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Effects of disruptive selection on genetic variance

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Summary. Theoretical predictions of changes in variance with disruptive selection have used models of infinitely many genes so the increase in variance was necessarily due to linkage disequilibrium. With small numbers of loci, the disequilibrium is shown still to comprise the major part of the changes in variance.

In a replicated experiment with *Drosophila melanogaster*, disruptive selection was practised for three generations, and this was followed by 5 or 7 generations of random mating. The heritability, as estimated from regression of progeny on parent, rose from 37% to 68% on selection, and subsequently declined to 45% on random mating. Changes of variance can be interpreted invoking the build up of linkage disequilibrium during selection followed by its breakdown upon relaxation. The results agree well with those obtained from Monte Carlo simulation.

Key words: Disruptive selection – Linkage disequilibrium – Genetic variance – *Drosophila*

1 Introduction

Variation in the environment over the range occupied by an interbreeding population may lead to differences in the optimum phenotype favoured by selection. This type of selection was termed centrifugal selection by Simpson (1944) and disruptive selection by Mather (1955), and the interest in it derives from Mather's (1955) suggestion that it could produce polymorphism and lead to sympatric speciation. There is now an extensive literature on results of selection for such phenotypic deviants (see Thoday 1972, for a review) much of which reported unsuccessful attempts to repeat Thoday and Gibson's (1962) experiment which produced sexual isolation.

There are many experiments substantiating predictions that disruptive selection on a quantitative trait will lead to an increase in the genetic variance (Thoday 1959; Gibson and Thoday 1963; Scharloo 1964; Scharloo et al. 1967; Barker and Cummins 1969). Attempts to quantify the change in genetic variance with disruptive selection were made initially by Robertson (1970b) and later on by Bulmer (1971, 1980). The latter interpreted the divergence between the means of lines derived from matings of individuals selected from opposite extremes in terms of linkage disequilibrium. Assuming normality and a large number of loci of small effect, Bulmer (1976, 1980, p. 156) showed that if the proportion selected at each extreme is greater than 0.226 a stable equilibrium will be reached, but that, if the proportion is less than this value "the variance would increase without limit". Bulmer (1976) checked some of his predictions by Monte Carlo simulations and obtained results in good agreement with theory.

In this paper we report an experiment using *Drosophila* in which disruptive selection was practised for a few generations and then selection was relaxed. Heritability was estimated each generation and after relaxation in order to test whether it would rise during selection and fall during random mating due to the breakdown of linkage disequilibrium, as predicted by Bulmer. In his theory both population size and number of loci are infinite so we also report theoretical studies in which these assumptions are relaxed in order to check the robustness of the model and to help in interpreting the experiment. The theory is reported first.

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2 Theory and Monte Carlo simulation

a) Two locus additive model

For a two locus additive model under disruptive selection analytic results can be derived. Consider the case of two loci each with two alleles A,a and B,b where p and q are the frequencies of the plus alleles A and B respectively. The genotypic values measured as deviations between homozygotes and heterozygotes are α and β respectively. The gamete frequencies are:

AB: $f_1 = p\,q + D$ aB: $f_3 = (1-p)\,q - D$

Ab: $f_2 = p\,(1-q) - D$ ab: $f_4 = (1-p)\,(1-q) + D$,

where $D = f_1 f_4 - f_2 f_3$ is the covariance of gene frequencies in gametes (i.e. linkage disequilibrium). Assuming Hardy-Weinberg equilibrium between chromosomes, the genotypic variance (VG) contributed by this pair of loci is:

$$VG = 2p\,(1-p)\,\alpha^2 + 2q\,(1-q)\,\beta^2 + 4\alpha\,\beta\,D\,. \qquad (1)$$

Following Bulmer (1971) we denote the sum of the first two terms in (1) as the equilibrium additive variance (Vg) and the last term as the joint disequilibrium (CL), i.e. VG = Vg + CL.

