SEX-LINKAGE AND SEX-LIMITATION IN QUANTITATIVE INHERITANCE

I. RANDOM MATING POPULATIONS

R. J. KILLICK*

Department of Genetics, University of Birmingham

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1. INTRODUCTION

INVESTIGATIONS into the genetical architecture of metrical traits generally proceed by one of two broad methods; (a) the analysis of the generations derived from a cross between two inbred lines (*e.g.* parents, F_1 , F_2 and back-crosses) or (b) the analysis of one of several multiple mating schemes which are more suitable when interest lies in a population rather than just two genotypes. These multiple mating schemes will be described in section 2 but the analysis of each involves a number of assumptions among which is that of autosomal inheritance.

Mather and Jinks (1963) gave the expectations for covariances among relatives arising from sex-linkage in a random mating population and more recently (1971) extended this to cover the analysis of biparental progenies (see section 2).

In this paper the effect of sex-linkage on the analysis and interpretation of data from multiple mating schemes using experimental material drawn from a panmictic base population will be considered. Since consideration of sex-linkage necessarily involves sexually dimorphic species the complications arising from sex-limitation must also be considered. In the present context sex-limitation implies a differential effect of the same autosomal gene in males and females. This might be a slight quantitative difference but in the extreme case the character may be expressed in only one sex, *e.g.* milk yield in cattle and egg production in fowl. Sex-limitation is not uncommon. For instance, in *Drosophila melanogaster* it has been reported by Breese and Mather (1957, 1960), Cooke and Mather (1962), Hill (1964) and Kearsey and Kojima (1967).

2. THE MULTIPLE MATING SCHEMES

The multiple mating schemes considered in this paper are:

(i) *Biparental progenies (BIPs) of Mather (1949)*

A sample of n male and n female parents drawn from a random mating population are crossed in pairs to give n families. The observed variation may be partitioned into that within families (= total phenotypic variance-covariance of full sibs) and between families (= covariance of full sibs).

* Present address: Scottish Plant Breeding Station, Pentlandsfield, Roslin, Midlothian.

(ii) *The North Carolina experiment I of Comstock and Robinson (1952)*

A sample of m male parents are each crossed to n female parents drawn from the same population to give mn families. The n half-sib families constitute a male parent array. The variation may be partitioned into that within and that between full-sib families. The latter item may be further subdivided into variation between male parent arrays (= covariance of half sibs) and variation between full-sib families within male parent arrays (= covariance of full sibs—covariance of half sibs).

TABLE 1
Expected mean squares from the analyses of variance of multiple mating schemes under method (a) (sexes separate)

Item	d.f.	e.m.s.
1. BIPs		
Between families	$n-1$	$\sigma_w^2 + r\sigma_b^2$
Within families	$n(r-1)$	σ_w^2
2. North Carolina experiment I		
Between male parent arrays	$m-1$	$\sigma_w^2 + r\sigma_{mb}^2 + m\sigma_m^2$
Between families in arrays	$m(n-1)$	$\sigma_w^2 + r\sigma_{mb}^2$
Within families	$nm(r-1)$	σ_w^2
3. North Carolina experiment II		
Between male parent arrays	$m-1$	$\sigma_w^2 + r\sigma_{mf}^2 + m\sigma_m^2$
Between female parent arrays	$n-1$	$\sigma_w^2 + r\sigma_{mf}^2 + m\sigma_f^2$
Male $\times$ female arrays	$(m-1)(n-1)$	$\sigma_w^2 + r\sigma_{mf}^2$
Within families	$nm(r-1)$	σ_w^2
4. North Carolina experiment III		
Sums	$(m-1)$	$\sigma_w^2 + 2r\sigma_m^2$
Differences	$(m-1)$	$\sigma_w^2 + 2r\sigma_{mI}^2$
Within families	$2m(r-1)$	σ_w^2

r = Number of sibs/family.

(iii) *The North Carolina experiment II of Comstock and Robinson (1952)*

A sample of m males are each crossed to the same n females in turn, giving mn families. The variation may be partitioned into that within and between full-sib families. Since there are n half-sib families per male parent and m half-sib families per female parent the variation between full-sib families may be subdivided into the variation between male parent arrays, between female parent arrays (both = covariance of half sibs) and the interaction of male arrays and female arrays (= covariance of full sibs—2 covariance of half sibs).

The above three designs form a series in which the variation between full-sib families is successively subdivided to provide more information as to the source of variation. The relative efficiencies of these designs are discussed by Kearsay (1965).

