774a + 6401) - \frac{15}{2} b^3 \\
 &= \frac{1}{2} a(a-1) [15(a^4 - 14a^3 + 66a^2 - 130a + 92) + 2] - \frac{1}{2} b [225(a-8)^4 + 461620(a^2 - 25a + 200) + 1480a - 44958]
 \end{aligned}$$

$$\begin{aligned}
 1-32+384-2048+4096 &= \frac{2899}{16} = 3 \times 1032 \\
 225-7200+86400-463800+921600 &= 258
 \end{aligned}$$

$$\begin{aligned}
 225-7200 &+ 86400 - 1,629,080 + 10,200,542 \\
 -225 &+ 7200 - 86,400 + 464,800 - 921,600 \\
 461,620 &- 1,169,280 + 9,278,194 \\
 -461,620 &+ 1,169,500 - 9324,000 \\
 15(a^4 - 14a^3 + 66a^2 - 130a + 92) &+ 2 \\
 1480) 44958(25 & \\
 3560 & \\
 \hline
 9258 & \\
 8480 & \\
 \hline
 458 &
 \end{aligned}$$

$$\begin{aligned}
 \frac{1380}{15} &= 92 \\
 255 \times 42 &= 10710 \\
 230 & \\
 460 & \\
 255 & \\
 9302410 & \div 965 \\
 3720 & \\
 42 & \\
 381300 & \\
 14205100 & \\
 2219085 &+ 4435 \\
 4.2.4.5 & \begin{array}{r} 100 + 1100 + 1000 \\ 11 + 33 + 38 + 1 \\ \hline 196 + 8868 + 1011 \\ \hline 1055 \end{array} \\
 465 &+ 381,300 \\
 255 &+ 23,460 + 23,205 \\
 113 &+ 2,280 + 18,300 \\
 833 & \begin{array}{r} 491020 \\ 42 \\ \hline 466200 \\ 116550 \end{array}
 \end{aligned}$$

$$K_5 = 128 \left[ 3(N+qn)^5 - 30(N+qn)^3(N+q^2n) + 20(N+qn) \{ 3(N+qn)(N+q^3n) + 2(N+q^2n)^2 \} \right. \\ \left. - 5 \{ 17(N+qn)(N+q^4n) + 10(N+q^2n)(N+q^3n) \} + 62(N+q^5n) \right].$$

$$K_6 = 256 \left[ 15(N+qn)^6 - 225(N+qn)^4(N+q^2n) + 600(N+qn)^2 \{ (N+qn)(N+q^3n) + (N+q^2n)^2 \} \right. \\ \left. - 15 \{ 85(N+qn)^2(N+q^4n) + 100(N+qn)(N+q^2n)(N+q^3n) + 11(N+q^2n)^3 \} \right. \\ \left. + 4 \{ 465(N+qn)(N+q^5n) + 255(N+q^2n)(N+q^4n) + 113(N+q^3n)^2 \} - 1382(N+q^6n) \right] \dots (1)$$

These expressions are considerably simplified if we write

$N+qn = A$ ,  $q^2n = B$ . We then have:-

$$K_2 = 4K_2, \quad K_2 = \frac{1}{2}A(A-1) - \frac{1}{2}B.$$

$$K_3 = 48K_3, \quad K_3 = \frac{1}{6}A(A-1)(A-2) - \frac{1}{6}B(3A-20).$$

$$K_4 = 32K_4, \quad K_4 = \frac{1}{2}A(A-1) \left[ 3(A-2)(A-3) - 1 \right] - \frac{1}{2}B \left[ 18(A-4)^2 - 4A + 66 \right] + 4B^2.$$

$$K_5 = 768K_5, \quad K_5 = \frac{1}{6}A(A-1)(A-2) \left[ 3(A-3)(A-4) - 5 \right] - \frac{5B}{6} \left[ 6(A-8)^2 + 8(A-12)(A+45) + A + 104 \right] \\ + \frac{10}{6}B^2(2A-25)$$

$$K_6 = 512K_6, \quad K_6 = \frac{1}{2}A(A-1) \left[ 15(A-2)^3 \{ (A-3)(A-4)(A-5) - 1 \} + 2 \right] - \frac{1}{2}B \left[ 15(A-8)^4 + 46,560(A^2 - 25A + 2000) \right. \\ \left. - 3,280A - 34,058 \right] + \frac{5}{2}B^2 \left[ 120(A-13)^2 + 23A + 14,324 \right] - \frac{65}{2}B^3 \dots (1a).$$

P70

$K_2, K_3$ , etc are integers, not always positive. Fisher (1936b) has tabulated  $2K_2$  in his Table XIV. I give tables of  $K_2, K_3$ , and  $K_4$  in Tables 1, 2, and 3.

The distribution of  $u_3$  deviates considerably from normality even when  $N$  and  $n$  are not very small. Thus for  $N=6, n=4$ ,  $y_1 = 2.00, y_2 = 4.33$ . Of course when a number of  $u$  values are summed, these values are reduced, but not always very greatly so, since a single family often contributes most of  $S(K_3)$  and  $S(K_4)$ , and a large fraction of  $S(K_2)$ , as appears, for example, in Table 4.

f.5v

$$K_4 = \frac{1}{2} A(A-1) [15(A-2) \{ (A-3) [(A-4)(A-5)-5] - 1 \} + 2] \sim$$

$$- \frac{1}{2} B [225(A-8)^4 + 6,620(A^2 - 25A + 200) + 1,480(A+25) + 558]$$

$$+ \sum_{n=0}^{\infty} B^n [120(A-13)^2 + 21(A+348) + 16] - \frac{165}{2} B^3 \dots (1a)$$

f6 150

$$K_n = \frac{1}{4} K_c$$

Table 1

$N_1$	1	2	3	4	5	6	7	8	9	10
0	0	81	243	486	810	1215	1701	2268	2916	3645
1	9	99	270	522	855	1269	1764	2340	2987	3735
2	19	118	298	559	901	1324	1828	2413	3079	3826
3	30	138	327	597	948	1380	1893	2487	3162	3918
4	42	159	357	636	996	1437	1959	2562	3246	4011
5	55	181	388	676	1045	1495	2026	2638	3331	4105
6	69	204	420	717	1095	1554	2094	2715	3417	4200
7	84	228	453	759	1146	1614				
8	100	253	489	802	1198	1675				
9	117	279	522	846						
10	135	306	558	891						
11	154	334								
12	174	363								



Table 2

 $\frac{1}{48} K_3$ 

$N$	1	2	3	4	5	6	7	8	9	10
0	0	0	124	2,416	4,240	14,580	25,515	40,824	61,236	87,480
1	0	81	942	3,402	8,100	15,795	27,216	43,092	64,152	91,125
2	9	180	1,242	3,924	<del>8,955</del> 9,856	<del>14,034</del> 14,034	28,980	45,432	67,144	94,860
3	28	248	1,540	4,483	9,856	18,388	30,808	47,845	70,228	98,686
4	58	436	1,837	5,080	10,804	19,468	32,701	50,332	73,390	102,604
5	100	595	2,224	5,716	11,800	21,205	34,660	52,894	76,636	106,615
6	155	776	2,612	6,392	12,845	23,700	36,686	55,532	79,968	110,720
7	224	980	3,032	7,109	13,940	24,254				
8	308	1,208	3,485	7,868	15,086	<del>25,446</del> 25,868				
9	408	1,461	3,942	8,640						
10	525	1,740	4,444	9,516						
11	660	<del>2,046</del> 2,048								
12	814	2,380		✓	✓	✓	✓	✓	✓	✓

Table 3  
 $\frac{1}{32} K_4$

$N \backslash n$	1	2	3	4	5	6	7
0	0	-6,561	-19,683	146,830	1,115,370	3,444,525	<del>8,129,049</del> 10,838,442
1	-81	-6,723	6,318	301,482	1,377,405	3,968,919	9,047,052
2	-163	-3,970	41,068	<del>423,629</del> 418,545	1,668,599	<del>4,537,112</del> 7,052	10,026,260
3	78	2,346	85,533	564,567	1,990,572	<del>5,111,188</del> 50,868	11,068,971
4	1,002	<del>12,404</del> 7,044	140,727	725,628	2,344,980	<del>5,815,187</del> 23,47	12,177,489
5	3,005	<del>28,439</del> 14,504	<del>284,642</del> 256,242	908,180	2,733,515	<del>6,511,705</del> 23,5	13,354,154
6	6,519	<del>49,692</del> 34,329	287,508	1,113,627	3,157,905	<del>7,284,794</del> 63	14,601,342
7	<del>12,012</del> 10,848	77,460	<del>383,448</del> 5291	1,343,407	3,619,914	<del>8,425,542</del> 103,10	
8	19,988	112,571	499,193	1,599,002	4,121,342	<del>8,965,643</del> 75,75	
9	<del>30,987</del> 35,367	155,889	615,402	1,881,918			
10	<del>45,485</del> 5	<del>208,314</del> 215,604	758,142	2,193,705			
11	64,394	279,782					
12	<del>88,062</del> 8,446	344,265					

$N \backslash n$	8	9	10
0	16,350,012	29,524,500	49,305,915
1	17,819,1028	31,728,267	52,454,385
2	19,369,691	34,037,009	55,734,074
3	21,004,593	36,453,642	59,148,222
4	22,726,362	38,981,118	62,700,105
5	24,537,662	41,622,425	66,393,035
6	26,441,193	44,380,587	70,230,360

When a dominant test factor, such as the gene for the A agglutino-  
-gen, is used ~~in~~ or for the power of tasting phenylthiourea, is used  
in place of maleness, a correction must be made for the fact  
that ~~no~~ families including no member recessive for ~~the~~ <sup>its</sup> alleloma-  
-phic gene are excluded. In such families  $c = d = 0$ , so

$$\begin{aligned} u_{31} &= (a-3b)^2 - (a+q b) \\ &= (N-3n)^2 - (N+q n), \end{aligned}$$

and the frequency of such families among those which ~~would segregate~~  
~~if they contained~~ have a heterozygous dominant parent is  $2^{-2} = 2^{-(N+n)}$ .  
In such families  $K_1 = (N-3n)^2 - (N+q n)$ , whilst the other cumulants are  
zero. Hence in summing the  $u_{31}$  scores for the remaining families,  
we must put in each case,

$$K_1 = \frac{N+q n - (N-3n)^2}{2^{N+n-1}},$$

whilst the other cumulants of equations (1) or (1a) are to be multiplied by  $\frac{2^{N+n}}{2^{N+n-1}}$ .

The  $u_{31}$  score is also applicable to families where one parent ~~is~~ is recessive  
for the rare gene, e.g. albinism, the other being heterozygous for it, whilst  
both are heterozygous for the test factor, e.g. that for an agglutininogen.

This case demands analysis along quite different lines, and will not be  
considered further, except in the special case of Finney's Family 25, for  
which we develop equations (4) on p.

correction must be made for the fact that families including no member recessive for the allelomorphous gene are excluded. In such families  $c = d = 0$ , so  $u_{31} = (a - 3b)^2 - (a + 4b)$   
 $= (N - 3n)^2 - (N + 4n),$

and the frequency of such families is  $2^{-s} = 2^{-(N+n)}$ . ~~In this case the~~  
~~cumulants of the distribution of  $u_{31}$  are as above in equations (1),~~  
~~except that  $K_1 = 2^{-(N+n)} [(N + 4n) - (N - 3n)^2]$ .~~ ~~75a~~

~~This is generally negative, but may be positive.~~

The distribution of  $u_{31}$  in the presence of linkage.

Let  $x$  be the recombination frequency, and let  $y = (1 - 2x)^2$ . Thus  $y = 0$  in the absence of linkage, and varies between 0 and 1 in presence of linkage. Its use leads to slightly simpler expressions than that of  $\xi = x(1-x) = \frac{1}{4}(1-y)$ . We have:

$$E(a) = \frac{1}{3}(2-x)N, E(c) = \frac{1}{3}(1+x)N, E(b) = xn, E(d) = (1-x)n, \text{ or}$$

$$E(a) = \frac{1}{3}(1+x)N, E(c) = \frac{1}{3}(2-x)N, E(b) = (1-x)n, E(d) = xn.$$

The cumulants of  $y = b - d = 2b - n$  can readily be found. For the distribution of  $y$  is binomial, the probability that  $b = r$  being the coefficient of  $\theta^r$  in  $(1-x + x\theta)^n$  or  $[x + (1-x)\theta]^n$ . Haldane (1940<sup>a</sup>) has given expressions for the first 12 cumulants of the binomial distribution in terms of  $\xi$ , the product of the frequencies, which is here  $x(1-x)$ , or  $\frac{1}{4}(1-y)$ , and  $y$ , their difference, which is here  $\pm(1-2x)$ , or  $\pm y^{\frac{1}{2}}$ . To obtain the appropriate values for  $y$  we must multiply the values of  $K_r$  given by Haldane by  $2^n$ . The cumulants of  $y$  up to  $k_0$  are:

$$K_1 = -gn = -y^{\frac{1}{2}}n$$

$$K_2 = 4cn = (1-y)n$$

$$K_3 = 8gc n = 2y^{\frac{1}{2}}(1-y)n$$

$$K_4 = 16c(1-6c)n = -2(1-y)(1-3y)n$$

$$K_5 = 32gc(1-12c)n = -8y^{\frac{1}{2}}(1-y)(2-3y)n$$

$$K_6 = 64c(1-30c+120c^2)n = 8(1-y)(2-15y+15y^2)n$$

$$K_7 = 128gc(1-60c+360c^2)n = 16y^{\frac{1}{2}}(1-y)(\frac{14}{3}-\frac{60}{45}y+45y^2)n$$

$$K_8 = 256c(1-126c+1680c^2-5040c^3)n = -16(1-y)(14-231y+525y^2-315y^3)n \dots (2)$$

Further cumulants can easily be calculated if desired. To find the cumulants of  $x$ . The signs of the odd cumulants are arbitrary, but if that of one is changed, that of all must be changed. To find the cumulants of  $x$  we must substitute  $c = \frac{1}{q}(1+x)(2-x) = \frac{1}{q}(1-\frac{y}{q})$ ,  $g = \frac{1}{2}(1-2x) = \frac{1}{2}(1-\frac{y}{q})$ . That is to say we must substitute  $N$  for  $n$  in the above expressions,  $\frac{y}{q}$  for  $y$ , and also change the sign of  $y^{\frac{1}{2}}$ . So putting  $y = q\eta$ , the cumulants of  $x-3y$  are:—

$$K_1 = -q^{\frac{1}{2}}(N - \eta^{\frac{1}{2}}(N+qN))$$

$$K_2 = N+qN - \eta(N+q^2N)$$

$$K_3 = 2\eta^{\frac{1}{2}}[N+q^2N - \eta(N+q^3N)]$$

$$K_4 = -2[N+q^2N - 4\eta(N+q^3N) + 3\eta^2(N+q^4N)]$$

$$K_5 = -8\eta^{\frac{1}{2}}[2(N+q^2N) - 5\eta(N+q^4N) + 3\eta^2(N+q^5N)]$$

$$K_6 = 8[2(N+q^3N) - 14\eta(N+q^4N) + 30\eta^2(N+q^5N) - 15\eta^3(N+q^6N)]$$

etc. The cumulants of  $n$ , after the first, are those of  $(x-3y)^2$ . They are obtained from the above by the expressions given by Haldane (1941) and are, putting  $N+qN = A$ ,  $\eta^2N = B$ ,:—



$$K_1 = \frac{\zeta}{q} [A(A-1) - B].$$

$$\frac{1}{2} K_2 = A(A-1) - B + 2 \frac{\zeta}{q} [A(A-1)(A-2) - B(3A-20)] - \left(\frac{\zeta}{q}\right)^2 [A(A-1)(2A-3) + B(2A^2 - 42A + 243) - B^2].$$

$$\begin{aligned} \frac{1}{6} K_3 = & A(A-1)(A-2) - B(3A-20) + \frac{\zeta}{q} [A(A-1) \{3(A-2)(A-3) - 1\} - B(18A^2 - 256A + 1544) + 8B^2] \\ & - \left(\frac{\zeta}{q}\right)^2 [3A(A-1)(2A^2 - 11A + 10) + B(6A^3 - 240A^2 + 3,793A - 24,600) - 5B^2(3A - 44)] \\ & + \left(\frac{\zeta}{q}\right)^3 [A(A-1)(3A^2 - 19A + 15) + B(6A^3 - 954A^2 + 15,710A - 110,715) + B^2(3A^2 - 123A + 1,339) - B^3] \dots (3) \end{aligned}$$