Let us assume that genotypic and environmental values are both normally and independently distributed, such that phenotypic values (their sum) are normal with mean M and variance σ^2. Of the many loci affecting the trait we focus on just two and assume that individuals of genotype ij have mean $\bar{x}_{ij}$ and variances σ^2_{ij} but that the difference between σ^2 and σ^2_{ij} is negligible. Disruptive selection is carried out such that an equal proportion at each end of the distribution is saved for breeding, these proportions remain the same each generation and the population is large enough that the absolute difference between the mean and the truncation points (+T and −T) is the same on each side. The probability of selection of the ij^{th} genotype formed by the random union of gametes i and j (i, j = 1, ..., 4) is (Robertson 1956):

$$W_{ij} = \frac{1}{\sigma\sqrt{2\pi}} \left\{ \int_{-\infty}^{-T} \exp\left[\frac{-(X-\bar{X}_{ij})^2}{2\sigma^2}\right] dX + \int_{T}^{\infty} \exp\left[\frac{-(X-\bar{X}_{ij})^2}{2\sigma^2}\right] dX \right\}. \qquad (2)$$

Expanding (2) in a Taylor series to second order terms about M gives:

$$W_{ij} \cong 2Q + \frac{Q\,i\,x_T}{\sigma^2}(X_{ij} - M)^2, \qquad (3)$$

where Q is the proportion selected at each end of the distribution, i is the difference between the mean of the selected group and M in standard units and x_T is the abscissa in standard units at the truncation point. The genotypic frequencies in selected individuals are obtained from (3) by multiplying by their initial values and dividing by Q. For our model of gene effects, this gives the second order approximation of the expected change in gene frequency as:

$$\Delta p \cong \frac{i\,x_T}{2\sigma^2}[\alpha^2 p\,(1-p)\,(1-2p) + \beta^2(1-2q)\,D + 2\alpha\,\beta(1-2p)\,D]\,. \qquad (4)$$

Therefore gene frequencies move towards intermediate values. Rates of change are of order $(\alpha/\sigma)^2$ and likely to be small except for genes of very large effect or with much contributing disequilibrium in the same direction to gene frequency change. We are mostly concerned with populations initially in linkage equilibrium (D (0) = 0). Then from (3),

$$D(1) = \frac{i\,x_T}{\sigma^2}\,\alpha\,p\,(1-p)\,\beta\,q\,(1-q)\,, \qquad (5)$$

so D values are also of order $(\alpha/\sigma)^2$ and unless effects are very large, do not contribute much to gene frequency change in the first few generations since they contribute terms of order $(\alpha/\sigma)^4$ (see 4).

Changes in genotypic variance. Assuming now that there are n loci, with effects α_i affecting the trait, and there is initial equilibrium, the increase in genotypic variance due to the generation of positive linkage disequilibrium in terms of parameters before selection is, by extension of (5):

$$CL(1) = \frac{i\,x_T}{\sigma^2(0)} \sum\sum_{j \neq k} 2\,\alpha_j^2\,\alpha_k^2\,p_j\,(1-p_j)\,p_k\,(1-p_k) = \frac{1}{2}\frac{i\,x_T}{\sigma^2} VG^2\left(1 - \frac{1+CV_v^2}{n}\right) \qquad (6)$$

where CV_v is the coefficient of variation of the quantities $\alpha_j^2\,p_j(1-p_j)$. If the number of loci is large and no single locus contributes a large part of the variance, the final terms in (6) drop out and it reduces to the expression obtained by Bulmer (1971). The change in genotypic variance due to gene frequency change can be obtained by extension of (4). This shows that unless CV_v^2 is much larger than unity, the change in genotypic variance due to gene frequency changes is a fraction of order 1/n (1/number of loci) of that due to linkage disequilibrium. Thus in laboratory experiments of short duration, provided population size is sufficiently large that random drift can be ignored, changes in additive variance due to gene frequency change are unlikely to be detected.

By assuming a model of infinitely many genes, Bulmer (1971) extended (6) to several generations,

$$CL(t+1) = \frac{1}{2}\frac{i\,x_T}{\sigma^2(t)} VG^2(t) + \frac{1}{2} CL(t)\,, \qquad (7)$$

$$VG(t) = VG(0) + CL(t) . \quad (8)$$

In large populations and in the presence of linkage, Bulmer (1974, 1980) showed that $\hat{V}G$, the genotypic variance at equilibrium, satisfies the equation:

$$[\{2H + 1 - (1 + i x_T)\}]/2H \hat{V}G^2 + [VE - VG(0)] \hat{V}G - VG(0) VE = 0 \quad (9)$$

where VE is the environmental variance and H is the harmonic mean of the recombination fraction among the loci involved. For unlinked loci (H = 1/2), (9) predicts that if the proportion selected at each extreme is greater than 22.6%, there is a stable equilibrium. With more intense selection there is no real solution, and Bulmer (1980) interprets this to mean that favourable loci at each extreme become fixed. Expression (9) also predicts that, if the steady state is reached, the amount of disequilibrium generated increases with tight linkage.