(iv) *The North Carolina experiment III of Comstock and Robinson (1952)*

This design has been extended by Kearsey and Jinks (1968) and Jinks, Perkins and Breese (1969). It involves crossing m males from a population

TABLE 2
Expected mean squares from the analyses of variance of multiple mating schemes under method (b) (sexes pooled)

	Item	d.f.	e.m.s.
1. BIPs			
	Between sexes (S)	1	$\sigma_w^2 + r\sigma_{sb}^2 + r\sigma_s^2$
	Between families (F)	$n-1$	$\sigma_w^2 + 2r\sigma_b^2$
	S $\times$ F	$n-1$	$\sigma_w^2 + r\sigma_{sb}^2$
	Within sexes and families	$2n(r-1)$	σ_w^2
2. North Carolina experiment I			
	Between sexes (S)	1	$\sigma_w^2 + r\sigma_{sb}^2 + r\sigma_{sm}^2 + r\sigma_s^2$
	Between male parent arrays (A)	$m-1$	$\sigma_w^2 + 2r\sigma_b^2 + 2r\sigma_m^2$
	Between families in arrays (F)	$m(n-1)$	$\sigma_w^2 + 2r\sigma_b^2$
	S $\times$ A	$m-1$	$\sigma_w^2 + r\sigma_{sb}^2 + r\sigma_{sm}^2$
	S $\times$ F	$m(n-1)$	$\sigma_w^2 + r\sigma_{sb}^2$
	Within sexes and families	$2mn(r-1)$	σ_w^2
3. North Carolina experiment II			
	Between sexes (S)	1	$\sigma_w^2 + r\sigma_{smf}^2 + r\sigma_{sm}^2 + r\sigma_{sf}^2 + r\sigma_s^2$
	Between male parent arrays (M)	$m-1$	$\sigma_w^2 + 2r\sigma_{mf}^2 + 2r\sigma_m^2$
	Between female parent arrays (F)	$n-1$	$\sigma_w^2 + 2r\sigma_{mf}^2 + 2r\sigma_f^2$
	M $\times$ F	$(m-1)(n-1)$	$\sigma_w^2 + 2r\sigma_{mf}^2$
	S $\times$ M	$m-1$	$\sigma_w^2 + r\sigma_{smf}^2 + r\sigma_{sm}^2$
	S $\times$ F	$n-1$	$\sigma_w^2 + r\sigma_{smf}^2 + r\sigma_{sf}^2$
	S $\times$ M $\times$ F	$(m-1)(n-1)$	$\sigma_w^2 + r\sigma_{smf}^2$
	Within sexes and families	$2mn(r-1)$	σ_w^2
4. North Carolina experiment III			
	Between sexes (S)	1	$\sigma_w^2 + 2r\sigma_{sm}^2 + r\sigma_s^2$
	Sums	$m-1$	$\sigma_w^2 + 4r\sigma_m^2$
	Differences	$m-1$	$\sigma_w^2 + 4r\sigma_{ml}^2$
	S $\times$ sums	$m-1$	$\sigma_w^2 + 2r\sigma_{sm}^2$
	S $\times$ differences	$m-1$	$\sigma_w^2 + 2r\sigma_{sml}^2$
	Within sexes and families	$2m(r-1)$	σ_w^2

r = Number of sibs of like sex per family.

to two female tester lines (preferably extreme high and low selection lines from the population), and to the F_1 between them, giving $3m$ families. Although of wide application, this design will be considered for a panmictic base population only, but mention will also be made of the result when the base population consists of inbred lines.

For all these designs two methods of analysis may be envisaged; (a) the two sexes among the progeny may be analysed quite separately or (b) the two sexes may be combined so that main effects and sex interactions are obtainable from an analysis of variance. The composition of mean squares obtainable from the analysis of these four designs is shown in table 1 for method (a) and are, of course, equally applicable for male or female progeny. The composition of the various mean squares when the designs are analysed by method (b) is shown in table 2.

3. MODEL AND PARAMETERS

The model and parameters describing sex-linkage used in this paper are those of Mather and Jinks (1963, 1971). A locus on the X chromosome having two alleles, A and a , gives rise in a random mating population to the following genotypes which have frequencies and mean expression in Mather's (1949) notation of

Sex	Female			Male	
	Genotype	AA	Aa	aa	
	Frequency	u^2	$2uv$	v^2	
	Mean value	d_x	h_x	$-d_x$	
				A	a
				u	v
				d'_x	$-d'_x$

where $u (= 1 - v)$ is the frequency of allele A . The distinction between d_x and d'_x automatically allows for sex-limitation on the sex-chromosome. Mather and Jinks (1971) use five parameters to describe the variation arising from sex-linked genes. These are:

$$D_{RX} = \Sigma 4uv[d_x + (v - u)h_x]^2$$

$$H_{RX} = \Sigma 16u^2v^2h_x^2$$

$$D'_X = \Sigma 4uvd'_x{}^2$$

$$D'_{XX} = \Sigma 4uvd_xd'_x$$

$$F'_{XX} = \Sigma 8uv(u - v)d'_xh_x.$$

In terms of their 1963 notation $D_{RX} = D_S$, $H_{RX} = H$, $D'_X = D_B$ and $D'_{XX} - \frac{1}{2}F'_{XX} = D_U$. The similarity between the D_R and H_R of Mather (1949) for autosomal genes and D_{RX} and H_{RX} is apparent.