(part 1 has to be checked)

$$K_1 = \frac{Y}{q} [(N+qn)^2 - (N+q^2n)]$$

$$\frac{1}{2} K_2 = (N+qn)^2 - (N+q^2n) + \frac{2Y}{q} [(N+qn)^3 - 3(N+qn)(N+q^2n) + 2(N+q^3n)] \\ - \left(\frac{Y}{q}\right)^2 [2(N+qn)(N+q^2n) - 4(N+qn)(N+q^3n) - (N+q^2n)^2 + 3(N+q^4n)]$$

$$\frac{1}{8} K_3 = (N+qn)^3 - 3(N+qn)(N+q^2n) + 2(N+q^3n) \\ + \frac{Y}{q} [3(N+qn)^4 - 18(N+qn)^2(N+q^2n) + 32(N^3 + 66.qNn + q^4n^2) - 14(N+q^4n)] \\ + \left(\frac{Y}{q}\right)^2 [8(N+qn)^3(N+q^2n) - 3(13N^3 + 75q.qN^2n + 14qq.q^2Nn^2 + 13.q^5n^3) \\ + (61N^2 + 30,450.qNn + 61.q^5n^2) - 30(N+q^5n)]$$

$$+ \left(\frac{Y}{q}\right)^3 [(5N^4 + 228.qN^3n + 846.q^2.N^2n^2 + 1028.q^3.Nn^3 + 5.q^6n^4) \\ - 2(11N^3 + 3,84q.qN^2n + 1,28q.q^3.Nn^2 + 11.q^6n^3) \\ + 8(4N^2 + 1,86q.q^2.Nn + 4.q^6n^2) - 15(N+q^6n)]. \quad \dots (3)$$

The expression for  $K_4$  is very heavy, being the sum of <sup>18</sup>~~20~~ products of the cumulants of  $x-zy$ . It is unlikely to be used, so I have not given it. It will be noted that the coefficient of  $\frac{Y}{q}$  in  $K_n$  is ~~it is~~ half the leading term of  $K_{n+1}$ . The general behaviour of  $K_3$  can be seen from the following considerations. When  $Y=0$  (no linkage) it is positive provided  $N+n > 2$ . When  $N=0$  and  $Yn$  is large it approximates to  $\frac{1}{2} \frac{18^3 n^4}{(5-3)} (1-Y)(3-5Y)$ . This vanishes when  $Y = \frac{3}{5}$ , or  $X = .112$ , and becomes negative for closer linkages, vanishing again when  $Y=1$ ,  $X=0$ . Thus for fairly close linkages the distribution may be pretty symmetrical, since most of the

$$* \frac{1}{2} 18^3 n^4 Y(1-Y)(3-5Y)$$

$S(n)$ 

value of  $S(K_2)$  comes from families with large  $n$ .

The distribution of  $\chi$  for a given value of  $S(\bar{a})_{K_2}$  can be deduced in a rough way.

The asymmetry noted above means that a surprisingly high value of  $\chi$  (considering the known variance of  $S(n)$ ), is compatible with a given value of  $Y$ . It follows that unexpectedly low values of  $Y$  are compatible with a given value of  $S(n)$ , i.e. that the distribution of  $Y$  is negatively skew. It <sup>further</sup> follows that the distribution of  $1-2\chi$  is even more negatively skew. That is to say, when linkage is not very tight,  $\chi$  may well exceed the value deduced from the data by several times its standard error, whereas <sup>a large</sup> error in the opposite direction is less probable than with a normal distribution.

When a dominant test factor is used in place of sex, the cumulants are as above, except that

$$K_2 = \frac{Y}{q} \left[ (N+qn)^2 - (N+q^2n) \right] - \frac{(N+n) \left[ (N-3n)^2 - (N+qn) \right]}{2}$$

The case of a back-cross for the recessive gene causing abnormality, and with both parents heterozygous for the test factor, will not be considered here.

$$K_1 = \frac{Y}{q} \cdot \frac{2^{N+n}}{2^{N+n}-1} \left[ (N+qn)^2 - (N+q^2n) \right] - \frac{[(N-3n)^2 - (N+qn)]}{2^{N+n}-1},$$

whilst the other cumulants of equation (3) are to be multiplied by  $\frac{2^{N+n}}{2^{N+n}-1}$ .

value of  $S(K_3)$  comes from families with large  $n$ .

When a ~~test~~ dominant test factor is used in place of sex, the cumulants are as above, except that  $K_1$

$$K_1 = \frac{y}{q} \left[ \frac{(N+qn)^2 - (N+q^2n)}{2^{-(N+n)}} - \frac{(N-3n)^2 - (N+q^2n)}{2^{-(N+n)}} \right].$$

The distribution of  $u_3$ , when the method of ascertainment is known.

The cases originally considered by Fisher (1935a, b) have not yet arisen in practice, and it therefore does not seem worth while to give the full expressions for the cumulants of  $u_3$  for them. However an example will show how they may be calculated. Let us suppose that a group of families in which partial sex linkage is suspected have been recorded by the method of single ascertainment, that is to say that the probability of recording a family <sup>of  $s$  members</sup> was proportional to the number of recessives,  $n$ , in it. It is required to find the value of  $K_3$  in the absence of linkage. The frequency of families containing  $n$  recessives among families of  $s$  ~~which~~ derived from two heterozygous parents is  $\frac{3^N s!}{4^s N! n!}$ . The frequency with which they are recorded is proportional

to  $n$  times this quantity, and is therefore  $P_n = \frac{3^{N-1} (s-1)!}{4^{s-1} N! (n-1)!}$ .

Hence  $\sum N P_n = \frac{3}{4} (s-1)$ ,  $\sum N(N-1) P_n = \frac{9}{16} (s-1)(s-2)$ ,  $\sum N(N-1)(N-2) P_n = \frac{27}{64} (s-1)(s-2)(s-3)$ ,  
 $\sum (n-1) P_n = \frac{1}{4} (s-1)$ ,  $\sum (n-1)(n-2) P_n = \frac{1}{16} (s-1)(s-2)$ ,  $\sum N(n-1) P_n = \frac{3}{16} s(s-1)(s-2)$ , etc.

We may write  $\frac{1}{8} K_3$  as:

$$N(N-1)(N-2) + 24 N(N-1)(n-1) + 243 N(n-1)(n-2) + 729 (n-1)(n-2)(n-3) \\ + 24 N(N-1) + 486 N(n-1) + 2187 (n-1)(n-2).$$

Summing over the different values of  $P_n$ , we find

$$K_3 = 216S(S-1)(S-2)(S+6). \text{ Similarly}$$

$$K_4 = 144(S-1)(27S^2 + 81S^2 - 964S + 1016).$$

### The Distribution of $u_{11}$ .

In the

~~In the absence of linkage,~~

$$u_{11} = (a-b-c+d)^2 - (a+b+c+d)$$

Now since the family  $\underline{s}$  falls into two sections  $a+d$  and  $b+c$ , whose ~~probab~~ expectations are fixed, the expressions for its moments are greatly simplified. In the absence of linkage  $u_{11} = S(X_s^2 - 1)$ , where  $X_s^2$  is the exact value of the Pearson's measure of divergence from expectation for a sample of  $\underline{s}$  members and one degree of freedom. The cumulants of  $X_s^2$  in <sup>the distribution of</sup> this case have been given in equations (8) by Haldane (1948). Those of the distribution of  $u_{11}$  are:

$$K_1 = 0$$

$$K_2 = 2S(S-1)$$

$$K_3 = 8S(S-1)(S-2)$$

$$K_4 = 16S(S-1)(3S^2 - 15S + 14)$$

$$K_5 = 128S(S-1)(S-2)(3S^2 - 21S + 31)$$

$$K_6 = 256S(S-1)(15S^4 - 210S^3 + 990S^2 - 1950S + 1382) - \dots - (4).$$

These are independent of the value of  $n$ , and hence of the method of ascertainment. They are also unaffected by dominance of the test factor. If there is linkage, the cumulants are to be derived as before from equations (2) of this paper, by substituting  $\underline{s}$  for  $\underline{n}$ . They are: -



$$K_1 = \gamma s(s-1)$$

$$K_2 = 2s(s-1)(1-\gamma) [1 + (2s-3)\gamma]$$

$$K_3 = 8s(s-1)(1-\gamma) [s-2 + (3s^2-14s+15)\gamma - (5s^2-14s+15)\gamma^2]$$

$$K_4 = 16s(s-1)(1-\gamma) [3s^2-15s+14 + (12s^3-105s^2+277s-231)\gamma - (50s^3-327s^2+715s-525)\gamma^2 + (42s^3-237s^2+465s-315)\gamma^3] \\ \dots \dots (s)$$

The Distribution of  $u_{33}$  is probably best studied by Fisher's operational method. As it is not used in the study of partial sex-linkage, it will not be discussed here.

# Application to data on partial sex-linkage.

Let us first consider the data concerning 28 sibships with normal parents, segregating for epidermolysis bullosa, summarized in Haldane's (1936) Table XIV, and Fisher's (1936b) Tables XVI and XVII. The values of  $u$  and its cumulants are given in Table 3.<sup>4</sup> The fourth column is obtained by halving the values of  $\frac{1}{2} K_2$  in Fisher's Table XIV, the fifth and sixth from my Tables 2<sup>2</sup> and 2<sup>3</sup>. If we write:

$$S(u) = U = 434,$$

$$\frac{1}{4} S(K_2) = K_2 = 5,379,$$

$$\frac{1}{48} S(K_3) = K_3 = 37,222,$$

$$\frac{1}{32} S(K_4) = K_4 = 5,4297,$$

then in the absence of linkage,  $U$  is distributed with cumulants:

$$K_1 = 0, K_2 = 4 K_2 = 21,516, K_3 = 32 K_3 = 1,186,656, K_4 = 32 K_4 = 18,495,408$$

$$\text{Hence } \gamma_1 = \frac{6 K_3}{K_2^3} = .566107, \gamma_2 = \frac{2 K_4}{K_2^2} = .397758. \text{ So the distribution}$$

of  $U$  is comparable with that of a  $\chi^2$  distribution with 25 degrees of freedom, which has  $\gamma_1 = .5658, \gamma_2 = .48$ , and is thus rather more platykurtic.

Several methods are available for the approximate non-normalization of moderately skew distributions by transformation of the variate. One type, in which the variate  $x$  is transformed into  $(x+a)^b$ , has been discussed by Haldane (1938, 1941<sup>2</sup>) and was intended for use on these  $u$  scores.

In the case of the  $\chi^2$  distribution for more than about three degrees of freedom it is found that the cube root is almost normally distributed.

This depends on the fact that the  $\chi^2$  distribution has  $K_3 = \frac{2 K_2^3}{K_1^3}$ ,

$$K_4 = \frac{6 K_2^2}{K_1^2}, \text{ whilst the distribution of the cube of a normal variate}$$

Table 3.<sup>4</sup>

Twenty-eight families segregating for epidermolysis bullosa.

Number of families	N	n	$S(n)$	$\frac{1}{4}S(k_2)$	$\frac{1}{48}S(k_3)$	$\frac{1}{32}S(k_4)$
5	1	1	+18	45	0	-405
5	2	1	-10	95	45	-815
1	3	1	-8	30	28	78
1	4	1	-12	42	58	1,002
1	5	1	+2	55	100	3,005
2	6	1	+20	138	310	13,038
1	7	1	+84	84	224	12,012
1	12	1	-12	174	814	<del>88062</del> <del>86,436</del>
1	1	2	-18	99	81	-6,723
1	2	2	-4	118	180	-3,940
1	5	2	+26	181	595	28,439
1	6	2	-8	204	776	49,692
1	1	3	-12	270	972	6,318
1	3	3	+34	327	1,540	85,533
1	5	3	-32	388	2,224	207,692
1	3	4	-14	597	4,483	564,567
1	4	4	+24	636	5,080	725,628
2	3	5	+356	1,896	19,712	<del>3,981,144</del> <del>1,440,572</del>
28	73	38	+434	5,379	37,222	<del>3,752,099</del>

~~5,742,641~~  
54,297

has approximately  $K_3 = \frac{2K_2^2}{K_1}$ ,  $K_4 = \frac{56K_2^2}{9K_1} = 6.2 \frac{K_2^2}{K_1}$ , if the coefficient of variation is small. Where this does not hold, we may use Haldane's (1938) transformation "B". We put:

$$Y = \left[ \left(1 + \frac{U}{g}\right)^{bg} + 2bd - 1 \right] \left[ 1 - d \left( b - \frac{d}{K_2} \right) \right] \div 2bK_2^{\frac{1}{2}} \dots \dots (6)$$

$$\text{where } b = \frac{32 K_3^2 - K_2 K_4}{8 K_2^2 K_1^2}, \quad d = \frac{K_3}{3 K_2}, \quad g = \frac{8 K_2^2 K_3}{40 K_2^2 - K_2 K_4}.$$

The terms omitted from equation (6) only affect the fifth decimal place of  $Y$  in the case here considered.  $Y$  is an almost normally distributed variable with mean zero, and unit standard deviation.

On the data of Table 3,  $U$  is 2.959 times its standard error, giving  $P = .0015$  were it normally distributed.  $b = .001, 560, 564$ ,  $d = 2.306, 625$ ,  $g = \frac{352.1412}{351.2434}$ ,  $bg = .548, 1341$ . Hence  $Y = 2.4499$ , and  $P = .00722$ . Thus the value of  $U$  must still be regarded as significant, but its significance is decidedly lessened.

If preferred the method of Cornish and Fisher (1939) may be used, putting  $a = 0$ ,  $b = 0$ ,  $c = y_1$ ,  $d = y_2$ , in the formulae of their p. 9. This gives  $P = .0074$ . This method is perhaps a little longer than that here given unless tables of Hermitean polynomials are available; and in theory the values of  $y_3$  and  $y_4$ , if not of higher deviations from normality, should be used. The  $Y$  transformation has the merit that, although only based on  $y_1$  and  $y_2$ , it is known to normalize the  $\chi^2$  distribution very accurately, and it is clearly analogous to  $\chi^2$ . It is also of interest as giving, at least approximately, the median value of  $U$ . If the

$$q \left[ (1-2bd)^{\frac{1}{2q-1}} \right]$$

sign

distribution of  $U$  is symmetrical, which is nearly the case, this is the value of  $U$  which makes  $V$  vanish, i.e.  $q \left[ 1 - (1-2bd)^{\frac{1}{2q-1}} \right]$ , or approximately  $\frac{4.60}{13.72}$ . In this case the median is  $-\frac{4.60}{13.72}$ . That is to say although, in the absence of linkage, the <sup>mean</sup> median value of  $U$  is zero, it is as likely to be less than  $-13.72$  as greater. ~~5~~ as greater.

The other most doubtful case of partial sex-linkage, based on data of this kind, is that of Oguchi's disease. Here  $U=294$ ,  $K_2=3,543$ ,  $K_3=17,381$ ,  $K_4=2,604,511$ . Thus  $U$  is 2.898 times its standard error, but  $V$  giving  $P=.0019$ . But  $V=2.2480$ , giving  $P=.01136$ . However in this case there is further information of two kinds. Back-crosses to affected females give  $S(u_{11})=24$ , and from equations (4),  $S(K_2)=160$ ,  $S(K_3)=2,400$ ,  $S(K_4)=39,040$ . Since  $\bar{u}_{11} = \frac{1}{2} K_2 \bar{y}$ , as compared with  $\bar{u}_{31} = \frac{1}{18} K_2 \bar{y}$ , the  $u_{11}$  must be given 9 times the weight of  $u_{31}$ . That is to say we must consider  $V = S(u_{31}) + 9 S(u_{11})$ . The variance of  $u_{11}$  must be multiplied by 81, its  $K_r$  by  $q^2$ . When this is done we find:

$U=510$ ,  $K_2=5,813$ ,  $K_3=53,831$ ,  $K_4=10,608,931$ , whence  $V=2.4245$ ,  $P=V=2.6148$ ,  $P=.004425$ . Further the direct data from cousin marriage give  $\frac{1}{2}x$  equal to 1.313 times its standard error, with  $P=.0946$ . Combining these probabilities by Fisher's (1934) method, we find  $\chi^2=15.557$  for 4 degrees of freedom. By Wilson and Hilferty's (1931) theorem,  $P=.00382$ . Thus the results are decidedly significant. However the probability of an explanation by chance is some ten times greater than appeared at first sight; and as the sex ratio is very aberrant, it is perhaps possible that the gene is not partially sex-linked. For the other cases of partial sex-linkage based on evidence of this type, the ~~prob~~ significances of the data are still greater.