Disruptive selection can also be viewed as a two way selection experiment in which there is limited migration between the high and low lines during the first few generations. The amount of migration that takes place depends upon the proportion selected at each extreme. After a first cycle of selection and mating, assuming the population size and number of loci are large, one can consider the whole population as being composed of a mixture of three normally distributed subpopulations, corresponding to the offspring of the high × high (H × H), H × low (L) and L × L matings in a ratio of 1:2:1. The expected mean of the H × H matings expressed as a deviation from the overall mean is, $\Delta M = i\, h(0)\, VG(0)$, where $h^2(0)$ is the heritability at generation zero. The expected mean of the L × L is, $-\Delta M = -i\, h(0)\, VG(0)$ and the L × H (and H × L) matings yield a distribution with zero mean and the genotypic variance within each of the three distributions is $Vw = VG(0)(1 - 1/2\, i(i - x_T)\, h^2(0))$. It then follows that the overall distribution has zero expected mean and expected genotypic variance equal to:

$$VG(1) = (\Delta M)^2/2 + Vw \quad (10)$$

$$= VG(0)(1 + 1/2\, i\, x_T\, h^2(0)) . \quad (11)$$

This approach to the problem was used by Robertson (1970b) though he ignored changes in within subpopulation variance.

Expression (10) provides further insight into the dynamics of the disruptive selection experiment and allows us to make some qualitative predictions. With linkage and small population size, response to selection (ΔM) is smaller than with free recombination (Robertson 1970a) and the decline in Vw is larger. Hence, from (10), contrary to expectations based on infinite population theory, the tighter the degree of linkage, the smaller the increase in genotypic variance as selection proceeds. This and other points are illustrated in the next section with Monte Carlo simulation.

b) Monte Carlo Simulation

Method. The processes of gamete formation, random mating, genotypic evaluation on the individual's own performance and selection of the same proportion at each extreme of the distribution were simulated directly. Only additive models were studied and phenotypic values were determined by adding a normally distributed random variable with mean zero and specified variance. The N highest (H) and N lowest (L) out of a total of M scored in each sex were selected and the N of each sex divided randomly into groups of size N/2. Individuals of one group of H males were pair mated to a group of H females, and the other group to L females, and similarly for the L males. Thus a zero phenotypic correlation among mates was expected. Thoday (1972) called this mating structure "quasi-random mating". Each pair of mates contributed the same number of offspring to the pool of individuals for the next generation. This mating plan was followed in each generation of selection. Unless otherwise stated, the number selected in each sex at each extreme was N = 20 out of M = 200 scored for each sex. A range of models were simulated.

Results. Table 1 shows values of genotypic variance and joint disequilibrium for models with free recombination obtained by Monte Carlo simulation for 30 loci an compared with predicted results (7, 8) from Bulmer (1971). Observed and predicted results are in

Table 1. Simulated values from 30 Monte Carlo replicates and predicted values (eq. 7 and 8) for the genotype variance (VG) and joint disequilibrium (CL) with disruptive selection. In each simulated model there are 30 unlinked loci each with two alleles and initial frequencies (q) and gene effects (α/σ) as shown, the initial heritability is 0.5 and 20/200 are selected at each extreme in each sex. The difference between VG at generation 0 and (VG-CL) at generation 4 reflects the change in variance due to gene frequency changes