A model which describes sex-limitation satisfactorily will take account of the following: the parameters should be (a) orthogonal, (b) meaningful and (c) epistatic in that the effect of a gene is determined by its genetic background (in this case the sex of the individual). The following model, devised in conjunction with Dr M. J. Kearsey, satisfies these requirements. Conventionally a segregating locus necessitates the estimation of three parameters, m , d and h , from generation means. With sex-limitation we consider each of these parameters to be increased by some function, f_m , f_d and f_h respectively in the female and decreased by the same amounts in the male. Thus we may specify the effect of a sex-limited locus $AA-aa$ as shown in table 3.

TABLE 3
Model for sex-limitation

	Parameters						
	m	f_m	d	f_d	h	f_h	
AA	1	1	1	1	0	0	Females
aa	1	1	-1	-1	0	0	
Aa	1	1	0	0	1	1	
AA	1	-1	1	-1	0	0	Males
aa	1	-1	-1	1	0	0	
Aa	1	-1	0	0	1	-1	

The parameters are therefore orthogonal and meaningful since we have defined

$$\begin{aligned}
 m &= \frac{1}{4}(AA+aa), \quad \text{♀} + \text{♂} \\
 d &= \frac{1}{4}(AA-aa), \quad \text{♀} + \text{♂} \\
 h &= \frac{1}{4}[2Aa - (AA+aa)], \quad \text{♀} + \text{♂} \\
 f_m &= \frac{1}{4}(AA+aa), \quad \text{♀} - \text{♂} \\
 f_d &= \frac{1}{4}(AA-aa), \quad \text{♀} - \text{♂} \\
 f_h &= \frac{1}{4}[2Aa - (AA+aa)], \quad \text{♀} - \text{♂}.
 \end{aligned}$$

The epistatic nature of the model is confirmed by the coefficients of f_d (and f_h) being the product of the coefficients of f_m and d (or h) in every case. We may therefore define

$$\begin{aligned}
 D_R &= \Sigma 4uv[d + (v-u)h]^2 \\
 H_R &= \Sigma 16u^2v^2h^2 && \text{(Mather, 1949)} \\
 D_{RS} &= \Sigma 4uw[f_d + (v-u)f_h]^2 \\
 H_{RS} &= \Sigma 16u^2v^2f_h^2
 \end{aligned}$$

Clearly when sex-limitation is absent f_d and f_h , and therefore D_{RS} and H_{RS} , will be zero. When sex-limitation is complete and the gene has no effect at all in the male (*e.g.* milk yield in cattle) $d = f_d$, $h = f_h$, $D_R = D_{RS}$ and $H_R = H_{RS}$. In other words the components for the main effects will equal those of their interactions with sex. This must be so since the former are derived after first adding the male scores to the female scores and the latter are derived after subtracting the male scores from the female scores; and if the male scores are all zero both sets of data will be identical.

4. ANALYSES

(i) *Covariances between relatives*

The covariances between relatives and the variances of males and females are shown in table 4. Those arising from sex-linked genes were given by Mather and Jinks (1963, 1971). Those arising from autosomal genes have been given by Falconer (1960) as $\frac{1}{2}V_A$ ($= \frac{1}{4}D_R$) for all four parent-offspring

covariances, $\frac{1}{4}D_R + \frac{1}{16}H_R$ for the three sib-sib covariances, and $\frac{1}{2}D_R + \frac{1}{4}H_R$ for the two variances, but these expectations take no account of the possibility of sex-limitation. However, when only one sex is considered the sex-limitation parameters developed in the previous section have complex and meaningless expectations. Thus it is necessary to sum complementary pairs of statistics, *e.g.* the covariance of father-son and that of mother-daughter, to obtain simple expectations. The number of independent statistics is therefore reduced to five, from which nine genetic parameters are to be

TABLE 4
Genetic components of covariances between relatives and progeny variances in a panmictic population