## Application to data on Friedreich's ataxia

Hogben and Pollack (1935) collected data on 12 families segregating for Friedreich's ataxia and for the blood-group genes. Using Bernstein's score they found no evidence of linkage. But Fisher (1936a) used the  $u_3$  score, and found a high positive value. On the method which he then used, it was 1.530 times its standard error. Using the methods of this paper we find  $S(u) = +14.6$ . But its owing to the dominance of the test factor its expectation in the absence of linkage is  $-2.45$ . Hence  $U = 14.8.45$ . On the method then used by Fisher  $S(u)$  was the ~~variance~~ sampling variance was 9.108, ~~on his data~~ so  $S(u)$  was 1.53 times its standard error. On the method used here, if the variance is 4.500, so  $U$  is 2.22 times its standard error, and would therefore be regarded as significant were it not for the correction for skewness.

Fisher points out that the positive value of  $S(u)$  is entirely due to one family. This family, from an  $A \times O$  marriage, consisted of

2 Af, 10 OF, 0 Af, 4 Of, where  $f$  is the gene for Friedreich's ataxia, and  $F$  its normal allele on ph.\* Fisher ~~remark~~ writes of this family it "The  $u$  score attained by this family is, however, over four times its standard error, and, if it is not to be attributed to linkage, it must be ascribed to some cause, or causes, of disturbance capable of obscuring the evidence for the presence or absence of linkage. It provides, in fact, decisive evidence either of linkage, or of the heterogeneity of the twelve families reported".

Actually on Fisher's new method of <sup>estimating the variance</sup> ~~scoring~~, the corrected value,  $u = 154.031$ , is 3.320 times its standard error. But even this would ~~\*, and gave~~  $u = 158$

be fairly decisive evidence, provided the distribution of  $\bar{u}$  were normal. However in the case of a single family it is grossly abnormal. The actual probability is best found by elementary methods. We can ask what fraction of all families consisting of 2 normals and 4 abnormal, would give this, the highest possible value of  $\bar{u}$ , in the absence of linkage. The probability that both the two normals should belong to group A is  $\frac{1}{4}$ . The probability that all four abnormal should belong to group O is  $\frac{1}{16}$ , giving a cumulative probability of  $\frac{1}{64}$ . The probability of observing a family of 0 AF, 2 OF, 4 Af, 0 Of, which would give the same  $\bar{u}$  score, is equal. Hence the probability of obtaining this score by chance is  $\frac{1}{32}$ , or .03125, as compared with .0005 if  $\bar{u}$  were normally distributed.\* There is nothing surprising in finding one such family among 12.

It is highly probable that there are several ~~genes~~ different genes for Friedreich's ~~ataxia~~ recessive Friedreich's ataxia (Haldane 1940b) and quite possible that some of them are in different chromosomes. One, but not all, of these genes may well prove to be linked with the blood group genes. B. & Hoyer and Pollack's data do not furnish decisive evidence either of linkage or of heterogeneity. Fisher's ~~arguments~~ further arguments, based on the analysis of variance, seem to be inapplicable to this case for the same reasons as the simpler arguments given above.

\* If allowance is made for the fact that a family of 2 AF, 0 OF, 4 Af, 0 Of would not be used for linkage work, though it has a probability  $\frac{1}{64}$ , the probability of obtaining a maximal  $\bar{u}$  is  $\frac{2}{63}$ , or .0317.

## Application to data on allergy.

Zieve, Weiner, and Freis (1936) recorded the segregation of allergy along with blood group and other genes. They used a relatively inefficient method of searching for linkage, and found none. However Finney (1940) has developed the use of the  $u$  scores with great ingenuity and in great detail, and applied it to this case. He concludes that the recessive gene  $h$  for allergy shows evidence of linkage with the blood group genes. The sum of his weighted  $u$  scores,  $S(1)$ , is 1.40 times its standard error, giving  $P = .040$ . Clearly this is so near the border-line of significance that a detailed analysis becomes of interest.

Table 4<sup>5</sup> is a summary of the 31 families including ~~both~~ members ~~recessive both for allergy and a recessive blood group gene~~ which were certainly segregating ~~for~~ for two gene pairs, to which  $u_{21}$  is applicable.\* The data are given more fully in Finney's pp. 186 and 187. Besides these, <sup>two</sup> segregating families, 44 and 66, were scored by  $u_{23}$ , and a number of families which were only certainly segregating for one gene pair. These latter only gave 5% of the information, and can be omitted without serious injustice. The  $u_{23}$  families contributed 2.5% of Finney's weighted  $u$  score, so their omission is also not serious.

Finney's

The families belonging to <sup>Finney's</sup> type  $\gamma$  are from  $Tt Rr \times tt Rr$ , and the cumulants are given by the modified form of equations (1) on p. 6(a). Type  $\gamma^*$  refers to the segregation of  $A$  and  $h$  among those progeny of  $A \times AB$  which inherit  $B$  from their  $AB$  parent. Here the correction is as for type  $\gamma$ , except that

\* Where a family ~~from~~ with  $A$  and  $B$  parents is segregating both for the  $A$  and  $B$  genes, it is scored twice.

since  $N$  and  $n$  only refer to the  $AB$  and  $B$  children, we use  $2^5$  instead of  $2^{N+n}$ . In family 52 this makes no difference to the result. Type 11 refers to the segregation of  $A$  and  $B$  from an  $AB$  parent. Since the parent is known to be heterozygous there is no connection, as in the case of partial sex linkage where the father is known to be heterozygous for sex.

Family 25, from  $TtRr \times TtRr$  contained abnormal (allergies) only. In this case  $N=0$ ,  $n=5$ , and

$$u_{31} = (c-3d)^2 - (c+q d) = (4d-n-1)^2 - (3n+1).$$

Neglecting for the moment the fact that  $d$  may be zero, and the family thus excluded from the record, we can calculate the cumulants of  $d$  from equations (2), putting  $c = \frac{3}{16}$ ,  $q = \frac{1}{2}$ . The cumulants of  $4d-n-1$  are therefore:

$$K_1 = -1, K_2 = 3n, K_3 = 6n, K_4 = -6n, K_5 = -120n, K_6 = -312n, K_7 = 3,696n, K_8 = 39,504n.$$

The cumulants of  $u$ , after the first, are those of  $(4d-n-1)^2$ . They are:

$$K_1 = 0.$$

$$K_2 = 18n(n-1).$$

$$K_3 = 12n(n-1)(3n-4).$$

$$K_4 = 144n(n-1)(24n^2 - 24n - 43).$$

But when  $d=0$ ,  $K_1 = n(n-1)$  and the other cumulants vanish. This occurs with a frequency  $(\frac{3}{4})^n$ . When allowance is made for this we find:

$$K_1 = \frac{3^n}{3^n - 4^n} n(n-1).$$

$$K_2 = \frac{4^n}{4^n - 3^n} 18n(n-1).$$

$$K_3 = \frac{4^n}{4^n - 3^n} 12n(n-1)(3n-4).$$

$$K_4 = \frac{4^n}{4^n - 3^n} 144n(n-1)(24n^2 - 24n - 43). \quad \dots \quad (7)$$



f.26 18a

Table 4<sup>5</sup>

Families segregating for allergy and blood groups.

Families	Type	N	n	S(u)	S(K <sub>1</sub> )	$\frac{1}{4}S(K_2)$	$\frac{1}{48}S(K_3)$	$\frac{1}{32}S(K_4)$
4, 15, 36a, 36b	m	1	1	+24	+8.000	48.00	0	-432 ✓
14, 16, 22, 38a, 38b	m	2	1	+22 <sup>16</sup>	+7.143	108.57	51.43	-931.4 ✓
23a, 23b	m	3	1	+12	+1.600	64.00	59.73	166.4 ✓
28, 42	m	4	1	-24	+0.714	86.71	119.74	2,068.6 ✓
46	m	m	1	-12	0	84.33	224.88	12,054.1 ✓
29, 57a, 57b	m	0	2	-18	-18.000	324.00	0	-26,244 ✓
30, 39, 44, 58a, 58b	m	1	2	-18	-4.286	565.71	462.86	-38,414.1 ✓
33, 59	m	3	2	+88	+0.714	284.90	615.23	<del>2,441.4</del> 4843.4 ✓
18a, 18b	m	4	2	+28	+0.571	323.05	885.84	26,224.8 ✓
13	m	m	3	-18	+0.029	453.44	3,034.96	381,663.7 ✓
52a	m*	1	2	+18	-0.857	113.14	92.57	-7,683.4 ✓
52b	II	1	2	+30	0	99.00	81	-6,723 ✓
60b	II	2	1	-2	0	19.00	9	-163 ✓
25	6	0	3	+54	-4.378	46.70	<del>77.84</del> 715.08	5,558 ✓
Total				+18 <sup>8</sup>	-8.630	2,620.55	<del>5,663.14</del> 715.08	<del>349,664.1</del> 351,993.1



On this basis we can calculate the last four columns of Table 4.<sup>5</sup>  
 $U = 192.63$ , which is  $1.88^{22}$  times its standard error, giving  $P = .027$ . Thus on  
 the data included in Table 4 the evidence for linkage is rather stronger  
 than when the data giving the remaining 7.5% of Finney's information<sup>data added</sup>.  
 Clearly no injustice is done to his case by leaving them latter out of  
 consideration.  $K_1 = 2,620.55$ ,  $K_2 = 5,715.08$ ,  $K_3 = 5,663.19$ ,  $K_4 = 351,993.1$ . Hence  
 $b = \gamma_1 = .25^{56}$ , so the distribution is a good deal more symmetrical  
 than those considered above. We find  $b = 3.9102 \times 10^{-4}$ ,  $d = .426957$ ,  
 $g = 848.644$ ,  $bg = .319658$ ,  $\gamma = 1.4^{958}$ , whence  $P = .03^{63}$ .

Hence the correction only diminishes the significance of Finney's  
 result to a slight extent. Probably if ~~the~~ all families were included we  
 should have  $P$  about .05. It must however be remembered that men have  
 23 pairs of autosomes, and that White (1940) has shown that two human  
 genes may be in the same chromosome, and yet show no appreciable linkage.  
 Hence the a priori probability of finding linkage between a given pair of  
 genes is less than .05. Thus the a priori probability that one of the two  
 pairs tested by Finney should show linkage is probably less than .1. Thus  
 the data in question must be regarded as giving a strong indication  
 of linkage, but not as indicating it with a high degree of probability.  
 About twice as much information would be needed to make linkage  
 highly probable. At present Burks' data (193 ) data seems to give  
 stronger evidence, but a full appreciation of their significance must await  
 their complete publication, which is much to be desired.

## Discussion

This paper is not intended to be polemical. Both Fisher and Finney have improved existing methods for the determination of linkage, including my own. ~~Never~~ And it is clear that the method of this paper is very far from final. The methods of detecting and measuring linkage in man ~~are~~ have developed very rapidly, since Bernstein's pioneer work, and have not reached ~~for~~ <sup>probably</sup> perfection. ~~Perhaps~~ <sup>Probably</sup> some better method than my own of treating these borderline cases will be found. Nevertheless it would seem that whenever  $U$  is less than three times its standard error, it is desirable to make some allowance for the skewness of its distribution. I have to thank Dr. N. Karm for reading the manuscript, and detecting several numerical errors.

## Summary.

The distribution of Fisher's  $u$  scores used in testing for human linkage, is not normal, but has a decided positive skewness. Hence large values of  $u$  ~~are~~ may occur more frequently in the absence of linkage than would be supposed from their standard error. The cumulants of  $u$  are tabulated in certain cases. It is shown that ~~when~~ <sup>when</sup> correction is made for skewness, the data for partial sex-linkage are still significant, though a good deal less so than had been thought. On the other hand the evidence for linkage of the blood group genes with Friedreich's ataxia is not significant. ~~And that for linkage of the blood group genes with allergy is barely so.~~ <sup>B-E</sup> On the other hand the significance of Finney the data on linkage of allergy and blood groups is only very slightly diminished.

$$4c = N - n, \quad 8c = 2N - 2n \quad B = 3d =$$

Cumulants of  $(x - 3y - 3c + qd)$  are:

$$K_1 = 0 \quad \text{If } N - 4c = x, \quad n - 4d = y, \quad \therefore u_{33} = (x - 3y)^2 - (3N - 2x + 2y - 18y) \\ = (x - 3y)^2 + 2(x + 4y) - 3(N + 4n)$$

To find variance of  $u_{33}$ , compared with  $u'_{33} = (x - 3y)^2 - 3(N + 4n)$ , in absence of linkage.

$$v = (x - 3y)^2, \quad v' = (x - 3y)^2 + 2(x + 4y), \quad \bar{v} = \bar{v}' = 3(N + 4n) \\ v'' = x^4 = \quad = v + 2(x + 4y)$$

$$\begin{array}{r} 2^2 - 6xy + 4y^2 \\ 2492 \\ 1 - 6 + 9 \\ + 9 - 5 - 4 + 81 \end{array}$$

Second if  $K_n$  is the cumulant of  $x - 3y$ , then

$$\begin{aligned} \Delta V_v &= 2K_2 + K_4 = 2[3(N + 4n)]^2 - 120(N + 4n) \\ &= 18(N + 4n)^2 - 120(N + 4n) = 6[3(N + 4n)^2 - 20(N + 4n)] \end{aligned}$$

$$v'' = v' + 4v(x + 4y) + 4(x + 4y)^2$$

$$\begin{aligned} V_{v''} &= \overline{v''} - (\bar{v}')^2 = 2V_v + 4\overline{v(x + 4y)} + 4\overline{(x + 4y)^2} \\ &= V_v + 4[x^3 + 3x^2y + 4xy^2 + 8y^3] + 4(x^2 + 8xy + 8y^2) \\ &= V_v + 4[x^3 + x^2 + 4(y^3 + y^2)] \\ &= V_v + 4[-6N + 3N + 4(-6n + 3n)] = V_v - 12(N + 4n) \end{aligned}$$

$$\begin{array}{r} 405 \\ 26 \\ 437 \\ 380 \\ 47 \end{array}$$

$\therefore v'$  is the less variable  $\therefore u_{33}$  is better than  $u'_{33}$

$$\begin{array}{r} D.H.M.N. \\ 825440 \\ 690 \end{array}$$

$$\begin{array}{r} 231 \\ 4 \\ 924 \\ 3690 \end{array}$$

$$v'^3 = v^3 + 6v^2(x + 4y) + 12v(x + 4y)^2 + 8(x + 4y)^3$$

$$C = \frac{3}{16}, \quad \theta = \frac{1}{2}, \quad K_4 = 128 \cdot \frac{3}{16} \cdot \frac{1}{2} \left( 1 - \frac{60 \cdot 3}{16} + \frac{360 \cdot 3^2}{16^2} \right) = 12 \left( 1 - \frac{360}{32} + \frac{45 \cdot 9}{32} \right) = \frac{77 \cdot 3}{8} = \frac{231}{8}$$

$$K_8 = 16 \cdot 3 \left( 1 - \frac{126 \cdot 3}{16} + \frac{1680 \cdot 3^2}{16^2} - \frac{5040 \cdot 3^3}{16^3} \right) + 3 \left( 16 - 378 + \frac{1680 \cdot 4}{16^2} - \frac{5040 \cdot 17}{16^3} \right) = 3 \left( 16 - 348 + 24 \frac{(560 - 315)}{16} \right)$$

$$= \frac{3}{16} (24 \times 245 - 16 \times 362) = \frac{72 \times 823}{16} = \frac{2469}{2}$$

$$\begin{array}{r} 2469 \\ 9876 \\ 36504 \checkmark \end{array}$$

$$\begin{array}{r} 245 \\ 2205 \\ 6615 \\ 5742 \\ 823 \end{array} \quad \begin{array}{r} 362 \\ 1448 \\ 5792 \end{array}$$

f. 29 v

$$\begin{array}{r} 2-11+10 \\ -2+11-10 \\ \hline 2-13+21-10 \\ \hline 6-34+63-30 \end{array}$$

$$P = \left(\frac{2-x}{3}\right)^a \left(\frac{1+x}{3}\right)^b x^c (1-x)^d + \left(\frac{1+x}{3}\right)^a \left[\frac{2-x}{3}\right]^b (x-x)^c x^d$$

Let  $a < c$ ,  $b < d$

$$= (9-4z)^2 (1-4z)^2$$

$$(-2+11)9 - (16+11)22 =$$

$$(-\frac{1}{2}h + \eta)g - (\frac{1}{2}h + 4\mu g + \frac{1}{2}\eta)h\tau$$

$$U_L = 24V^2 - 6V + 6 \cdot 9 + 30 \cdot 3 + 9^2 = 24(24 - 2.5) = 450$$

$$3h_2b + e(h_2)x + -h_2x \cdot 9 + x(h_2)x + -x = -x$$

$$(h_2 + c) + (h_3 - c) = 2, (h_3 - c) =$$

$$x_0 = x, \quad x_1 = -6N, \quad x_2 = 27N^2, \quad x_3 = -6N^3, \quad x_4 = 27N^4, \quad x_5 = -6N^5$$

$$(-h+r)z - (h+r)z + (h-r)z =$$

$$(281 - 247 + x^2 - 149) - (49 - x) =$$

$$\therefore x + x = 1' + 1' = 2'$$

$$f(n) = n \quad \text{and} \quad f(n) = n$$

$$a^2 - 3b^2 - 3c^2 + 9d^2 = (a + 3d + 9)(a - 3d + 9)$$

\_\_\_\_\_

\_\_\_\_\_

## References.

Burks, B. [Proc. Nat. Ac. Sci.]