	Simulated						Predicted	
q	0.5 (30 loci)		0.2 (30 loci)		0.2 (5 loci) 0.5 (25 loci)			
α/σ	0.18		0.23		0.46 0.11			
Generation	VG	CL	VG	CL	VG	CL	VG	CL
0	10.0	−0.1	10.0	0.2	10.0	0.2	10.0	0.0
1	15.6	5.6	15.6	5.7	15.6	5.5	15.6	5.6
2	27.0	16.9	26.3	16.0	26.9	15.7	23.5	13.5
3	39.3	29.0	38.5	28.0	38.8	27.0	35.3	25.3
4	53.1	43.2	53.0	42.5	51.0	38.8	53.6	43.6
	SE(VG) = 1.0		Se(CL) = 1.0					

good agreement. The change in genotypic variance as predicted from two locus theory is almost exclusively due to joint disequilibrium. Even with initial frequencies of 0.2 (or 0.8, since there is symmetry around frequencies of 0.5 for additive genes), gene frequencies move slowly towards intermediate values but only 1% of the change in genotypic variance is due to changes in gene frequency over four generations. The similarity of results of models with ranges of initial frequency (Table 1) shows that for a given amount of initial genetic variation, the system is not much affected by the effects, frequencies and numbers of loci.

Table 2. Simulated values from 30 Monte Carlo replicates of joint disequilibrium for various degrees of linkage for models with 30 additive loce each with initial frequency 0.5 and effect (α/σ) of 0.18, and 20/200 are selected at each extreme in each sex. Predicted values (from eq. 7 and 8) for unlinked loci are also shown

Generation	Simulated					Predicted
	Recombination fraction between adjacent loci					
	0.5	0.1	0.01	0.00		
	Joint disequilibrium (CL)				Mean SE	
0	−0.1	0.1	−0.1	−0.1	0.17	0.0
1	5.6	5.6	5.7	5.6	0.50	5.6
2	16.9	16.7	16.7	16.6	1.07	13.5
3	29.0	29.5	28.1	27.6	1.50	25.3
4	43.2	41.9	39.9	37.0	2.00	43.6

Table 3. Monte Carlo simulation of models of 4 loci (15 replicates) and 20 loci (7 replicates) giving the joint disequilibrium (CL) and the ratio of the observed mean of H × H matings ($\bar{X}_H$) to the maximum value ($\bar{X}_{MAX}$) which would be obtained if the plus allele were fixed at all loci. The recombination fraction between adjacent loci is c, intitial gene frequencies are 0.4 at each locus, the equilibrium additive variance is 10.0, and 20/200 are selected at each extreme in each sex

Generation	c	0.50	0.05	0.00		0.50	0.05	0.00
	Loci	CL			AvSE	$\bar{X}_H/\bar{X}_{MAX}$		
0	4	−0.1	−0.1	0.1	0.1	0.40	0.40	0.40
	20	0.0	−0.3	−0.2	0.2	0.40	0.40	0.40
2	4	12.6	13.1	12.8	0.7	0.76	0.77	0.76
	20	16.0	13.5	14.1	1.1	0.54	0.54	0.54
5	4	26.3	26.6	26.4	0.6	0.95	0.95	0.94
	20	59.8	44.4	42.4	3.8	0.68	0.66	0.66
10	4	30.2	30.4	30.4	0.1	1.00	1.00	1.00
	20	108.9	86.9	54.0	5.8	0.82	0.77	0.70
20	4	30.1	30.2	30.2	0.1	1.00	1.00	1.00
	20	176.7	135.4	59.3	6.5	0.97	0.87	0.71

Table 2 illustrates the effect of degree of linkage for models with initial gene frequency 0.5. During the first three cycles of selection linkage has very little effect. At generation 4, however, there is a clear indication that the tighter the linkage, the smaller the amount of disequilibrium produced. As mentioned earlier, this is probably a direct consequence of the finiteness of the population. The maximum amount of disequilibrium produced is when the selected individuals at each extreme are fixed for either the plus or minus alleles. With complete linkage we can do no better than fix the best gamete out of the initial sample. The probability of obtaining the desirable allele at all loci in the initial sample will depend on the gene frequency, the number of loci and the sample size. Provided the population size is not too small, the critical parameters are the number of loci and the initial gene frequencies. The larger the number of loci, the higher the required initial gene frequency in the base population to have a given probability of obtaining the extreme gamete in the initial sample (Robertson 1970a). With few loci there is a high probability of picking up the extreme gamete in the first cycle of selection and therefore linkage has no effect. With more loci, the looser the degree of linkage the more likely the extreme gametes will be produced as selection proceeds. This is illustrated in Table 3.