		Sex-linkage parameters					Autosomal parameters			
		D_{RX}	D'_X	D'_{XX}	H_{RX}	F'_{XX}	D_R	H_R	D_{RS}	H_{RS}
Covariances	Mother-son	—	—	$\frac{1}{2}$	—	$-\frac{1}{4}$	$\frac{1}{4}$	—	$-\frac{1}{4}$	—
	Father-daughter	—	—	$\frac{1}{2}$	—	$-\frac{1}{4}$	$\frac{1}{4}$	—	$-\frac{1}{4}$	—
	Mother-daughter	$\frac{1}{4}$	—	—	—	—	see text			
	Father-son	—	—	—	—	—	see text			
	Mother-daughter									
	+									
	Father-son	$\frac{1}{4}$	—	—	—	—	$\frac{1}{2}$	—	$\frac{1}{2}$	—
	Brother-sister	—	—	$\frac{1}{4}$	—	$-\frac{1}{8}$	$\frac{1}{4}$	$\frac{1}{16}$	$-\frac{1}{4}$	$-\frac{1}{16}$
	Brother-brother	—	$\frac{1}{2}$	—	—	—	see text			
	Sister-sister	$\frac{3}{8}$	—	—	$\frac{1}{8}$	—	see text			
Variances	Brother-brother									
	+									
	Sister-sister	$\frac{3}{8}$	$\frac{1}{2}$	—	$\frac{1}{8}$	—	$\frac{1}{2}$	$\frac{1}{8}$	$\frac{1}{2}$	$\frac{1}{8}$
	Female	$\frac{1}{2}$	—	—	$\frac{1}{4}$	—	see text			
	Male	—	1	—	—	—	see text			
	Female									
	+									
	Male	$\frac{1}{2}$	1	—	$\frac{1}{4}$	—	1	$\frac{1}{2}$	1	$\frac{1}{2}$

estimated (this reduces to eight parameters when D_u is substituted for $D'_{XX} - \frac{1}{2}F'_{XX}$), together with the environmental parameter, E , which enters the female and male variances. It is only possible to estimate these parameters by assuming sex-limitation to be absent, and there is no way to test this assumption. Consequently, any estimates of sex-linkage parameters derived from the covariances between relatives will be subject to an uncontrolled error.

(ii) *Biparental progenies and North Carolina experiments I and II*

These three designs are conveniently considered together since they form a series of increasing restraints. The expectations of the components of the mean squares given in tables 1 and 2 are shown in table 5 for method (a) and table 6 for method (b). The analyses will be considered for method (a) first.

(a) *Method (a)* (see table 5)

It is important to remember that if the sexes are analysed separately it is not possible to extrapolate from one sex to the other. Thus the autosomal

components D_R and H_R estimated from males may not be applied to females, unless sex-limitation is known to be negligible.

Biparental progenies provide only two statistics. There are two autosomal parameters and at least one environmental parameter to be estimated and consequently the design is inadequate, though this difficulty may be overcome by assuming dominance to be absent (Kearsey, 1965). The same restriction applies to the estimation of sex-linkage parameters in females but

TABLE 5

Genetic components of variation under method (a) i.e. sexes separate

	Sex-linkage parameters			Autosomal parameters	
	Females		Males	Either sex	
	D_{RX}	H_{RX}	D'_X	D_R	H_R
(i) Biparental progenies					
σ_b^2	$\frac{3}{8}$	$\frac{1}{8}$	$\frac{1}{2}$	$\frac{1}{4}$	$\frac{1}{16}$
σ_w^2	$\frac{1}{8}$	$\frac{1}{8}$	$\frac{1}{2}$	$\frac{1}{4}$	$\frac{3}{16}$
(ii) North Carolina experiment I					
σ_m^2	$\frac{1}{4}$	—	—	$\frac{1}{8}$	—
σ_{mb}^2	$\frac{1}{8}$	$\frac{1}{8}$	$\frac{1}{2}$	$\frac{1}{8}$	$\frac{1}{16}$
σ_w^2	$\frac{1}{8}$	$\frac{1}{8}$	$\frac{1}{2}$	$\frac{1}{4}$	$\frac{3}{16}$
(iii) North Carolina experiment II					
σ_m^2	$\frac{1}{4}$	—	—	$\frac{1}{8}$	—
σ_f^2	$\frac{1}{8}$	—	$\frac{1}{2}$	$\frac{1}{8}$	—
σ_{mf}^2	—	$\frac{1}{8}$	—	—	$\frac{1}{16}$
σ_w^2	$\frac{1}{8}$	$\frac{1}{8}$	$\frac{1}{2}$	$\frac{1}{4}$	$\frac{3}{16}$
(iv) North Carolina experiment III					
	D_{IX}	H_{IX}		D	H
σ_m^2	$\frac{1}{4}$	—	—	$\frac{1}{8}$	—
σ_{ml}^2	—	$\frac{1}{4}$	—	—	$\frac{1}{8}$
σ_w^2	—	—	—	$\frac{1}{8}$	$\frac{1}{8}$

not in males. Thus BIPs are suitable for estimating the environmental and sex-linkage parameters from data on males alone, provided that there is no autosomal variation. It is not at all suitable for the analysis of female data.

The North Carolina experiment I provides three statistics. There are two sex-linkage parameters in the females and one sex-linkage parameter in the males, and in addition an environmental and two autosomal parameters must be allowed for. Thus this design is suitable for the analysis of either sex-linked or autosomal variation in both sexes, but if the genetical variation is distributed between the sex-chromosome and the autosomes it is suitable for neither sex.