Fisher, R. A. (1934). Statistical methods for research workers Ch IV, para 21.1.

" " (1935a). "The detection of linkage with 'dominant' abnormalities"  
Ann. Eng. 6, 187-201

" " (1935b). "The detection of linkage with recessive abnormalities."  
Ann. Eng. 6, 339-351.

" " (1936a) "Heterogeneity of linkage data for Friedreich's ataxia and the spontaneous antigens". Ann. Eng. 7, 17-21.

(1940)  
Finney, D. J. "The Detection of Linkage". Ann. Eng. 10, 171-214.

Bernstein, F. (1931). "Zur Grundlegung der Chromosomentheorie der Vererbung beim Menschen mit besonderer Berücksichtigung der Blutgruppen". Z. ind. Abst. u. Vererb. 57, 113-138.

Haldane, J. B. S. (1936). "A search for incomplete sex-linkage in man"  
Ann. Eng. 7, 28-57

Fisher, R. A. (1936b). "Tests of significance applied to Haldane's data on partial sex linkage". Ann. Eng. 7, 87-104.

Haldane J. B. S. (1938a). "The approximate normalization of a class of frequency distributions". Biometrika 29, 392-404.



f. 30 v

J. B. S. Haldane (1938) "The first six moments of  $\chi^2$  for an  $n$ -fold table with  $n$  degrees

J. B. S. Haldane (1940) "The cumulants and moments of the binomial distribution, and the cumulants of  $\chi^2$  for a  $(n \times 2)$ -fold table.

*Biometrika* 31, 392-395.

J. B. S. Haldane (1941a), (1941b) (*Biometrika*)

Hogben, L. and Pollack R. (1935) "A contribution to the relation of the gene loci involved in the isoagglutinin reaction, taste blindness, Friedreich's ataxia, and major brachydactyly of man". *J. Gen.* 31, 353-361.

J. B. S. Haldane (1940b). [Paper on modifiers in *J. Gen.*] *Rel. Imp. of*  
- *Princ. & Modif.* - gives in det. some human diseases.  
XL, 149-157

Wilson, E. B. and Hafferty M. M. (1931). "The distribution of Chi-square".  
*Proc Nat. Ac. Sci.* 17, 684-

White, T. (1940) [*J. Gen.*] Linkage & Crossing Over in the  
Human Sex Chromosomes. 40. 3. 403-437

Zieve, I., Wiener, A. S., and Fries J. H. (1936). "On the linkage relations of the genes for allergic disease, and the genes determining the blood groups, MN types and eye colour in man". *Ann. E. 4*, 163-178.

Cornish, E. A. and Fisher R. A. (1939) "Moments and cumulants in the specification of distributions" *Revue de l'Institut International de Statistique*, 1937, IV. 1-14.

## References.

- Bernstein F. (1931). "Zur Grundlegung der Chromosomentheorie der Vererbung beim Menschen mit besonderer Berücksichtigung der Blutgruppen." Z. ind Abst. u. Vererb. 57, 113-138.
- Burks, B. (1938) "Autosomal linkage in man- the recombination ratio between congenital tooth deficiency and hair colour. J.Nat.Acad.Sci. 24.7.276-282.
- Fisher, R.A. (1934). Statistical methods for research workers. Ch. IV, para 21.1.
- .. .. (1935a) "The detection of linkage with dominant abnormalities." Ann. Eug. 6, 187-201.
- .. .. (1935b) "The detection of linkage with recessive abnormalities." Ann. Eug. 6, 339-551.
- .. .. (1936a) "Heterogeneity of linkage data for Friedreich's ataxia and the spontaneous antigens." Ann. Eug. 7, 17-21.
- .. .. (1936b) "Tests of significance applied to Haldane's data on partial sex linkage." Ann. Eug. 7, 87-104.
- Finney D.J. (1940) "The Detection of Linkage." Ann. Eug. 10, 171-214
- Haldane J.B.S. (1936) "A search for incomplete sex-linkage in man." Ann. Eug. 7, 28-57.
- .. .. (1938a) "The approximate normalization of a class of frequency distributions." Biometrika 29, 392-404.
- .. .. (1940a) "The cumulants and moments of the binomial distribution, and the cumulants of for a (n 2) fold table. Biometrika 31, 392-395.
- .. .. (1940b) "The Relative importance of principal and modifying genes in determining some human characters. J.Gen. XLI. 149.
- .. .. (1941a), (1941b) "The Cumulants of the Distribution of the Square of a Variate." Biometrika. XXXII 199-200.
- Hogben, L and Pollack R. (1935) "A contribution to the relation of the gene loci involved in the isoagglutinin reaction, taste blindness, Friedreich's ataxia, and major brachydactyly of man". J.Gen. 31. 353-361.
- Wilson, E.B. and Hefferty M.M. (1931) "The distribution of Chi-Square Proc. Nat. Ac.Sci. 17, 684-
- White, T. (1940) "Linkage and Crossing over in the Human Sex Chromosomes. 40. 403-437.
- Zieve, I, Wiener, A.S., and Fries J.H. (1936) "On the linkage relations of the genes for allergic disease, and

the genes determining the blood groups, MN types and eye colour in man." Ann. Eug. 7, 163-178.

Cornish, E.A. and Fisher R.A. (1937) "Moments and cumulants in the specification of distributions." Revue de l'Institut International de Statistique, 1937, IV.1-14.

$$\begin{aligned}
 \frac{K_3'}{8} &= 8K_1^2(K_1K_3+3K_2K_4) + K_1^2(K_1K_3+3K_2^2) + \frac{1}{2}(3K_1^2K_4+12K_1K_2K_3+2K_2^3) + \frac{1}{4}(3K_1K_5+6K_2K_4+5K_3^2) + K_6 \\
 &= K_1^3K_3 + 3K_1^2K_2^2 + \frac{3}{2}K_1^2K_4 + 6K_1K_2K_3 + K_2^3 + \frac{3}{2}K_1K_5 + \frac{3}{2}K_2K_4 + \frac{5}{4}K_3^2 + \frac{1}{8}K_6 \\
 &= -2\eta^2a^3[a+b-\eta(u+10b)] + 3\eta a^2[u-\eta(u+b)]^2 - 3\eta a^2[a+b-4\eta(u+10b) + 3\eta^2(u+9b)] \\
 &\quad - 12\eta a[a-\eta(u+b)][a+b-\eta(u+10b)] + [a-\eta(u+b)]^3 + 6\eta a[2(u+10b)-5\eta(u+9b) + 3\eta^2(u+8b)] \\
 &\quad - 3[a-\eta(u+b)][a+b-4\eta(u+10b) + 3\eta^2(u+9b)] + 5\eta[a+b-\eta(u+10b)]^2 + \frac{1}{8}K_6
 \end{aligned}$$

$$\begin{aligned}
 &= -2\eta^2a^3[a+b-\eta(u+10b)] + 3\eta a^2[a^2-2\eta a(u+b) + \eta^2(u+b)^2] - 3\eta a^2[a+b-4\eta(u+10b) + 3\eta^2(u+9b)] \\
 &\quad - 12\eta a[a(u+b)-\eta(u+b)^2-\eta a(u+10b) + \eta^2(u+b)(u+10b)] + a^3-3\eta a^2(u+b) + 3\eta^2a(u+b)^2 - \eta^3(a+b)^3 \\
 &\quad + 6\eta a[2(u+10b)-5\eta(u+9b) + 3\eta^2(u+8b)] - 3[a(u+b)-\eta(u+b)^2-4\eta a(u+10b) + 4\eta^2(u+b)(u+10b) \\
 &\quad + 3\eta^2a(u+9b) - 3\eta^2(u+b)(u+9b)] + 5\eta[u(u+b)^2-2\eta(u+b)(u+10b) + \eta^2(u+10b)^2] \\
 &\quad + 2(u+10b)-14\eta(u+9b) + 30\eta^2(u+8b) - 15\eta^3(u+738b) \\
 &= a(u-1)(u-2) - b(3a-20) + \eta[2a^4-18a^2(u+b) + 24a(u+10b) + 8(u+b)^2-14(u+9b)] \\
 &\quad + \eta^2[-8a^3(u+b) + 24a^2(u+10b) + 15a(u+b)^2-34a(u+9b) - 22(u+b)(u+10b) + 30(u+8b)] \\
 &\quad + \eta^3[2a^3(u+10b) + 3a^2(u+b)^2-4a^2(u+9b) - 11a(u+b)(u+10b) - (u+b)^3 + 18a(u+8b) + 9(a+b)(u+9b) \\
 &\quad + 5(u+10b)^2-15(u+738b)]
 \end{aligned}$$

$$\begin{aligned}
 &= a(a-1)(a-2) - b(3a-20) + \eta[a(u-1)(3a^2-15a+14) - b(18a^2-256a+1544) + 8b^2] \\
 &\quad - \eta^2[a(u-1)(8a^2-31a+30) + b(8a^3-240a^2+3491a-24600) - 5b^2(3a-44)] \\
 &\quad + \eta^3[a(u-1)(5a^2-14a+15) + b(26a^3-954a^2+16688a-110715) + b^2(3a^2-123a+1319) - b^3]
 \end{aligned}$$

$$\begin{aligned}
 &= a(a-1)(a-2) - b(3a-20) + \eta[a(u-1)\{3(u-2)(u-3)-1\} - b\{18[(u-4)^2+34]-(4a+1)\} + 8b^2] \\
 &\quad - \eta^2[a(u-1)(u-2)(8a-15) + b\{8(u-11)^3 - 6(u-3)^2(u+538)\} - 6(a-18)(a-130) - (u+912)\} - 5b^2(3a-44)] \\
 &\quad + \eta^3[a(u-1)(5a^2-14a+15) + b\{26(u-12)^3 - 9(u-12)(u-44) + 12a-2635\} + b^2\{3(u-24)(u-21) + 54\} + b^3]
 \end{aligned}$$



ct sm cp cv q (E) x oth fs (average)

2 regular daughters, one cv q (alleged)

cv q x oth fs

1 cv oth fs, 1 + oth fs, 1 + + +

1 + q, 1 + + fs q.

? was she  $\frac{+}{cv}$  wrongly sworn as cv?

$$\begin{array}{r} 815040 \\ 630 \end{array}$$

$$1680.4 - 315.27$$

$$= 24(560 - 315)$$

$$\frac{3.5}{24}$$

$$\frac{2205}{2}$$

$$\frac{6615}{2}$$

$$\frac{3307.5}{2}$$

$$\frac{1653.75}{2}$$

$$\frac{826.875}{2}$$

$$\frac{413.4375}{2}$$

$$\frac{206.71875}{2}$$

$$\frac{103.359375}{2}$$

$$\frac{51.6796875}{2}$$

$$\frac{25.83984375}{2}$$

$$\frac{12.919921875}{2}$$

$$\frac{6.4599609375}{2}$$

$$\frac{3.22998046875}{2}$$

$$\frac{1.614990234375}{2}$$

$$\frac{0.8074951171875}{2}$$

$$\frac{0.40374755859375}{2}$$

$$\frac{0.201873779296875}{2}$$

$$\frac{0.1009368896484375}{2}$$

$$\frac{0.05046844482421875}{2}$$

$$\frac{0.025234222412109375}{2}$$

$$\frac{0.0126171112060546875}{2}$$

$$\frac{0.00630855560302734375}{2}$$

$$\frac{0.003154277801513671875}{2}$$

$$\frac{0.0015771389007568359375}{2}$$

$$\frac{0.00078856945037841796875}{2}$$

$$\frac{0.000394284725189208984375}{2}$$

$$\frac{0.0001971423625946044921875}{2}$$

$$\frac{9.857118129730224609375 \times 10^{-5}}{2}$$

$$\frac{4.9285590648651123046875 \times 10^{-5}}{2}$$

$$\frac{2.46427953243255615234375 \times 10^{-5}}{2}$$

$$\frac{1.232139766216278076171875 \times 10^{-5}}{2}$$

$$\frac{6.160698831081390380859375 \times 10^{-6}}{2}$$

$$\frac{3.0803494155406951904296875 \times 10^{-6}}{2}$$

$$\frac{1.54017470777034759521484375 \times 10^{-6}}{2}$$

$$\frac{7.700873538851737976072421875 \times 10^{-7}}{2}$$

$$\frac{3.8504367694258689880362109375 \times 10^{-7}}{2}$$

$$\frac{1.92521838471293449401810546875 \times 10^{-7}}{2}$$

$$\frac{9.62609192356467247009052734375 \times 10^{-8}}{2}$$

$$\frac{4.813045961782336235045263671875 \times 10^{-8}}{2}$$

$$\frac{2.4065229808911681175226318359375 \times 10^{-8}}{2}$$

$$\frac{1.20326149044558405876131591796875 \times 10^{-8}}{2}$$

$$\frac{6.01630745222792029380657958984375 \times 10^{-9}}{2}$$

$$\frac{3.008153726113960146903289794921875 \times 10^{-9}}{2}$$

$$\frac{1.5040768630569800734516448974609375 \times 10^{-9}}{2}$$

$$\frac{7.52038431528490036725822448873046875 \times 10^{-10}}{2}$$

$$\frac{3.760192157642450183629112244365234375 \times 10^{-10}}{2}$$

$$\frac{1.8800960788212250918145561221826171875 \times 10^{-10}}{2}$$

$$.0465^i$$

$$4.056$$

$$.186248$$

$$2328$$

$$279$$

$$.188847$$

$$.216$$

$$.216$$

$$0432$$

$$216$$

$$1296$$

$$046656$$

$$3.2$$

$$2.8$$

$$4.48$$

$$1.92$$

$$.36$$

$$6.76$$

$$\begin{aligned} & \text{1 Count of 8. If } p = .4, \text{ prob is } .6^8 + 8 \times .6^7 \times .4 = .6^7 (.6 + 8 \times .4) \\ & = 3.8 \times .6^7 \text{ (out of 9. } P = .6^9 + 8 \times .4 \times .6^8 + 28 \times .4^2 \times .6^7 = .6^7 (.36 + 1.92 + 4.48) \\ & = 6.76 \times .6^7 = 4.056 \times .216 = .189 \end{aligned}$$

$u_{33}$

a ND, c NR, b n D, d n R

$$E u_{33} = [a - 3b - (3b - qd)] - (a + qb + qc + 8d)$$

$$= [N - 4c - 3(N - 4d)] - [N + 8c + q(n + 8d)]$$

Cumulants of  $c$  are:

$$K_1 = \frac{N}{4}$$

$$K_2 = \frac{3}{16}$$

$$K_3 = \frac{3}{32}$$

$$K_4 = \frac{3}{16} (1 - \frac{9}{8}) = -\frac{3}{16} \times 2^{-1}$$

$$K_5 = \frac{1}{2} \times \frac{3}{16} (1 - \frac{9}{4}) = -\frac{3}{16}$$

$$K_6 = \frac{3}{16} (1 - \frac{30.3}{16} + \frac{120.3^2}{16^2}) = \frac{3}{16} (1 - \frac{180}{32} + \frac{135}{32}) = \frac{-3}{16}$$

$$K_7 = \frac{1}{2} \times \frac{3}{16} (1 - \frac{60.3}{16} + \frac{360.9}{16^2}) = \frac{3}{32} (1 - \frac{360}{32} + \frac{605}{32}) = \frac{3.67}{2^{10}}$$

$$K_8 = \frac{3}{16} (1 - \frac{126.3}{16} + \frac{1680.7}{16^2} - \frac{5040.27}{16^3}) = \frac{3}{16} (1 - \frac{378}{16} + \frac{245.27}{16^2}) = \frac{2464}{2^{12}}$$

Cumulants of  $x$  are:

$$K_1 = 3 - 3N, K_2 = -2.3N, K_3 = 2.3N, K_4 = 2^3 \cdot 3.5N, K_5 = 2^4 \cdot 3.13N, K_6 = -2^4 \cdot 3.67N, K_7 = -2^4 \cdot 3.823N$$

Cumulants of  $-N + 4c$  are:

$$K_1 = 0$$

$$K_2 = 3N$$

$$K_3 = 6N$$

$$K_4 = -6N$$

$$K_5 = -120N = -15.2^3N$$

$$K_6 = -48 - 312N = -39.2^4N$$

$$K_7 = 3216N = 201.2^5N$$

$$K_8 = 2464 \cdot 2^4N$$



$$c+d=n$$

$$c+d=n, c=n-d$$

$$n-d$$

f.33v

$$u_3 = \frac{(c-3d)^2}{(n-4d)^2} (c+4d)$$

[From *Biometrika*, Vol. XXXII. Part II. October, 1941.]

