Summary

In intercrosses the product formula yields an estimate of θ, which with undisturbed viability is fully efficient, and, with a single disturbed viability, results in the loss of a small amount of information for moderate disturbances. With two disturbed viabilities, however, the estimate is again fully efficient and is in fact then identical with the maximum likelihood solution. It may also be noted that the maximum likelihood solution for θ is the same in both the undisturbed case and the case of a single disturbed viability.

References

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III. A METHOD OF ALLOWING FOR DIFFERENTIAL VIABILITY IN ESTIMATING LINKAGE FROM BACKCROSS MATINGS IN COUPLING ONLY OR REPULSION ONLY

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A coupling mating of the type : AB/ab = ab/ab, gives rise to four kinds of offspring which are, phenotypically : AB, ab (parentals) and Ab, aB (recombinants). It is usual to group the two parental types and the two recombinant types to give a pair of observed numbers. Corresponding results may be obtained for matings in repulsion. It has been shown by Fisher (1935-47) that the joint use of coupling and repulsion data can be made to yield maximum likelihood estimates of (a) the linkage between the two loci and (b) the relative viability of the two groups AB, ab and Ab, aB.

Often, however, results are available for matings in coupling only or repulsion only. We can still take into account the effects of differential viability by considering the numbers observed in all four classes : AB, ab, Ab and aB, on the assumption that the presence of each dominant gene modifies the expected values by a certain factor and that the two viability effects are independent.

Let the recombination fraction be p ; the factors corresponding to the presence of A and B be u and v respectively ; and the sample number be n. Let the observed and expected numbers for matings in coupling be given by the following table :—

	AB	ab	Ab	aB	
Expected . .	$nuvq$	nq	nup	nvp	$\div(uvq+q+up+vp)$
Observed . .	a	b	c	d	

where $$p+q = 1 \quad . \quad . \quad . \quad . \quad . \quad (1)$$
and $$a+b+c+d = n \quad . \quad . \quad . \quad . \quad (2)$$

For matings in repulsion we merely interchange p and q.

Special case, $v = 1$

It will be as well to dispose of the special case, $v = 1$, first. This implies that one pair of factors only, A and a, have differential viability.

We have

$$e^{L} \propto \frac{u^{a+c}p^{c+d}q^{a+b}}{(1+u)^{n}} \quad . \quad . \quad . \quad . \quad (3)$$

Therefore :

$$\frac{\partial L}{\partial p} = \frac{c+d}{p} - \frac{a+b}{q} \qquad \therefore \hat{p} = \frac{c+d}{n} \quad . \quad . \quad . \quad (4)$$

$$\frac{\partial L}{\partial u} = \frac{a+c}{u} - \frac{n}{1+u} \qquad \therefore \hat{u} = \frac{a+c}{b+d} \quad . \quad . \quad . \quad (5)$$

and

$$I_{pp} = \frac{n}{pq}, \quad I_{pu} = 0, \quad I_{uu} = \frac{n}{u(1+u)^2} \quad . \quad . \quad (6)$$

$$\therefore \text{var } \hat{p} = \frac{pq}{n} \quad . \quad . \quad . \quad (7)$$

and

$$\text{var } \hat{u} = \frac{u(1+u)^2}{n} \quad . \quad . \quad (8)$$

I am indebted to Professor R. A. Fisher for the transformation

$$u = \tan^2 \theta \quad . \quad . \quad . \quad . \quad (9)$$

which has the useful property of transforming to a variable whose variance is a function of the sample number only, *viz.*

$$\text{var } \theta = \frac{1}{4n} \quad . \quad . \quad . \quad . \quad . \quad (10)$$