Four statistics are available from the analysis of the North Carolina experiment II. This is adequate for the analysis of sex-linkage or autosomal

variation in both males and females. It is also adequate for the simultaneous analysis of autosomal and sex-linked variation in males, but not in females as there are then five parameters (including one environmental) to be estimated. Even so, this design is useful for the analysis of female progeny since the

TABLE 6

Genetic components of variation under method (b) i.e. sexes pooled

	Sex-linkage parameters					Autosomal parameters			
	D_{RX}	D'_X	D'_{XX}	H_{RX}	F'_{XX}	D_R	H_R	D_{RS}	H_{RS}
(i) Biparental progenies									
σ_b^2	$\frac{3}{32}$	$\frac{1}{8}$	$\frac{1}{8}$	$\frac{1}{32}$	$-\frac{1}{16}$	$\frac{1}{4}$	$\frac{1}{16}$	—	—
σ_{sb}^2	$\frac{3}{32}$	$\frac{1}{8}$	$-\frac{1}{8}$	$\frac{1}{32}$	$\frac{1}{16}$	—	—	$\frac{1}{4}$	$\frac{1}{16}$
σ_w^2	$\frac{1}{16}$	$\frac{1}{4}$	—	$\frac{1}{16}$	—	$\frac{1}{4}$	$\frac{3}{16}$	$\frac{1}{4}$	$\frac{3}{16}$
(ii) North Carolina experiment I									
σ_m^2	$\frac{1}{16}$	—	—	—	—	$\frac{1}{8}$	—	—	—
σ_{mb}^2	$\frac{3}{32}$	$\frac{1}{8}$	$\frac{1}{8}$	$\frac{1}{32}$	$-\frac{1}{16}$	$\frac{1}{8}$	$\frac{1}{16}$	—	—
σ_{sm}^2	$\frac{1}{16}$	—	—	—	—	—	—	$\frac{1}{8}$	—
σ_{smb}^2	$\frac{3}{32}$	$\frac{1}{8}$	$-\frac{1}{8}$	$\frac{1}{32}$	$\frac{1}{16}$	—	—	$\frac{1}{8}$	$\frac{1}{16}$
σ_w^2	$\frac{1}{16}$	$\frac{1}{4}$	—	$\frac{1}{16}$	—	$\frac{1}{4}$	$\frac{3}{16}$	$\frac{1}{4}$	$\frac{3}{16}$
(iii) North Carolina experiment II									
σ_m^2	$\frac{1}{16}$	—	—	—	—	$\frac{1}{8}$	—	—	—
σ_f^2	$\frac{3}{32}$	$\frac{1}{8}$	$\frac{1}{8}$	—	$-\frac{1}{16}$	$\frac{1}{8}$	—	—	—
σ_{mf}^2	—	—	—	$\frac{1}{32}$	—	—	$\frac{1}{16}$	—	—
σ_{sm}^2	$\frac{1}{16}$	—	—	—	—	—	—	$\frac{1}{8}$	—
σ_{sf}^2	$\frac{3}{32}$	$\frac{1}{8}$	$-\frac{1}{8}$	—	$\frac{1}{16}$	—	—	$\frac{1}{8}$	—
σ_{smf}^2	—	—	—	$\frac{1}{32}$	—	—	—	—	$\frac{1}{16}$
σ_w^2	$\frac{1}{16}$	$\frac{1}{4}$	—	$\frac{1}{16}$	—	$\frac{1}{4}$	$\frac{3}{16}$	$\frac{1}{4}$	$\frac{3}{16}$
(iv) North Carolina experiment III									
	D_{IX}	H_{IX}				D	H_1	D_S	H_{1S}
σ_m^2	$\frac{1}{16}$	—	—	—	—	$\frac{1}{8}$	—	—	—
σ_{ml}^2	—	$\frac{1}{16}$	—	—	—	—	$\frac{1}{8}$	—	—
σ_{sm}^2	$\frac{1}{16}$	—	—	—	—	—	—	$\frac{1}{8}$	—
σ_{sml}^2	—	$\frac{1}{16}$	—	—	—	—	—	—	$\frac{1}{8}$
σ_w^2	—	—	—	—	—	$\frac{1}{8}$	$\frac{1}{8}$	$\frac{1}{8}$	$\frac{1}{8}$

interaction component σ_{mf}^2 tests exclusively for dominance, though without regard to its source and weighted towards sex-chromosomal dominance. It is also possible to estimate D_{RX} and D_R from σ_f^2 and σ_m^2 as the coefficients of these parameters are not the same in both statistics. Thus sex-linked and autosomal additive effects but not dominance effects can be separated. Of the three designs, the North Carolina experiment II alone permits the estimation of both autosomal and sex-linked gene effects in males, and, whilst

less satisfactory for females, does permit an unambiguous test for dominance and allow separation of sex-linked and additive gene effects in that sex.