[All Rights reserved.]

PRINTED IN GREAT BRITAIN

(v) The Cumulants of the Distribution of the Square of a Variate

By J. B. S. HALDANE, F.R.S.

The following problem has arisen in several biometric investigations. The cumulants of the distribution of  $x$  are known, and it is desired to find the cumulants of the distribution of  $x^2$ . As this problem is likely to arise in future, it seems desirable to give the appropriate transformations for the first few cumulants.

Let  $\kappa_1, \kappa_2, \kappa_3, \dots$  be the cumulants of  $x$ .

Let  $\mu'_1, \mu'_2, \mu'_3, \dots$  be the moments of  $x^2$  about zero.

Let  $\mu_2, \mu_3, \mu_4, \dots$  be the moments of  $x^2$  about its mean.

Let  $\kappa'_1, \kappa'_2, \kappa'_3, \dots$  be the cumulants of  $x^2$ .

Then  $\mu'_r$  is the  $r$ th moment of  $x$ . These have been given in terms of the cumulants up to the 10th, i.e.  $\mu'_{10}$ , in the general case by Kendall (1940), and up to the 12th, i.e.  $\mu'_{12}$ , by Haldane (1938) when  $\kappa_1 = 0$ . We consider the general case first. We have such expressions as

$$\mu'_2 = \kappa_1^2 + 6\kappa_1^2\kappa_2 + 4\kappa_1\kappa_3 + 3\kappa_2^2 + \kappa_4.$$

From these we calculate the moments  $\mu_r$ , and hence the cumulants. The results are:

$$\left. \begin{aligned} \kappa'_1 &= \kappa_1^2 + \kappa_2, \\ \kappa'_2 &= 4\kappa_1^2\kappa_2 + 2(2\kappa_1\kappa_3 + \kappa_2^2) + \kappa_4, \\ \kappa'_3 &= 8\kappa_1^2(\kappa_1\kappa_3 + 3\kappa_2^2) + 4(3\kappa_1^2\kappa_4 + 12\kappa_1\kappa_2\kappa_3 + 2\kappa_2^3) + 2(3\kappa_1\kappa_5 + 6\kappa_2\kappa_4 + 5\kappa_3^2) + \kappa_6, \\ \kappa'_4 &= 16\kappa_1^2(\kappa_1^2\kappa_4 + 12\kappa_1\kappa_2\kappa_3 + 12\kappa_2^3) \\ &\quad + 16(2\kappa_1^2\kappa_5 + 18\kappa_1^2\kappa_2\kappa_4 + 12\kappa_1^2\kappa_3^2 + 36\kappa_1\kappa_2^2\kappa_3 + 3\kappa_2^4) \\ &\quad + 8(3\kappa_1^2\kappa_6 + 18\kappa_1\kappa_2\kappa_5 + 32\kappa_1\kappa_3\kappa_4 + 18\kappa_2^2\kappa_4 + 30\kappa_2\kappa_3^2) \\ &\quad + 8(\kappa_1\kappa_7 + 3\kappa_2\kappa_6 + 7\kappa_3\kappa_5 + 4\kappa_4^2) + \kappa_8. \end{aligned} \right\} \quad (1)$$

After this the expressions become very heavy. When  $\kappa_1 = 0$ , i.e.  $x$  has its mean zero, most of the terms vanish, and we have

$$\left. \begin{aligned} \kappa'_1 &= \kappa_2, \\ \kappa'_2 &= 2\kappa_2^2 + \kappa_4, \\ \kappa'_3 &= 8\kappa_2^3 + 2(6\kappa_2\kappa_4 + 5\kappa_3^2) + \kappa_6, \\ \kappa'_4 &= 48\kappa_2^4 + 48\kappa_2(3\kappa_2\kappa_4 + 5\kappa_3^2) + 8(3\kappa_2\kappa_6 + 7\kappa_3\kappa_5 + 4\kappa_4^2) + \kappa_8, \\ \kappa'_5 &= 384\kappa_2^5 + 960\kappa_2^2(\kappa_2\kappa_4 + 5\kappa_3^2) + 80(16\kappa_2\kappa_6 + 28\kappa_2\kappa_3\kappa_5 + 6\kappa_2^2\kappa_6 + 25\kappa_3^2\kappa_4) \\ &\quad + 2(20\kappa_2\kappa_8 + 60\kappa_3\kappa_7 + 100\kappa_4\kappa_6 + 63\kappa_5^2) + \kappa_{10}, \\ \kappa'_6 &= 3840\kappa_2^6 + 9600\kappa_2^3(3\kappa_2\kappa_4 + 10\kappa_3^2) + 4800(2\kappa_2^2\kappa_6 + 14\kappa_2^2\kappa_3\kappa_5 + 8\kappa_2^2\kappa_4^2 + 25\kappa_2\kappa_3^2\kappa_4 + 3\kappa_3^4) \\ &\quad + 40(30\kappa_2^2\kappa_8 + 180\kappa_2\kappa_3\kappa_7 + 300\kappa_2\kappa_4\kappa_6 + 226\kappa_3^2\kappa_6 + 189\kappa_2\kappa_5^2 + 672\kappa_3\kappa_4\kappa_5 + 132\kappa_4^2) \\ &\quad + 4(15\kappa_2\kappa_{10} + 55\kappa_3\kappa_9 + 120\kappa_4\kappa_8 + 198\kappa_5\kappa_7 + 113\kappa_6^2) + \kappa_{12}. \end{aligned} \right\} \quad (2)$$

Finally, if  $x$  be symmetrically distributed, so that all its odd cumulants vanish,

$$\left. \begin{aligned} \kappa'_1 &= \kappa_2, \\ \kappa'_2 &= 2\kappa_2^2 + \kappa_4, \\ \kappa'_3 &= 8\kappa_2^3 + 12\kappa_2\kappa_4 + \kappa_6, \\ \kappa'_4 &= 48\kappa_2^4 + 144\kappa_2^2\kappa_4 + 8(3\kappa_2\kappa_6 + 4\kappa_4^2) + \kappa_8, \\ \kappa'_5 &= 384\kappa_2^5 + 1920\kappa_2^3\kappa_4 + 160\kappa_2(3\kappa_2\kappa_6 + 8\kappa_4^2) + 40(\kappa_2\kappa_8 + 5\kappa_4\kappa_6) + \kappa_{10}, \\ \kappa'_6 &= 3840\kappa_2^6 + 28800\kappa_2^4\kappa_4 + 9600\kappa_2^2(\kappa_2\kappa_6 + 4\kappa_4^2) + 240(5\kappa_2^2\kappa_8 + 50\kappa_2\kappa_4\kappa_6 + 22\kappa_4^3) \\ &\quad + 4(15\kappa_2\kappa_{10} + 120\kappa_4\kappa_8 + 113\kappa_6^2) + \kappa_{12}. \end{aligned} \right\} \quad (3)$$

I have bracketed together terms which are products of the same number of  $\kappa_r$ 's. If  $x$  is a linear function of observed numbers in a sample of  $n$ , every  $\kappa_n$  is proportional to  $x$ , so the terms in brackets will all be multiples of the same power of  $n$ .

#### REFERENCES

- HALDANE, J. B. S. (1938). 'The first six moments of  $\chi^2$  for an  $n$ -fold table with  $n$  degrees of freedom when some expectations are small.' *Biometrika*, **29**, 389-91.  
 KENDALL, M. G. (1940). 'The derivation of multivariate sampling formulae from univariate formulae by symbolic operation.' *Ann. Eugen., Lond.*, **10**, 392-402.

[From *Biometrika*, Vol. XXXII. Part II. October, 1941.]

[All Rights reserved.]

PRINTED IN GREAT BRITAIN

(v) The Cumulants of the Distribution of the Square of a Variate

By J. B. S. HALDANE, F.R.S.

The following problem has arisen in several biometric investigations. The cumulants of the distribution of  $x$  are known, and it is desired to find the cumulants of the distribution of  $x^2$ . As this problem is likely to arise in future, it seems desirable to give the appropriate transformations for the first few cumulants.

Let  $\kappa_1, \kappa_2, \kappa_3, \dots$  be the cumulants of  $x$ .

Let  $\mu'_1, \mu'_2, \mu'_3, \dots$  be the moments of  $x^2$  about zero.

Let  $\mu_2, \mu_3, \mu_4, \dots$  be the moments of  $x^2$  about its mean.

Let  $\kappa'_1, \kappa'_2, \kappa'_3, \dots$  be the cumulants of  $x^2$ .

Then  $\mu'_r$  is the  $2r$ th moment of  $x$ . These have been given in terms of the cumulants up to the 10th, i.e.  $\mu'_{10}$ , in the general case by Kendall (1940), and up to the 12th, i.e.  $\mu'_{12}$ , by Haldane (1938) when  $\kappa_1 = 0$ . We consider the general case first. We have such expressions as

$$\mu'_2 = \kappa_1^4 + 6\kappa_1^2\kappa_2 + 4\kappa_1\kappa_3 + 3\kappa_2^2 + \kappa_4.$$

From these we calculate the moments  $\mu_r$ , and hence the cumulants. The results are:

$$\left. \begin{aligned} \kappa'_1 &= \kappa_1^2 + \kappa_2, \\ \kappa'_2 &= 4\kappa_1^2\kappa_2 + 2(2\kappa_1\kappa_3 + \kappa_2^2) + \kappa_4, \\ \kappa'_3 &= 8\kappa_1^2(\kappa_1\kappa_3 + 3\kappa_2^2) + 4(3\kappa_1^2\kappa_4 + 12\kappa_1\kappa_2\kappa_3 + 2\kappa_2^3) + 2(3\kappa_1\kappa_5 + 6\kappa_2\kappa_4 + 5\kappa_3^2) + \kappa_6, \\ \kappa'_4 &= 16\kappa_1^2(\kappa_1^2\kappa_4 + 12\kappa_1\kappa_2\kappa_3 + 12\kappa_2^3) \\ &\quad + 16(2\kappa_1^2\kappa_5 + 18\kappa_1^2\kappa_2\kappa_4 + 12\kappa_1^2\kappa_3^2 + 36\kappa_1\kappa_2^2\kappa_3 + 3\kappa_2^4) \\ &\quad + 8(3\kappa_1^2\kappa_6 + 18\kappa_1\kappa_2\kappa_5 + 32\kappa_1\kappa_3\kappa_4 + 18\kappa_2^2\kappa_4 + 30\kappa_2\kappa_3^2) \\ &\quad + 8(\kappa_1\kappa_7 + 3\kappa_2\kappa_6 + 7\kappa_3\kappa_5 + 4\kappa_4^2) + \kappa_8. \end{aligned} \right\} \quad (1)$$

After this the expressions become very heavy. When  $\kappa_1 = 0$ , i.e.  $x$  has its mean zero, most of the terms vanish, and we have

$$\left. \begin{aligned} \kappa'_1 &= \kappa_2, \\ \kappa'_2 &= 2\kappa_2^2 + \kappa_4, \\ \kappa'_3 &= 8\kappa_2^3 + 2(6\kappa_2\kappa_4 + 5\kappa_3^2) + 6, \\ \kappa'_4 &= 48\kappa_2^4 + 48\kappa_2(3\kappa_2\kappa_4 + 5\kappa_3^2) + 8(3\kappa_2\kappa_6 + 7\kappa_3\kappa_5 + 4\kappa_4^2) + \kappa_8, \\ \kappa'_5 &= 384\kappa_2^5 + 960\kappa_2^2(\kappa_2\kappa_4 + 5\kappa_3^2) + 80(16\kappa_2\kappa_4^2 + 28\kappa_2\kappa_3\kappa_5 + 6\kappa_2^2\kappa_6 + 25\kappa_3^2\kappa_4) \\ &\quad + 2(20\kappa_2\kappa_8 + 60\kappa_3\kappa_7 + 100\kappa_4\kappa_6 + 63\kappa_5^2) + \kappa_{10}, \\ \kappa'_6 &= 3840\kappa_2^6 + 9600\kappa_2^3(3\kappa_2\kappa_4 + 10\kappa_3^2) + 4800(2\kappa_2^2\kappa_6 + 14\kappa_2^2\kappa_3\kappa_5 + 8\kappa_2^2\kappa_4^2 + 25\kappa_2\kappa_3^2\kappa_4 + 3\kappa_3^4) \\ &\quad + 40(30\kappa_2^2\kappa_8 + 180\kappa_2\kappa_3\kappa_7 + 300\kappa_2\kappa_4\kappa_6 + 226\kappa_3^2\kappa_6 + 189\kappa_2\kappa_5^2 + 672\kappa_3\kappa_4\kappa_5 + 132\kappa_4^3) \\ &\quad + 4(15\kappa_2\kappa_{10} + 55\kappa_3\kappa_9 + 120\kappa_4\kappa_8 + 198\kappa_5\kappa_7 + 113\kappa_6^2) + \kappa_{12}. \end{aligned} \right\} \quad (2)$$

Finally, if  $x$  be symmetrically distributed, so that all its odd cumulants vanish,

$$\left. \begin{aligned} \kappa'_1 &= \kappa_2, \\ \kappa'_2 &= 2\kappa_2^2 + \kappa_4, \\ \kappa'_3 &= 8\kappa_2^3 + 12\kappa_2\kappa_4 + \kappa_6, \\ \kappa'_4 &= 48\kappa_2^4 + 144\kappa_2^2\kappa_4 + 8(3\kappa_2\kappa_6 + 4\kappa_4^2) + \kappa_8, \\ \kappa'_5 &= 384\kappa_2^5 + 1920\kappa_2^3\kappa_4 + 160\kappa_2(3\kappa_2\kappa_6 + 8\kappa_4^2) + 40(\kappa_2\kappa_8 + 5\kappa_4\kappa_6) + \kappa_{10}, \\ \kappa'_6 &= 3840\kappa_2^6 + 28800\kappa_2^4\kappa_4 + 9600\kappa_2^2(\kappa_2\kappa_6 + 4\kappa_4^2) + 240(5\kappa_2^3\kappa_8 + 50\kappa_2\kappa_4\kappa_6 + 22\kappa_4^3) \\ &\quad + 4(15\kappa_2\kappa_{10} + 120\kappa_4\kappa_8 + 113\kappa_6^2) + \kappa_{12}. \end{aligned} \right\} \quad (3)$$

I have bracketed together terms which are products of the same number of  $\kappa_r$ 's. If  $x$  is a linear function of observed numbers in a sample of  $n$ , every  $\kappa_r$  is proportional to  $n$ , so the terms in brackets will all be multiples of the same power of  $n$ .

#### REFERENCES

- HALDANE, J. B. S. (1938). 'The first six moments of  $\chi^2$  for an  $n$ -fold table with  $n$  degrees of freedom when some expectations are small.' *Biometrika*, **29**, 389-91.  
 KENDALL, M. G. (1940). 'The derivation of multivariate sampling formulae from univariate formulae by symbolic operation.' *Ann. Eugen., Lond.*, **10**, 392-402.