The appropriate χ^2 for testing the significance of departures of u from unity is the following with one degree of freedom :

$$\chi^2 = \frac{[(a+c)-(b+d)]^2}{n} \quad . \quad . \quad . \quad (11)$$

General case

Returning now to the general case of two disturbed viabilities it will be convenient to designate the four expected numbers by m_1, m_2, m_3 and m_4, where

$$m_1+m_2+m_3+m_4 = n \quad . \quad . \quad . \quad (12)$$

We have

$$e^{L} \propto \frac{p^{c+d}q^{a+b}u^{a+c}v^{a+d}}{(uvq+q+pu+pv)^{n}} \quad . \quad . \quad . \quad . \quad (13)$$

$$\therefore \frac{\partial L}{\partial p} = \frac{(c+d)-(m_3+m_4)}{p} - \frac{(a+b)-(m_1+m_2)}{q} \quad . \quad (14)$$

$$\frac{\partial L}{\partial u} = \frac{(a+c)-(m_1+m_3)}{u} \quad . \quad . \quad . \quad . \quad . \quad (15)$$

and

$$\frac{\partial L}{\partial v} = \frac{(a+d)-(m_1+m_4)}{v} \quad . \quad . \quad . \quad . \quad . \quad (16)$$

Equating each of (14), (15) and (16) to zero, in order to maximise likelihood, we obtain after a little reduction :

$$a = m_1,\ b = m_2,\ c = m_3,\ d = m_4 \quad . \quad . \quad . \quad (17)$$

We can now solve (17) for the estimates $\hat{p}$, $\hat{u}$ and $\hat{v}$, *i.e.*

$$\frac{\hat{p}}{\hat{q}} = \frac{\hat{p}}{1-\hat{p}} = \left(\frac{cd}{ab}\right)^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad (18)$$

$$\hat{u} = \left(\frac{ac}{bd}\right)^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad (19)$$

$$\hat{v} = \left(\frac{ad}{bc}\right)^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad (20)$$

These formulæ are analogous to those obtained from the four numbers arising when both coupling and repulsion data are available. Applying the familiar formula

$$\text{var T} = \Sigma m \left(\frac{\partial \text{T}}{\partial a}\right)^2 - n\left(\frac{\partial \text{T}}{\partial n}\right)^2$$

to the estimates in (18), (19) and (20), we can derive the following sampling variances :

$$\text{var } \hat{p} = p^2q^2/h \quad . \quad . \quad . \quad . \quad (21)$$

$$\text{var } \hat{u} = u^2/h \quad . \quad . \quad . \quad . \quad . \quad (22)$$

$$\text{var } \hat{v} = v^2/h \quad . \quad . \quad . \quad . \quad . \quad (23)$$

where
$$\frac{4}{h} = \frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}.$$

Suppose now we wish to test the significance of departures of, say, v from unity where linkage and one disturbed viability are admitted The expectations for $v = 1$ are :

$$\frac{nuq}{1+u},\ \frac{nq}{1+u},\ \frac{nup}{1+u},\ \frac{np}{1+u} \quad . \quad . \quad . \quad . \quad (24)$$

If we employ the usual χ^2 measuring the agreement between the observed and the expected numbers, two of the three available degrees of freedom will be used up in estimating p and u, leaving one degree of freedom to test the significance of the second viability. Taking the estimates of p and u from (4) and (5), we can write the expectations :

$$\frac{(a+b)(a+c)}{n},\ \frac{(a+b)(b+d)}{n},\ \frac{(a+c)(c+d)}{n},\ \frac{(b+d)(c+d)}{n} \quad . \quad (25)$$

$$\therefore \chi^2 = \frac{na^2}{(a+b)(a+c)} + \frac{nb^2}{(a+b)(b+d)} + \frac{nc^2}{(a+c)(c+d)} + \frac{nd^2}{(b+d)(c+d)} - n$$

$$\textit{i.e.}\ \chi^2 = \frac{n(ad-bc)^2}{(a+b)(a+c)(b+d)(c+d)} \quad . \quad . \quad (26)$$

We are in fact testing the proportionality of the elements in the

2×2 table
$$\begin{array}{c|c} a & b \\ \hline c & d \end{array}$$

where the marginal totals are fixed by the estimation of p and u.

Reference

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