(b) *Method (b)* (see table 6)

When the sexes are pooled the analyses of variance yield the usual main effects, their interaction with sexes and a sex effect. The latter statistic is a fixed (model 1) effect and has a very complex expectation which cannot be expressed in terms of the parameters used in this paper. Any overall sex-limitation caused by factors other than segregating genes also enters this statistic. Consequently it will be ignored. The expectations of the statistics are more complex under method (b) than method (a); two extra sex-linkage parameters, D'_{XX} and F'_{XX} are required as a result of cross-product terms between male and female genetic effects.

If there is no sex-limitation the expectations of the sex interaction components all reduce to zero for autosomal genes and exclusively measure sex-linked gene effects. This contrasts with method (a) where every component was compounded of both sex-linked and autosomal gene effects.

Biparental progenies yield only three statistics for the estimation of up to nine parameters.

The North Carolina experiment I provides five statistics which, while inadequate for the estimation of all the parameters, do allow their partial separation. If there is no autosomal variation, i.e. $\sigma_m^2 = \sigma_{sm}^2$, then D_{RX} may be estimated directly from σ_m^2 . The addition of σ_{mb}^2 and σ_{smb}^2 eliminates D'_{XX} and F'_{XX} and provides an estimate of the joint effect of D'_X and H_{RX} . These two parameters are completely correlated in the three statistics in which they occur and hence their separation is impossible. However, their joint estimate and that of D_{RX} allows estimation of the environmental component, E , from σ_v^2 . Consequently D_{RX} and E may be compared provided there is no autosomal variation. If autosomal variation is present it is possible to estimate the additive components of variation only by assuming there is no sex-limitation ($D_{RS} = 0$) for which there is no test. In this case $\sigma_m^2 = \frac{1}{16}D_{RX} + \frac{1}{8}D_R$ and $\sigma_{sm}^2 = \frac{1}{16}D_{RX}$. Thus, although this design is superior to BIPs it is still inadequate for the joint analysis of sex-linked and autosomal variation.

The North Carolina experiment II provides seven statistics. If there is no sex-linked variation (nor any other cause of reciprocal differences) $\sigma_m^2 = \sigma_f^2$, and all the autosomal parameters may be estimated. In the unlikely event of there being no autosomal variation (which may be tested by $\sigma_m^2 = \sigma_{sm}^2$ and $\sigma_{mf}^2 = \sigma_{smf}^2$, provided sex-limitation is not complete) the sex-linkage parameters may be estimated. The most common case, however, will be that in which the genetical variation is distributed between the autosomes and sex-chromosome. In this case separation of all the parameters is impossible but some useful estimates may be obtained. Thus $\sigma_{mf}^2 + \sigma_{smf}^2 = \frac{1}{16}(H_{RX} + H_R + H_{RS})$ which measures exclusively dominance, though without regard to its source.

Also $\sigma_{mf}^2 - \sigma_{smf}^2 = \frac{1}{16}(H_R - H_{RS})$, so an estimate of autosomal dominance less the sex-limited dominance is obtainable. Similarly,

$$\sigma_m^2 - \sigma_{sm}^2 = \frac{1}{8}(D_R - D_{RS})$$

provides an estimate of autosomal additive, less sex-limited additive, gene

effects. If sex-limitation is assumed to be absent these two estimates simplify to estimates of H_R and D_R respectively. Estimates of exclusively sex-linked gene activity may also be obtained from

$$(\sigma_m^2 + \sigma_{sm}^2) - (\sigma_f^2 + \sigma_{sf}^2) = \frac{1}{16}D_{RX} - \frac{1}{4}D'_X$$

$$(\sigma_m^2 - \sigma_{sm}^2) - (\sigma_f^2 - \sigma_{sf}^2) = \frac{1}{8}F'_{XX} - \frac{1}{4}D'_{XX}$$

although these expressions are, of course, confounded.

(iii) *North Carolina experiment III*

Unlike the previous mating schemes, this design provides a test for epistasis which should be made prior to the estimation of parameters since these are liable to be distorted by genic interactions. The effect of sex-linkage on this test will be considered first. Let the two (female) tester lines be designated L_1 and L_2 and their F_1 as L_3 . If the progeny mean of the i th male crossed to these lines is L_{1i} , L_{2i} and L_{3i} respectively the test consists of calculating for each male the value of

$$L_{1i} + L_{2i} - 2L_{3i}.$$

The variance of these values should be zero in the absence of epistasis (Kearsey and Jinks, 1968). It can easily be shown that for sex-linked genes the value of $L_{1i} + L_{2i} - 2L_{3i}$ is zero for male progeny, female progeny and for the two sexes pooled irrespective of which allele the male parent possesses. Hence the variance of these values must also be zero and the test is not impaired by sex-linkage. In the case where the sexes are pooled it can be shown that sex-limitation is also without effect. Kearsey and Jinks (1968) mention a second test for epistasis which is developed by Jinks, Perkins and Breese (1969). Its advantage lies in dispensing with the L_3 line though its use is restricted to a base population consisting only of inbred lines. If $\bar{P}_i$ is the mean of the inbred line to which the i th male belongs, the test consists of calculating for every male the value of