REPRINTED FROM  
 ANNALS OF EUGENICS, Vol. 11, PART 2, pp. 179-181, 1941  
 [All rights reserved.] PRINTED IN GREAT BRITAIN

## THE FITTING OF BINOMIAL DISTRIBUTIONS

By J. B. S. HALDANE, F.R.S.

A NUMBER of cases arise where on different occasions an event has occurred 0, 1, 2, 3, ...,  $r$ , ... times. Sometimes a Poisson distribution gives a good fit, the probability of the event occurring  $r$  times being  $P_r = e^{-m} \frac{m^r}{r!}$ . In other cases a good fit may be obtained to a binomial

distribution where  $P_r$  is the coefficient of  $t^r$  in  $(1 - p + pt)^k$ . Here  $p$  and  $k$  are both positive or both negative. Where they are negative it is convenient to write  $p' = -p$ ,  $k' = -k$ . Hence

$$P_r = \frac{k(k-1) \dots (k-r+1)}{r!} p^r (1-p)^{k-r},$$

$$\text{or} \quad \frac{k'(k'+1) \dots (k'+r-1)}{r!} p'^r (1+p')^{-k'-r}.$$

Such distributions have been discussed, with numerical examples, by Whitaker (1914), and Greenwood & Yule (1920) have paid special attention to the negative binomial distribution where  $p$  and  $k$  are negative.

In the past these distributions have, I think, always been fitted by the first two moments. For if  $m$  and  $v$  are the observed mean and variance, their expectations are  $E(m) = kp$ ,  $E(v) = kp(1-p)$ . Whence we obtain consistent estimates,  $\hat{p} = \frac{m-v}{m}$ ,  $\hat{k} = \frac{m^2}{m-v}$ . However, this method of estimation does not appear to be fully efficient. Fitting by maximum likelihood is so. Jeffreys (1939) states (pp. 260, 374) that tables of digamma functions are required for such fitting. It is the object of this note to show that the fitting may be done by elementary methods.

Let  $q = 1 - p$ . Let  $n_r$  be the observed frequency of  $r$ ,  $R$  the maximum value of  $r$ . Let  $N = \sum_{r=0}^R n_r$ , the total number of observations, and  $m = \frac{1}{N} \sum_{r=0}^R r n_r$ , the mean value of  $r$ . Then the logarithm of the likelihood is

$$L = \sum_{r=0}^R n_r \log P_r = \sum_{r=0}^R n_r \left[ r \log p + (k-r) \log q + \sum_{s=0}^{r-1} \log(k-s) - \log r! \right],$$

$$\frac{\partial L}{\partial p} = \frac{1}{pq} \sum n_r (r - kp) = 0,$$

$$\text{whence} \quad kp = m. \quad (1)$$

$$\frac{\partial L}{\partial k} = \sum n_r \left( \log q + \sum_{s=0}^{r-1} \frac{1}{k-s} \right) = 0.$$

$$\therefore N \log q + \sum_{r=0}^R \frac{1}{k-r} \sum_{s=r+1}^R n_s = 0,$$

$$\text{or} \quad N[\log k - \log(k-m)] = \frac{n_1 + n_2 + \dots + n_R}{k} + \frac{n_2 + n_3 + \dots + n_R}{k-1} + \dots + \frac{n_R}{k-R+1}. \quad (2)$$

When  $k$  and  $p$  are negative, this becomes

$$N[\log(k' + m) - \log k'] = \frac{n_1 + n_2 + \dots + n_R}{k'} + \frac{n_2 + n_3 + \dots + n_R}{k' + 1} + \dots + \frac{n_R}{k' + R - 1}. \quad (2.1)$$

These equations can be stated in terms of digamma functions, but this is quite unnecessary, and they can be solved without great difficulty by trial and interpolation, rejecting the infinite root.

We further have

$$\begin{aligned} \frac{-\partial^2 L}{\partial p^2} &= \frac{kN}{pq}, \quad \frac{-\partial^2 L}{\partial p \partial k} = \frac{N}{q}, \\ \frac{-\partial^2 L}{\partial k^2} &= \sum_{r=0}^R (k-r)^{-2} \sum_{s=r+1}^R n_s \\ &= \frac{n_1 + n_2 + \dots + n_R}{k^2} + \frac{n_2 + n_3 + \dots + n_R}{(k-1)^2} + \dots + \frac{n_R}{(k-R+1)^2} \\ &= \frac{n_1 + n_2 + \dots + n_R}{k'^2} + \frac{n_2 + n_3 + \dots + n_R}{(k'+1)^2} + \dots + \frac{n_R}{(k'+R-1)^2}. \end{aligned}$$

Hence the amounts of information concerning  $p$  and  $k$  are

$$\begin{aligned} I_p &= -\frac{\partial^2 L}{\partial p^2} + \left( \frac{\partial^2 L}{\partial p \partial k} \right)^2 \frac{1}{\partial^2 L / \partial k^2} \\ &= \frac{N}{q} \left[ \frac{k}{p} - \frac{N}{q \sum_{r=0}^R (k-r)^{-2} \sum_{s=r+1}^R n_s} \right], \end{aligned} \quad (3)$$

$$I_k = \sum_{r=0}^R (k-r)^{-2} \sum_{s=r+1}^R n_s - \frac{pN}{kq}. \quad (4)$$

Whitaker's values, in my terminology, are

$$I_p = \frac{kn}{1 + (2k-3)p}, \quad I_k = \frac{q^2 N}{2k(k-1)p^2}.$$

The numerical calculation of  $k$  to more than four significant figures is rather tedious; however, this does not matter in view of its large standard error. But as the numbers to be subtracted in the calculations of  $I_p$  and  $I_k$  are very nearly equal,  $p$ ,  $q$  and  $\frac{-\partial^2 L}{\partial k^2}$  should be calculated to seven or eight significant figures.

As an example, we take Whitaker's data for the numbers of days out of 1096 on which  $r$  deaths of women over 80 were reported in *The Times* of 1910-12. They are:  $n_0 = 162$ ,  $n_1 = 267$ ,  $n_2 = 271$ ,  $n_3 = 185$ ,  $n_4 = 111$ ,  $n_5 = 61$ ,  $n_6 = 27$ ,  $n_7 = 8$ ,  $n_8 = 3$ ,  $n_9 = 1$ .  $k' = 10.0$  gives the R.H.S. of equation (2.1) as 213.78, the L.H.S. as 213.97.  $k' = 9.9$  gives the R.H.S. as 216.029, the L.H.S. as 216.028. Hence  $k' = 9.900$ . From equations (1), (3) and (4) we have

$$p = -0.21787 \pm 0.05292, \quad k = -9.900 \pm 2.492.$$

By the method of moments, Whitaker found

$$p = -0.20770 \pm 0.04862, \quad k = -10.440 \pm 2.702.$$

Thus the two results only differ by about one-fifth of the standard error, and in this case, at least, the method of moments is quite satisfactory. However with a smaller total, it would be less reliable. In any case it is useful to take  $(m-v)/m^2$  as a first approximation to  $k$  in solving equation (2) or (2.1). It is also convenient to multiply both sides of this equation by  $k$ . If this is done, one side increases with  $k$ , whilst the other diminishes, and interpolation becomes easier. I have to thank Dr Jeffreys for a correction.

## SUMMARY

A binomial law can readily be fitted to observed data by the method of maximum likelihood.

## REFERENCES

- M. GREENWOOD & G. U. YULE (1920). 'An enquiry into the nature of frequency distributions representative of multiple happenings with particular reference to the occurrence of multiple attacks of disease or of repeated accidents.' *J.R. Stat. Soc.* **83**, 255-79.  
H. JEFFREYS (1939). *Theory of Probability*. Oxford.  
L. WHITAKER (1914). 'On the Poisson Law of small numbers.' *Biometrika*, **10**, 36-71.

That is to say we must substitute  $N$  for  $n$  in the above expressions,  $\frac{J}{9}$  for  $J$ , and also change the sign of  $J^{\frac{1}{2}}$ . So putting  $J = 9\eta$  the cumulants of  $x-3y$  are:-

$$k_1 = -\eta^{\frac{1}{2}}(N+9n)$$

$$k_2 = N+9n - \eta(N+9^2n)$$

$$k_3 = 2\eta^{\frac{1}{2}}[N+9^2n - \eta(N+9^3n)]$$

$$k_4 = -2[N+9^2n - 4\eta(N+9^3n) + 3\eta^2(N+9^4n)]$$

$$k_5 = -8\eta^{\frac{1}{2}}[2(N+9^3n) - 5\eta(N+9^4n) + 3\eta^2(N+9^5n)]$$

$$k_6 = 8[2(N+9^3n) - 14\eta(N+9^4n) + 30\eta^2(N+9^5n) - 15\eta^3(N+9^6n)].$$

etc. The cumulants of  $u$ , after the first, are those of  $(x-3y)^2$ .

They are obtained from the above by the expressions (1) given

by Haldane (1941a) and are, putting  $N+9n=A$ ,  $72n=B$ ,:-

$$k_1 = \frac{J}{9} [A(A-1) - B]$$

$$\frac{1}{2} k_2 = A(A-1) - B + 2\frac{J}{9} [A(A-1)(A-2) - B(3A-20)] - \left(\frac{J}{9}\right)^2 [A(A-1)(2A-3) + B(2A^2-42A+273) - B^2].$$

$$\frac{1}{6} k_3 = A(A-1)(A-2) - B(3A-20) + \frac{J}{9} [A(A-1)\{3(A-2)(A-3) - 1\} - B(18A^2-256A+1547) + 8B^2] - \left(\frac{J}{9}\right)^2 [3A(A-1)(2A^2-11A+10) + B(6A^3-270A^2+3,793A-24,600) - 5B^2(3A-44)] + \left(\frac{J}{9}\right)^3 [A(A-1)(3A^2-19A+15) + B(6A^3-954A^2+15,710A-110,715) + B^2(3A^2-123A+1,339) - B^3] \dots (3)$$

The expression for  $k_4$  is very heavy, being the sum of 18 products of the cumulants of  $x-3y$ . It is unlikely to be used, so I have not given it. It will be noted that the coefficient of  $J$  in  $k_r$  is half the leading term of  $k_{r+1}$ . The general behaviour of  $k_3$  can be seen from the following considerations. When  $J=0$  (no linkage) it is positive provided  $N+n > 2$ . When  $N=0$  and  $J$  is large

f.39 11a

$$\begin{aligned}
\frac{1}{8} K_3 = & A(A-1)(A-2) - B(3A-20) + \frac{Y}{q} \left[ A(A-1) \{ 3(A-2)(A-3) - 1 \} - B \{ 18[(A-4)^2 + 37] - (4A+1) \} + 8B^2 \right] \\
& - \left( \frac{Y}{q} \right)^2 \left[ A(A-1)(A-2)(8A-15) + B \{ 8(A-11)^2 - 6(A-10)(A-130) - (A+912) \} - 5B^2(3A-44) \right] \\
& + \left( \frac{Y}{q} \right)^3 \left[ A(A-1)(5A^2 - 17A + 15) + B \{ 26(A-12)^2 - 9(A-12)(A-494) + 2A - 2635 \} + B^2 \{ 3(A-20)(A-21) + 59 \} \right. \\
& \left. + B^3 \right]
\end{aligned}$$

--- (3)



the cumulants of  $u_{31}$ :-

$$k_1 = 0$$

$$k_2 = 2 [(N+qn)^2 - (N+q^2n)]$$

$$k_3 = 8 [(N+qn)^3 - 3(N+qn)(N+q^2n) + 2(N+q^3n)]$$

$$k_4 = 16 [3(N+qn)^4 - 18(N+qn)^2(N+q^2n) + 8\{3(N+qn)(N+q^3n) + (N+q^2n)^2\} - 17(N+q^4n)]$$

$$k_5 = 128 [3(N+qn)^5 - 30(N+qn)^3(N+q^2n) + 20(N+qn)\{3(N+qn)(N+q^3n) + 2(N+q^2n)^2\} - 5\{17(N+qn)(N+q^4n) + 10(N+q^2n)(N+q^3n)\} + 62(N+q^5n)]$$

$$k_6 = 256 [15(N+qn)^6 - 225(N+qn)^4(N+q^2n) + 600(N+qn)^2\{3(N+qn)(N+q^3n) + (N+q^2n)^2\} - 15\{85(N+qn)^2(N+q^4n) + 100(N+qn)(N+q^2n)(N+q^3n) + 11(N+q^2n)^3\} + 4\{465(N+qn)(N+q^5n) + 255(N+q^2n)(N+q^4n) + 113(N+q^3n)^2\} - 1382(N+q^6n)] \dots (1)$$

These expressions are considerably simplified if we write

$N+qn=A$ ,  $72n=B$ . We then have:-

$$k_2 = 4K_2, \quad K_2 = \frac{1}{2}A(A-1) - \frac{1}{2}B.$$

$$k_3 = 48K_3, \quad K_3 = \frac{1}{6}A(A-1)(A-2) - \frac{1}{6}B(3A-20)$$

$$k_4 = 32K_4, \quad K_4 = \frac{1}{2}A(A-1)[3(A-2)(A-3) - 1] - \frac{1}{2}B[18(A-7)^2 - 4A + 665] + 4B^2$$

$$k_5 = 768K_5, \quad K_5 = \frac{1}{6}A(A-1)(A-2)[3(A-3)(A-4) - 5] - \frac{5B}{6}[6(A-8)^3 + 8(A-12)(A+75) + A+104] + \frac{10}{3}B^2(2A-25)$$

$$k_6 = 512K_6, \quad K_6 = \frac{1}{2}A(A-1)[15(A-2)\{(A-3)[(A-4)(A-5) - 5] - 1\} + 2] + \frac{1}{2}B[225(A-8)^4 + 46,620(A^2 - 25A + 200) + 1,780(A+25) + 558] + \frac{5}{2}B^2[120(A-13)^2 + 21(A+348) + 16] - \frac{165}{2}B^3 \dots (1a)$$

$K_2, K_3$ , etc are integers, not always positive. Fisher (1936b) has tabulated  $2K_2$  in his Table XIV. I give tables of  $K_1, K_2$ , and  $K_4$  in Tables 1, 2, and 3.

The distribution of  $u_{31}$ , deviates considerably from

One parent 0 other  $\frac{n}{2}$ ,  $n_{21}$

F41r

Family	A B N	O N	A B P	O P	N	n	n
2	1	2	0	1	3	1	-8
94	1	1	0	1	2	1	-2
144	2	2	0	1	4	1	-4
18	1	3	3	0	4	3	+90
29	0	1	0	1	1	2	-6
31	0	2	1	0	2	1	+14
32	2	1	0	1	3	1	+4
34	1	0	1	1	1	2	-18
37	0	1	1	1	1	2	-18
41	1	2	0	1	3	1	-18
W	2	2	0	2	4	2	+14

10

One parent 0, other bet

+34

	x N	y N	x P	y P		
3	1	4	0	3	5	3
4	1	0	1	1	1	2
18	1	3	3	0	4	3
23	0	0	1	1	0	2
36	1	4	1	1		
44	1	0	0	1		
A <sub>10</sub> 48	0	2	1	3		
B <sub>0</sub> 46	2	0	2	2		
A <sub>10</sub> 48	1	1	2	0		
A <sub>20</sub> 11	1	1	2	0		
Lockyer A <sub>10</sub>	1	0	0	2		
" B	0	1	1	1		

(2+1) - (2+1)



$N+q^2n = a$	$\begin{array}{r} 91 \\ 224 \\ \hline 820 \end{array}$	$\begin{array}{r} 85 + 7735 \\ 100 + 1100 + 1000 \\ 11 + 33 + 33 + 11 \end{array}$	$\begin{array}{r} 465 + 381,300 \\ 255 + 23,460 + 23,205 \\ 113 + 2,280 + 11,300 \end{array}$
$N+q^3n = a+b$	$\begin{array}{r} 6561 \\ 2381 \\ \hline 765 \end{array}$	$\begin{array}{r} 930 \times 410 \\ 410 \\ \hline 372 \end{array}$	$\begin{array}{r} 833 + 407,020 \\ 1030 \\ \hline 51650 \end{array}$
$N+q^4n = a+q1b$	$\begin{array}{r} 765 \\ 733 \end{array}$	$\begin{array}{r} 460 \\ 51 \\ \hline 230 \end{array}$	$\begin{array}{r} 1381 \\ 1381 \\ \hline 22143 \end{array}$
$N+q^5n = a+820b$		$\begin{array}{r} 460 \\ 253 \\ \hline 23205 \end{array}$	$\begin{array}{r} 59048 \\ 4462 \\ \hline 10200542 \end{array}$
$N+q^6n = a+4381b$			$\begin{array}{r} 1030 \\ 51650 \\ \hline 154950 \end{array}$

$$\begin{aligned}
 R_6 &= \frac{1}{2} [15a^6 - 225a^4(a+b) + 600a^2\{a(a+10b) + (a+b)^2\} - 15\{85a^2(a+q1b) + 100a(a+b)(a+1ab) \\
 &\quad + 11(a+b)^2\} + 4\{465a(a+820b) + 255(a+b)(a+q1b) + 113(a+10b)^2\} - 1382(a+4381b)] \\
 &= \frac{1}{2} [15a^6 - 225a^4(a+b) + 600a^2(a^2 + 10ab + a^2 + 2ab + b^2) - 15\{85a^2(a+q1b) + 100a(a^2 + 11ab + 10b^2) \\
 &\quad + 11(a^3 + 3a^2b + 3ab^2 + b^3)\} + 4\{465a(a+820b) + 255(a^2 + 92ab + q1b^2) + 113(a^2 + 20ab + 100b^2)\} - 1382(a+4381b)] \\
 &= \frac{1}{2} [15a^6 - 225a^4(a+b) + 600a^2(2a^2 + 12ab + b^2) - 15\{196a^3 + 8868a^2b + 1033ab^2 + 11b^3\} \\
 &\quad + 4\{833a^2 + 407,020ab + 34,505b^2\} + 1382(a+4381b)] \\
 &= \frac{1}{2} a(15a^5 - 225a^4 + 1200a^3 - 2440a^2 + 3332a - 1382) - \frac{1}{2} b(225a^4 - 4200a^3 + 133,020a^2 \\
 &\quad - 1,628,080a + 10,100,542) + \frac{1}{2} b^2(600a^2 - 15,495a + 138,020) - \frac{165}{2} b^3 \\
 &= \frac{1}{2} a(a-1)(15a^4 - 210a^3 + 990a^2 - 1950a + 1382) - \frac{1}{2} b[15(a-8)^4 + 46,620a^2 - 1,167,280a + 9,278,942] \\
 &\quad + \frac{1}{2} b^2(120a^2 - 3,099a + 27,604) - \frac{165}{2} b^3 \\
 &= \frac{1}{2} a(a-1)[15(a^4 - 14a^3 + 66a^2 - 130a + 92) + 2] - \frac{1}{2} b[225(a-8)^4 + 46,620(a^2 - 25a + 200) \\
 &\quad + 1780a - 445,058] + \frac{1}{2} b^2[120(a-13)^2 - 21a + 7,324] - \frac{165}{2} b^3 \\
 &= \frac{1}{2} a(a-1)[15\{(a-2)(a-3)(a-4)(a-5) - 5(a-2)(a-3) - (a-2)^2\} + 2] - \frac{1}{2} b[225(a-8)^4 + 46,620(a^2 - 25a + 200) \\
 &\quad + 1780(a-25) + 882] + \frac{1}{2} b^2[120(a-13)^2 + 21(a+348) + 10] - \frac{165}{2} b^3 \\
 &\quad a(a-1) + \frac{15}{2} a(a-1)(a-2)(a-3)(a-4)(a-5) - 5a + 14 \\
 &\quad 15(a-2)\{(a-3)(a-4)(a-5) - 5(a-3)\} + (-1) + 2
 \end{aligned}$$

$$\begin{aligned}
 225(a-8)^4 &= 225a^4 - 225 \cdot 8 \cdot 4a^3 + 225 \cdot 6 \cdot 8^2 a^2 - 225 \cdot 4 \cdot 8^3 + 225 \cdot 8^4 \\
 &= 225a^4 - 7200a^3 + 86,400a^2 - 460,800a + 921,600 \\
 &\quad 133,020 - 1,628,080 + 10,200,542 \\
 &\quad - 86,400 + 460,800 - 921,600 \\
 &\quad 46,620 - 1,167,280 + 9,278,942 \\
 &\quad - 46,620 + 1,167,280 - 9,278,942 \\
 &\quad 120 - 3099 + 27,604 \\
 &\quad - 120 + 3120 - 20,280 \\
 &\quad 1 - 5 + 6 + 21 + 7,324 \\
 &\quad 15 \times (120 - 3099 + 27,604) = 15 \times 24,425 = 366,375 \\
 &\quad 5(a-2)(a-3)(a-4)(a-5) = (a-2)(a-15) \\
 &\quad = (a-2)(a-15)
 \end{aligned}$$



$$a^3 - 3a(u+b) + 2(u+10b) = a^3 - 3a + 2 - b(3a-20)$$

$$\eta [3a^4 - 3a^2(u+b) + 12a(u+10b) + 3(u+b)^2 + 12a(u+b) - 12a^2(u+b) + 12a(u+10b) + 5(u+b)^2 - 14(u+10b) - 3a^2(u+b)]$$

$$\eta^2 [-2a^3(u+b) + 12a^2(u+10b) + 12a(u+b)^2 - 30a(u+10b) - 12(u+b)(u+10b) - 6a^3(u+b) + 12a^2(u+10b) + 3a(u+b)^2 - 4a(u+10b) - 10(u+b)(u+10b) + 30(u+10b)]$$

$$\begin{aligned} & (a-12)(a-544) = a^2 - 606a + 4200 \\ & (a-4)(a-600) = a^2 - 604a + 2400 \\ & (a-2)(a-21) = a^2 - 23a + 42 \\ & (a-20)(a-21) = a^2 - 41a + 420 \end{aligned}$$

3-

f42v

$$\begin{aligned} & 3a^4 - 18a^3 + 15a^2a - 12a \\ & + 4(-18a^2 + 126a - 154b) + 3b^2 \\ & = 3[a^4 - 6a^3 + 5a^2a - 4] \end{aligned}$$

$$\eta^3 [12a^3(u+10b) + 3a^2(u+b)^2 - 9a(u+10b) - 12a(u+b)(u+10b) - (u+b)^3 + 18a(u+10b) + 9(a+b)(u+10b) + 5(u+10b)^2 - 15(u+10b)(u+b)]$$

$$12a^3 + 120ab^2 + 3a^2 + 6ab - 15b^2$$

$$\frac{26}{156} \frac{156}{936} \frac{936}{1232} \frac{1232}{12}$$

$$\frac{26}{156} \frac{156}{936} \frac{936}{1232} \frac{1232}{12}$$

$$3 - 18 + 20 - 17$$

$$4a^3 - 3a(u+b) + 2(u+10b)$$

$$= a^3 - 3a^2u + 3ab + 20b$$

$$4a^3 - 3a(u+b) + 2(u+10b) = 8[3a^2 - 3a(u+b) + 2(u+10b)]$$

$$3a^2 - 6a(u+b) + 3(u+b)^2 + 2(u+10b)$$

$$-24a^2 + 24a(u+b) - 24(u+b)^2$$

$$\begin{aligned} & (a-20)(a-21) = a^2 - 41a + 420 \\ & 3a^2 - 123a + 1314 \\ & -3a^2 + 123a - 1260 \\ & \frac{54}{54} \end{aligned}$$

$$\begin{aligned} & (a-12)^2 = a^2 - 24a + 144 \\ & 26a^2 - 445a^2 + 16,688a - 110,415 \\ & -26a^2 + 936a^2 - 11,232a + 44,428 \\ & -4a^2 + 5,456a - 66,187 \\ & + 4a^2 - 5,454a + 64,152 \\ & + 2a - 2635 \end{aligned}$$



$$\eta = \frac{y}{4}$$

f43r

$$K_1 = -\eta^{\frac{1}{2}}a$$

$$K_2 = a - \eta(a+b)$$

$$K_3 = 2\eta^{\frac{1}{2}}[a+b-\eta(a+10b)]$$

$$K_4 = -2[a+b-4\eta(a+10b)+3\eta^2(a+91b)]$$

$$K_5 = -8\eta^{\frac{1}{2}}[2(a+10b)-5\eta(a+91b)+3\eta^2(a+820b)]$$

$$K_6 = 8[2(a+10b)-14\eta(a+91b)+30\eta^2(a+820b)-15\eta^3(a+4381b)]$$

$$\begin{aligned} K_3' &= 8K_1^2(K_1K_3+3K_2^2)+4[3K_1^2K_4+12K_1K_2K_3+2K_2^3]+2[3K_1K_3+6K_2K_4+5K_3^2]+12K_6 \\ &= 8\eta a^2[-2\eta a\{a+b-\eta(a+10b)\}+3\{a-\eta(a+b)\}^2]+4[3\eta a^2-6\eta a\{a+b-4\eta(a+10b)+3\eta^2(a+91b)\} \\ &\quad -24\eta a\{a-\eta(a+b)\}\{a+b-\eta(a+10b)\}+8\eta\{a+b-\eta(a+10b)\}^2]8\{a-\eta(a+b)\}^3 \\ &\quad +2[24\eta a\{2(a+10b)-5\eta(a+91b)+3\eta^2(a+820b)\}-12\{a-\eta(a+b)\}\{a+b-4\eta(a+10b)+3\eta^2(a+91b)\} \\ &\quad +20\eta\{a+b-\eta(a+10b)\}^2]+16(a+10b)-136\eta(a+91b)+240\eta^2(a+820b)-120\eta^3(a+4381b) \end{aligned}$$

$$\begin{aligned} &= 8\eta a^2[3a^2-2\eta a(4a+3b)+\eta^2\{3(a+b)^2+4a(a+10b)\}]-24\eta a^2[a+b-4\eta(a+10b)+3\eta^2(a+91b)] \\ &\quad -96\eta a[a(a+b)-\eta\{(a+b)^2+a(a+10b)\}+\eta^2(a+b)(a+10b)]+32\eta[(a+b)^2-2\eta(a+b)(a+10b)+\eta^2(a+10b)^2] \\ &\quad +48\eta a[2(a+10b)-5\eta(a+91b)+3\eta^2(a+820b)]-24[a(a+b)-\eta\{(a+b)^2+4a(a+10b)\}+\eta^2\{4(a+b)(a+10b)+3a(a+10b)^2\} \\ &\quad -3\eta^3(a+b)(a+91b)]+40\eta[(a+b)^2-2\eta(a+b)(a+10b)+\eta^2(a+10b)^2]+16(a+10b)-136\eta(a+91b) \\ &\quad +240\eta^2(a+820b)-120\eta^3(a+4381b). \end{aligned}$$

$$\begin{aligned} \frac{K_3'}{8} &= a(a-1)(a-2)-b(3a-20)+\eta[3a^2-18a^2(a+b)+12a(a+10b)+3(a+b)^2+5(a+b)-14(a+91b)] \\ &\quad +\eta^2[-2a^3(4a+3b)+12a^2(a+10b)+12\eta(a+b)^2+12a^2(a+10b)+3a(a+b)^2-30a(a+91b)+3(a+b)^2+12a(a+10b) \\ &\quad -12(a+b)(a+10b)-9a(a+91b) \\ &\quad -10(a+b)(a+10b)+30(a+820b)]+\eta^3[3a^2(a+b)+6a^2(a+10b)-4a^2(a+91b)-12a(a+b)(a+10b)-(a+b)^3 \\ &\quad +18a(a+820b)+9(a+b)(a+91b)+5(a+10b)^2-15(a+4381b)] \\ &= a(a-1)(a-2)-b(3a-20)+\eta[ \end{aligned}$$

$$* + \frac{1}{8}[a^3-3\eta a^2(a+b)+3\eta^2 a(a+b)^2-(a+b)^3]$$

$$0z+19-bz+7-$$

$$\begin{aligned} &(-\eta^2+7\eta^2)\eta^2+(-\eta^2+7\eta^2)\eta^2- \\ &2(\eta^2+7\eta^2)\eta^2+(-\eta^2+7\eta^2)\eta^2+(-\eta^2+7\eta^2)\eta^2 \end{aligned}$$

$$\begin{aligned}
 &2a^4 + 20a^3b \\
 &3a^4 + 6a^3b + 3a^2b^2 \\
 &-9a^3 - 819a^2b \\
 &-12a^2 - 132a^2b - 120ab^2 \\
 &-a^3 - 3a^2b - 3ab^2 - b^3 \\
 &+18a^2 + 14760ab \\
 &+9a^2 + 828ab + 814b^2 \\
 &+5a^2 + 100ab + 500b^2 \\
 &-15a = 110,415b
 \end{aligned}$$

$$5a^4 - 22a^3 + 32a^2 - 15a = a(a-1)(5a^2 - 14a + 15)$$

$$b(26a^3 - 454a^2 + 16,688a - 110,415)$$

$$+ b^2(3a^2 - 123a + 131a)$$

$$\begin{aligned}
 (a-4)^2 &= a^2 - 8a + 16 \\
 (a-130) &= a^2 - 130a + 16900 \\
 &= a^2 - 148a + 2340
 \end{aligned}$$

$$\begin{aligned}
 (a-34)^2 &= a^2 - 68a + 1156 \\
 (a-44)^2 &= a^2 - 88a + 1936 \\
 &= (a-44)^2 - 3151 \\
 &= 8(1-33 + 363 - 3443)
 \end{aligned}$$

$$\begin{aligned}
 18a^2 - 256a + 1544 \\
 = 18(a^2 - 14a + 86) - 24a - 1 \\
 = 18\{(a-7)^2 + 34\} - (4a+1)
 \end{aligned}$$

$$\begin{aligned}
 8a^2 - 31a + 30 &= 8a^2 - 32a + 32 + a - 2 \\
 &= 8(a^2 - 4a + 4) + (a-2) \\
 &= 8(a-2)^2 + (a-2)
 \end{aligned}$$

$$\begin{aligned}
 &8a^3 - 240a^2 + 3741a - 24,600 \\
 &-8 + 264 - 2404 + 10848 \\
 &\hline
 &-6a^2 + 887a - 48 \\
 &+ 6a^2 - 888a + 824 \\
 &\hline
 &-a - 412 \\
 &+ 6a^2 - 888a + 5638 \\
 &\hline
 &-a - 412
 \end{aligned}$$

$$-24.51 - 186.7 - 100.7 + 100.7 + 100.7 + 100.7$$

$$\begin{aligned}
 &1640 \\
 &a(11+92+91) \\
 &5(1+20+100) \\
 &7381 \\
 &22143 \\
 &110715
 \end{aligned}$$

$$\begin{aligned}
 &8a^3(a+b) - [12a^2(a+b) + 15a(a+b)^2] + 39a(a+b)(a+b) - 20(a+b)(a+b) \\
 &+ 39a^2 + 8a^2b \\
 &- 24a^3 - 24a^2b - 15a^2b^2 \\
 &- 15a^3 - 30a^2b - 15a^2b^2 \\
 &+ 39a^2 + 3544ab \\
 &+ 22a^2 + 242ab \\
 &- 30a - 24600
 \end{aligned}$$

$$\begin{aligned}
 &4a^3 - 240a^2 + 3741a - 24,600 \\
 &= a(a+b)(4a^2 - 240a + 3741) - 24,600 \\
 &= a(a+b)(4a^2 - 240a + 3741) - 24,600 \\
 &= a(a+b)(4a^2 - 240a + 3741) - 24,600 \\
 &= a(a+b)(4a^2 - 240a + 3741) - 24,600 \\
 &= a(a+b)(4a^2 - 240a + 3741) - 24,600
 \end{aligned}$$

$$(2.51 + 79.52 - 181) \cdot 2$$

$$(41 + 2.51 - 181) \cdot 2 = 2.51 - 14a^2 - 14a^2 - 14a^2 - 14a^2$$

Egyptian craft, w q's

F44

w q

45 45	44	<del>55</del> 44	64	<del>34</del> 62	64	62
52 44	94	64	84	<u>44</u>	84	44
66 41	116	48	44	2,136	44	54
40 49	104	44	102	1,73	102	<del>48</del>
94 121	68	<u>38</u>	101		101	<del>4273</del>
103 123	85	5,309	81		81	138
107 116	45		56		56	
96 103	58		83		83	
102 106	84		42		42	
84 43	97		9,423		9,428	
10 981	<u>51</u>					

11,904

292  
144  
392  
137  
192  
1210

10  
11  
5  
9  
2  
9  
4  
50

51) 4124 (80.92  
408  
44.0  
454  
1.10

981 10 981  
904 11 904  
309 5 309  
423 9 423  
136 4 136  
428 39 3195  
243 1 43  
40 3268  
2 137  
3 3131

38) 3131 (82.394  
304  
91  
76  
150  
114  
360  
180

53) 4572 (86.27  
424  
332  
310  
140  
106  
340

Total 5 crafts, 4124 eggs, 80.92 eggs per raft  
=  $81 - \frac{4}{51}$

Total 39 crafts, 3268 eggs mean 81.7  
38 " , 3131 eggs, mean 82.4  
=  $82 - \frac{15}{19}$

9 428  
2 138  
1 43  
24 2104  
4 548  
10 981  
53 4572

424572  
1311 43.00  
84.92  
Mean 84.92  
86.3

Eggs per raft + 75

F45

Rafts Eggs

13 1222

4 2294

10 808

18 1544

2 144

9 402

2 134

2 134

58 4860

24) 2430 (83.8

232

112

87

250

232

180

4860

3131

4891 (81.