$$L_{1i} + L_{2i} - \bar{P}_i.$$

When dealing with a sexually dimorphic species, the test $L_{1i} + L_{2i} - \bar{P}_i$ works for females only, and has a value of $m + h_x$ for all i . The variance of these values is therefore zero. With male progeny the test is disturbed by sex-linkage. If the i th male parent has the sex-linked allele 'A', the value of $L_{1i} + L_{2i} - \bar{P}_i$ is $m + d'_x$ and if it has the 'a' allele the appropriate value is $m - d'_x$. The variance of these values will be equivalent to D'_x . When sexes are pooled the test generally fails; the variance of the values is equivalent to $uv(d_x - d'_x)^2$ so that it will succeed only if $d_x = d'_x$. Since there is no test for such equality it would be wise to regard sex-linkage as a factor certain to upset the validity of this test for epistasis when sexes are pooled.

Estimates of autosomal additive gene effects are obtained from the variance of the sums $L_{1i} + L_{2i}$ and estimates of autosomal dominance effects are obtained from the variance of the differences $L_{1i} - L_{2i}$. The sign of the covariance of the sums and differences indicates the direction of dominance. Unlike the designs described earlier, the autosomal gene effects cannot be

described by the D_R and H_R parameters of Mather (1949) but have to be specified by those of Jinks (1954). Under this notation we have

$$D = \Sigma 4uvd^2$$

$$H_1 = \Sigma 4uvh^2$$

$$F = \Sigma 4uvdh$$

(Jinks, Perkins and Breese, 1969))

Similarly, we require new parameters to describe the sex-linked variation analogous to those for the autosomes. Thus we define

$$D_{IX} = \Sigma 4uvd_x^2$$

$$H_{IX} = \Sigma 4uvh_x^2$$

$$F_{IX} = \Sigma 4uvd_x h_x.$$

The expectations for the statistics when the male and female progeny are analysed separately are shown at the foot of table 5. Sex-linked variation is not detected among males and hence the analysis on this sex permits estimation of the autosomal components regardless of sex-linkage. For the female progeny σ_m^2 detects additive sex-linked and autosomal variation and σ_{ml}^2 detects sex-linked and autosomal dominance variation, and each of these are weighted in favour of sex-linked genes because their coefficients are larger. Thus although the location of the genetical variation cannot be identified the two types of gene action can be separated. The covariance of sums and differences is $-\frac{1}{4}F_{IX} - \frac{1}{8}F$ for females and $-\frac{1}{8}F$ for males. If the base population consists of inbred lines the sex-linkage parameters are unaltered but the autosomal expectations become:

$$\sigma_m^2 = \frac{1}{4}D$$

$$\sigma_{ml}^2 = \frac{1}{4}H$$

$$\sigma_w^2 = \text{zero}$$

$$\text{Covariance sums/differences} = -\frac{1}{4}F$$

In this case additive and dominance effects can be separated but without regard to their location. There is no weighting in favour of sex-linked genes as the coefficients of the autosomal and sex-linkage parameters are equal.

The expectations of the components for a panmictic base population using method (b) (*i.e.* sexes pooled) are shown in table 6. The parameters D_S and H_{1S} represent autosomal sex-limitation such that

$$D_S = \Sigma 4uvf_d^2$$

$$H_{1S} = \Sigma 4uvf_h^2$$

$$F_S = \Sigma 4uvf_d f_h$$

It is only possible to separate sex-linked from autosomal variation by making the untestable assumption of no sex-limitation. However, σ_m^2 measures all the additive, and σ_{ml}^2 all the dominance, variation so that these two types of gene action can be separated. There is a weighting towards autosomal

genes. Some measure of autosomal minus sex-limited variation may be obtained by

$$\begin{aligned}\sigma_m^2 - \sigma_{sm}^2 &= \frac{1}{8}(D - D_S) \\ \sigma_{ml}^2 - \sigma_{sml}^2 &= \frac{1}{8}(H_1 - H_{1S}).\end{aligned}$$

The covariance of sums and differences is $-\frac{1}{16}F$ for sex-linked genes and $-\frac{1}{8}F$ for autosomal genes. The interaction of this covariance with sexes is $-\frac{1}{16}F$ for sex-linked genes and $-\frac{1}{8}F_S$ for autosomal genes so that

$$\text{Cov. sums/diffs} - \text{Sex} \times \text{Cov. sums/diffs} = -\frac{1}{8}(F - F_S).$$

If the base population consists of inbred lines the sex-linkage parameters do not change but the expectations for autosomal genes become

$$\begin{aligned}\sigma_m^2 &= \frac{1}{4}D \\ \sigma_{ml}^2 &= \frac{1}{4}H_1 \\ \sigma_{sm}^2 &= \frac{1}{4}D_S \\ \sigma_{sml}^2 &= \frac{1}{4}H_{1S} \\ \sigma_w^2 &= \text{zero} \\ \text{Cov. sums/diffs.} &= -\frac{1}{4}F \\ \text{Sex} \times \text{Cov. sums/diffs.} &= -\frac{1}{4}F_S.\end{aligned}$$

This is as restrictive as with a panmictic base population and has the further disadvantage that the joint estimates of autosomal and sex-linked gene effects are more heavily weighted towards the former.

5. DISCUSSION

The analysis of sex-linked quantitative inheritance would be a straightforward process were it not for the simultaneous existence of autosomal variation and the added complication that this may be sex-limited. Of the two methods of analysis suggested, method (a) is the simplest but is not helpful with either BIPs or the North Carolina experiment I designs, neither of which provide sufficient statistics for the estimation of parameters. The North Carolina experiment II design is perfectly adequate for male progeny and satisfactory for female progeny, the only restriction here being that the dominance effect of the sex-chromosome cannot be separated from that of the autosomes. There is, however, a more serious difficulty in that sex-linkage is not the only possible cause of reciprocal differences. Cytoplasmic and maternal effects will tend to inflate σ_f^2 which will lead to overestimation of D'_X in male progeny and underestimation of D_{RX} in female progeny. There is no test for the existence of these effects, in the presence of sex-linkage, so they must be assumed absent, though the potential distortion they cause should be remembered. The epistasis test of Kearsy and Jinks (1968) in the North Carolina experiment III is undisturbed by sex-linkage in either sex but the test of Jinks, Perkins and Breese (1969) is suitable only for female progeny. This experimental design fails to detect or measure sex-linkage in males, but is of course quite adequate for the analysis of

autosomal variation in that sex. In females it yields estimates of additive and dominance components compounded of sex-linked and autosomal gene effects.

When sexes are pooled (method (b)) neither BIPs nor the North Carolina experiment I design provide enough statistics for the purposes of estimation; BIPs merely allow the detection of genetical variation and the North Carolina experiment I further permits the detection of additive genetic variation. The North Carolina experiment II allows the significance of additive and dominance variation to be tested and provides estimates of these effects though compounded of more than one parameter. The North Carolina experiment III test for epistasis of Kearsy and Jinks (1968) is valid but that of Jinks, Perkins and Breese (1969) is not. Estimates of additive and dominance gene effects may be obtained but are compounded of sex-linked and autosomal gene effects weighted towards the latter.

Probably the most satisfactory design is the North Carolina experiment II analysed first by method (a). This allows estimation of D_R in both sexes and if these two values are similar sex-limitation may be taken to be unimportant; analysis by method (b) then becomes quite informative.

Whilst this approach to the analysis of such experimental designs is traditional it is not the only approach possible. It is possible to determine the expectations of the various mean squares by combining the expectations of the constituent components of variance in the proportions appropriate to the size of the experiment. The parameters may then be estimated by weighted least squares. Where the total number of parameters exceeds the number of statistics, making estimation impossible, simpler models may be tried sequentially and their adequacy assessed by means of a χ^2 test (Cavalli, 1952). Thus a typical sequence here might be to fit the usual autosomal parameters, then to add the sex-linkage parameter and finally to substitute the sex-limitation model for the sex-linkage model. The relative sizes of the χ^2 s will provide a guide as to which types of gene action are of most importance. (See Perkins and Jinks (1970) for a description of this approach).

Finally it may be noted that autosomal sex-limitation is not the only potential complication in estimating sex-linkage parameters. For instance, Garn and Rohmann (1962) published sib-sib correlations for three skeletal characters in man. For two characters the correlation between sisters exceeded 0.5 (which is not possible with autosomal inheritance) and was invariably larger than that between brothers and that between sisters and brothers which were roughly equal. Garn and Rohmann's suggestion that sex-linkage was responsible was disproved by Mather and Jinks (1963) as this makes $r_{SS} > r_{BB} > r_{SB}$. In this case sex-limitation does not explain the results either. One possible explanation is that, in addition to sex-linkage, the environmental component was smaller for females than for males. Such a difference would cause $r_{SS} > r_{SB} > r_{BB}$. A combination of sex-linkage and differential sensitivity to the environment could therefore give correlations of the same relative size of Garn and Rohmann's.

6. SUMMARY

1. A model describing sex-limitation of autosomal genes is developed.
2. The expectations of statistics from analyses of several multiple mating schemes are given for sex-linked and sex-limited gene effects. Two types of

analysis are considered; where sexes are analysed separately and where they are pooled.

3. The relative efficiencies of these multiple mating schemes in allowing separation of sex-linked and autosomal gene effects are discussed.

4. The influence of sex-linkage on the test for epistasis, allowed by one design (the North Carolina experiment III) is considered.

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