184

154

96) 4441 (83.24

768

311

286

230

182

380

33) 2801 (84.9

264

161

132

290

44) 6824 (85.1

632

404

375

9

504

444

300

44) 6824

53 4546

132 11396

11) 11346

41036

31254

86.3

73

244

3511

85

253

1484

64

304

1547

82

238

96

423

102

492

1464

58 rafts, 4860 eggs, mean 83.86 eggs

Crash test 98 rafts, 4491 eggs, mean 83.24 eggs

All families 66 rafts, 5602 eggs, mean 84.9

79 rafts, 6824 eggs, mean 86.38

9 402

2 134

4 294

2 144

1 86

34 3511

9 422

66 5602

13 1222

79 6824

[From *Biometrika*, Vol. XXXI. Parts III and IV. March, 1940.]

[All Rights reserved.]

PRINTED IN GREAT BRITAIN

(iii) The cumulants and moments of the binomial distribution, and the cumulants of  $\chi^2$  for a  $(n \times 2)$ -fold table

By J. B. S. HALDANE, F.R.S.

*From the Department of Biometry, University College, London*

The first four cumulants of the distribution of  $\chi^2$  for a  $(n \times 2)$ -fold table when samples are finite, have already been given (Haldane, 1937). These and higher cumulants and moments can be calculated by a simpler method. Consider a sample of  $s$ , the probability of a success being  $p$ , and  $p + q = 1$ . Pearson (1919) pointed out that for moments of  $(p + q)^s$  about its mean, the generating function is  $(qe^{pt} + pe^{-qt})^s$ , and Romanovsky (1923) gave a recurrence formula for the moments. That for the cumulants is much simpler.

Let  $U = qe^{pt} + pe^{-qt}$ .

Then the cumulant-generating function

$$K(t) \equiv \sum_{r=2}^{\infty} \frac{\kappa_r t^r}{r!} = s \log U.$$

To find the cumulants for  $s = 1$ , we note that

$$\frac{\partial}{\partial q} K(t) = \frac{e^{pt} - e^{-qt}}{U} - t,$$

$$\frac{\partial}{\partial t} K(t) = \frac{pq(e^{pt} - e^{-qt})}{U}$$



So 
$$\frac{\partial}{\partial t} K(t) = pq \frac{\partial}{\partial q} K(t) + pqt,$$

or 
$$\sum_{r=2}^{\infty} \frac{\kappa_r t^{r-1}}{(r-1)!} \equiv pq \sum_{r=2}^{\infty} \frac{t^r}{r!} \frac{d\kappa_r}{dq} + pqt.$$

Equating the coefficients of  $t^r/r!$ , we find

$$\kappa_2 = pq,$$

and if  $r > 2$  
$$\kappa_{r+1} = pq \frac{d\kappa_r}{dq}. \quad \dots\dots(1)$$

Let  $pq = c$ ,  $p - q = g$ ; then

$$\kappa_{r+1} = c \frac{d\kappa_r}{dq}, \quad \frac{dc}{dq} = g, \quad \frac{dg}{dq} = -2, \quad g^2 = 1 - 4c.$$

Hence if  $\kappa_{2r} = f(c)$ ,

$$\left. \begin{aligned} \kappa_{2r+1} &= gcf'(c), \\ \kappa_{2r+2} &= c(1-6c)f'(c) + c^2(1-4c)f''(c). \end{aligned} \right\} \quad \dots\dots(2)$$

From these equations we can very rapidly calculate successive values of  $\kappa_r$ , since  $\kappa_2 = c$ , and find:

$$\begin{aligned} \kappa_1 &= 0, \\ \kappa_2 &= c, \\ \kappa_3 &= cg, \\ \kappa_4 &= c - 6c^2, \\ \kappa_5 &= g(c - 12c^2), \\ \kappa_6 &= c - 30c^2 + 120c^3, \\ \kappa_7 &= g(c - 60c^2 + 360c^3), \\ \kappa_8 &= c - 126c^2 + 1,680c^3 - 5,040c^4, \\ \kappa_9 &= g(c - 252c^2 + 5,040c^3 - 20,160c^4), \\ \kappa_{10} &= c - 510c^2 + 17,640c^3 - 151,200c^4 + 362,880c^5, \\ \kappa_{11} &= g(c - 1,020c^2 + 52,920c^3 - 604,800c^4 + 1,814,400c^5), \\ \kappa_{12} &= c - 2,046c^2 + 168,960c^3 - 3,160,080c^4 + 19,958,400c^5 - 39,916,800c^6. \quad \dots\dots(3) \end{aligned}$$

If each of the above cumulants be multiplied by  $s$ , the moments about the mean can now be calculated from the expressions given by Fisher (1928) and Haldane (1938). If  $p = \frac{1}{2}$  we have

$$K(t) = s \log \cosh \frac{1}{2}t,$$

so 
$$\kappa_2 = \frac{s}{4}, \quad \kappa_4 = -\frac{s}{8}, \quad \kappa_6 = \frac{s}{4}, \quad \kappa_8 = -\frac{17s}{16}, \quad \kappa_{10} = \frac{31s}{4}, \quad \kappa_{12} = -\frac{691s}{8},$$

while if  $q$  is very small we have for the cumulant-generating function of a Poisson series

$$K(t) = sq(e^t - 1 - t).$$

The coefficient of  $c^2$  is  $-[s^r + (-1)^r - 3]$ . So when  $q$  is small, but its square is not neglected, the first order correction to the Poisson cumulant-generating function is

$$K(t) = sq(e^t - 1 - t) + sq^2(e^{2t} - e^t).$$

The numerical coefficient of the highest power of  $c$  in  $\kappa_r$  is  $(r-1)!$  when  $r$  is even, and  $\frac{1}{2}(r-1)!$  when  $r$  is odd.

Consider a sample of  $s$ , in which  $a$  successes are recorded. Then

$$\chi^2 = \frac{(a - sp)^2}{spq}.$$

But  $a - sp$  is the departure from the mean of the binomial distribution  $(p+q)^n$ . Hence the  $r$ th moment of the distribution of  $\chi^2$  (for one degree of freedom) about zero, is

$$\nu'_r = \frac{\mu_{2r}}{s^r c^r},$$

where  $\mu_{2r}$  is the  $2r$ th moment of  $(p+q)^n$ .

But if  $\mu'_r$  and  $\kappa'_r$  be the  $r$ th moment about the mean, and the  $r$ th cumulant, of the  $\chi^2$  distribution, then

$$\mu'_2 = \nu'_2 - \nu_1^2, \text{ etc.}, \quad \kappa'_2 = \mu'_2, \text{ etc.}$$

Making the necessary substitutions, we find, for the cumulants of  $\chi^2$  in terms of those of the binomial distribution:

$$\begin{aligned} \kappa'_1 &= (sc)^{-1} \kappa_2, \\ \kappa'_2 &= (sc)^{-2} (2\kappa_2^2 + \kappa_4), \\ \kappa'_3 &= (sc)^{-3} [8\kappa_2^3 + 2(5\kappa_2^2 + 6\kappa_2 \kappa_4) + \kappa_6], \\ \kappa'_4 &= (sc)^{-4} [48\kappa_2^4 + 48(5\kappa_2 \kappa_3^2 + 3\kappa_2^2 \kappa_4) + 8(4\kappa_4^2 + 7\kappa_3 \kappa_5 + 3\kappa_2 \kappa_6) + \kappa_8], \\ \kappa'_5 &= (sc)^{-5} [384\kappa_2^5 + 960(5\kappa_2^3 \kappa_3^2 + 2\kappa_2^2 \kappa_4) + 80(25\kappa_3^3 \kappa_4 + 16\kappa_2 \kappa_4^2 + 28\kappa_2 \kappa_3 \kappa_5 \\ &\quad + 6\kappa_2^2 \kappa_6) + 2(63\kappa_2^2 + 100\kappa_4 \kappa_6 + 60\kappa_3 \kappa_7 + 20\kappa_2 \kappa_8) + \kappa_{10}], \\ \kappa'_6 &= (sc)^{-6} [3,840\kappa_2^6 + 9,600(10\kappa_2^3 \kappa_3^2 + 3\kappa_2^2 \kappa_4) + 4,800(3\kappa_4^3 + 25\kappa_2 \kappa_3^2 \kappa_4 \\ &\quad + 8\kappa_2^2 \kappa_4^2 + 14\kappa_2^2 \kappa_3 \kappa_5 + 2\kappa_2^2 \kappa_6) + 40(132\kappa_4^2 + 672\kappa_3 \kappa_4 \kappa_5 + 189\kappa_2 \kappa_5^2 \\ &\quad + 226\kappa_2^2 \kappa_6 + 300\kappa_2 \kappa_4 \kappa_6 + 180\kappa_2 \kappa_3 \kappa_7 + 30\kappa_2^2 \kappa_8) + 4(113\kappa_6^2 + 198\kappa_5 \kappa_7 \\ &\quad + 120\kappa_4 \kappa_8 + 55\kappa_3 \kappa_9 + 15\kappa_2 \kappa_{10}) + \kappa_{12}]. \end{aligned} \quad \dots\dots(4).$$

We now substitute the values of  $\kappa_r$  given in equations (3) multiplied by  $s$ , putting

$$k = (pq)^{-1} = c^{-1}.$$

We therefore have, for the cumulants of  $\chi^2$  with one degree of freedom:

$$\begin{aligned} \kappa_1 &= 1, \\ \kappa_2 &= 2 + (k-6)s^{-1}, \\ \kappa_3 &= 8 + 2(11k-56)s^{-1} + (k^2-30k+120)s^{-2}, \\ \kappa_4 &= 48 + 96(4k-19)s^{-1} + 16(7k^2-125k+420)s^{-2} + (k^3-125k^2+1,680k-5,040)s^{-3}, \\ \kappa_5 &= 384 + 960(7k-32)s^{-1} + 400(15k^2-214k+648)s^{-2} + 6(81k^3 \\ &\quad - 3,908k^2 + 38,420k - 98,496)s^{-3} + (k^4-510k^3+17,640k^2 \\ &\quad - 151,200k + 362,880)s^{-4}, \\ \kappa_6 &= 3,840 + 9,600(13k-58)s^{-1} + 9,600(26k^2-327k+924)s^{-2} \\ &\quad + 40(1,729k^3-56,236k^2+459,024k-1,065,792)s^{-3} + 4(501k^4 \\ &\quad - 59,398k^3+1,289,244k^2-8,824,320k+18,555,840)s^{-4} \\ &\quad + (k^5-2,046k^4+168,960k^3-3,160,080k^2+19,958,400k \\ &\quad - 39,916,800)s^{-5}. \end{aligned} \quad \dots\dots(5)$$

When  $p = \frac{1}{2}$ ,  $k = 4$ , and we have, for  $n$  degrees of freedom:

$$\begin{aligned} \kappa_1 &= n, \\ \kappa_2 &= 2ns^{-1}(s-1), \\ \kappa_3 &= 8ns^{-2}(s-1)(s-2), \\ \kappa_4 &= 16ns^{-3}(s-1)(3s^2-15s+17), \\ \kappa_5 &= 128ns^{-4}(s-1)(s-2)(3s^2-21s+31), \\ \kappa_6 &= 256ns^{-5}(s-1)(15s^4-210s^3+990s^2-1,950s+1,382). \end{aligned} \quad \dots\dots(6)$$

If there are  $n$  samples, with different values of  $s$ , we have, for the cumulants of  $\chi^2$ , where  $h = \frac{1}{2pq}$ , and  $R_i = \sum s^{-i}$ ,

$$\begin{aligned}\kappa_1 &= n, \\ \kappa_2 &= 2n[1 + (h-3)R_1], \\ \kappa_3 &= 4n[2 + (11h-28)R_1 + (h^2-15h+30)R_2], \\ \kappa_4 &= 8n[6 + 12(8h-19)R_1 + 4(14h^2-125h+210)R_2 + (h^3-63h^2+420h-630)R_3], \\ \kappa_5 &= 16n[24 + 120(7h-16)R_1 + 100(15h^2-107h+162)R_2 + 3(81h^3 \\ &\quad - 1,954h^2 + 9,560h - 12,312)R_3 + (h^4-255h^3+4,410h^2-18,900h+22,680)R_4], \\ \kappa_6 &= 32n[120 + 600(13h-29)R_1 + 600(52h^2-327h+462)R_2 + 10(1,729h^3 \\ &\quad - 28,118h^2 + 114,756h - 133,228)R_3 + 2(501h^4 - 29,699h^3 + 322,311h^2 \\ &\quad - 1,103,040h + 1,159,740)R_4 + (h^5-1,023h^4+42,240h^3-395,010h^2 \\ &\quad + 1,247,400h-1,247,400)R_5]. \dots\dots(7)\end{aligned}$$

When  $p = q = \frac{1}{2}$ , we have:

$$\begin{aligned}\kappa_1 &= n, \\ \kappa_2 &= 2(n-R_1), \\ \kappa_3 &= 8(n-3R_1+4R_2), \\ \kappa_4 &= 16(3n-18R_1+32R_2-17R_3), \\ \kappa_5 &= 128(3n-30R_1+100R_2-135R_3+62R_4), \\ \kappa_6 &= 256(15n-225R_1+1,200R_2-2,940R_3+3,332R_4-1,382R_5). \dots\dots(8)\end{aligned}$$

The first four of equations (5, 6, 7, 8) have already been given in a slightly different form by Haldane (1937). The limiting forms of equations (5) and (7) when  $s$  tends to infinity and  $k$  to zero, while  $ks = g$ , have been given by Haldane (1938). However, the expression for  $\kappa_6$  there given is incorrect. The coefficient of  $R_1$  in the expression for  $\kappa_6$  should be 124,800.

The extension of equations (7) would be rather tedious. However, those of equations (6) and (8) would not be very difficult. The coefficient of  $x^{2r}/2r!$  in the expansion of  $\log \cosh t$  is the value of  $(d/dx)^{2r-1}(1-\tanh^2 x)$  when  $x = 0$ , and can easily be calculated, since this differential coefficient is a polynomial in  $\tanh x$ . The equations for moments in terms of cumulants can easily be extended when all odd cumulants vanish. In this case a useful check can be obtained from the fact that when  $s = 2$  the cumulant-generating function of  $\chi^2$  is  $t + \log \cosh t$ .

#### SUMMARY

Expressions are obtained for the first twelve cumulants of the binomial distribution, and a simple recurrence formula for further cumulants. The first six cumulants of  $\chi^2$  for a  $(n \times 2)$ -fold table when expectations are small, are deduced.

#### REFERENCES

- FISHER, R. A. (1928). "Moments and product moments of sampling distributions." *Proc. Lond. Math. Soc.* **30**, 200-38.  
 HALDANE, J. B. S. (1937). "The exact value of the moments of the distribution of  $\chi^2$ , used as a test of goodness of fit, when expectations are small." *Biometrika*, **29**, 133-43.  
 — (1938). "The first six moments of  $\chi^2$  for an  $n$ -fold table with  $n$  degrees of freedom when some expectations are small." *Biometrika*, **29**, 389-91.  
 PEARSON, K. (1919). "Peccavimus" (Footnote, p. 270). *Biometrika*, **12**, 259-81.  
 ROMANOVSKY, V. (1923). "Note on the moments of a binomial  $(p+q)^2$  about its mean." *Biometrika*, **15**, 410-12.

f. 48

[published 1946]