Changes of genetic parameters are usually monitored in practice by estimating the heritability using offspring parent regressions or intra-class correlations between sibs. An offspring mid-parent regression estimates $\left[\sum_j 2\alpha_j^2 p(1-p_j) + 4\sum\sum_{i<j} \alpha_i \alpha_j D_{ij}\right]/\sigma^2$, but is a useful predictor of selection response only if there is linearity of the offspring-parent regression. Table 4 shows Monte Carlo results for the observed ratio of genotypic to phenotypic variance and single generation realized heritabilities. The latter was obtained from the ratio of the differences between the mean of the offspring of the H × H (L × L) matings and the parental population mean, over the differences between the mean of the parents of the H × H (L × L) matings and the overall population mean. The denominator of this ratio is the selection differential. The realized heritabilities obtained from both extremes were averaged and the resultant estimate would equal the ratio of genotypic to phenotypic variance if the regression were linear.

It is clear that after a first cycle of selection the ratio and the realized heritability do not agree (Table 4). The first cycle of selection produces considerable divergence between the progeny means of H × H, H × L (L × H) and L × L matings to generate three subpopulations. In a second cycle of selection, for high say, those selected individuals which are them-

selves offspring of H × H matings will have progeny whose mean will regress towards the mean of the H × H subpopulation they were selected from rather than to the overall population mean. This clearly leads to a higher realized heritability estimate than if there had been no genetic differentiation among subpopulations. More generally, disruptive selection leads to a relationship between the conditional offspring means and the parental values of a double sigmoid type with minimum slopes at the two extremes and in the middle. Therefore the response to selection at each end of the distribution is symmetrical but realized heritability depends on the selection pressure applied.

After a first cycle of disruptive selection, the positive disequilibrium generated will bias upwards estimates of heritability based on intra-class correlation between sibs, relative to estimates derived from populations in equilibrium (Robertson 1977). The positive disequilibrium affects the variance component between families and the genetic component of the variance within families tends to zero as the extreme gametes tend to fixation. These points are clearly illustrated in Table 5.

Table 4. Monte Carlo simulation showing the observed ratio of genotypic to phenotypic variance (VG/VP), and the observed single generation realized heritabilities (h_R^2). The h_R^2 were computed from ratios of response to selection differential for high × high and low × low matings and averaged. Models as in Table 1 with 30 unlinked loci and 30 replicates

q	0.5 (30 loci)		0.2 (30 loci)		0.2 (5 loci) 0.5 (25 loci)	
a/σ	0.18		0.23		0.11	
Generation	VG/VP	h_R^2	Vg/VP	h_R^2	VG/VP	h_R^2
0	0.50	0.50	0.50	0.51	0.50	0.52
1	0.60	0.69	0.61	0.71	0.62	0.70
2	0.72	0.76	0.72	0.77	0.72	0.75
3	0.79	0.80	0.80	0.80	0.79	0.79

SE (h_R^2) = 0.01

3 Experiments with *Drosophila melanogaster*

a) Materials and methods

The lines were derived from the Dahomey population which had been kept in cages in this laboratory for many generations. The character studied was the sum of the abdominal bristles on the fourth and fifth segment in males and fifth and sixth segments in females.

The experiment was run with two replicates. In replicate 1 at generation 0, eggs were sampled from the cage in half-pint milk bottles and when the adults emerged, 160 males and 160 females were scored and constituted generation zero. The highest (H) and lowest (L) 16 males and 16 females were selected and each divided randomly into two groups of 8. Four types of mating were made: H × H, H × L, L × H and L × L using pair matings in individual vials. Within each type of mating flies were paired at random and the choice of which flies within each extreme were mated with high or low partners was random. At generations 1 and 2, 5 males and 5 females from each full-sib family (vial) were chosen at random, scored, selected on phenotype regardless of family of origin and mated as in generation 0, with spare matings kept to replace unsuccessful ones. At generation 3, after three cycles of disruptive selection, one male and one female were chosen at random from each of the 32 families and transferred to half-pint milk bottles for 6 cycles of random mating. During this period, each generation 32 pairs of flies were sampled from a bottle to produce offspring, and at generation 9, after 6 cycles of relaxation, 160 flies of each sex were sampled and

Table 5. Variance component between full-sib families (σ_b^2), within full-sib families (σ_w^2), intra-class correlation (t_c) and realized heritability (h_R^2, see Table 4) for models of Table 3 with different values of recombination fraction (c) between adjacent loci. The initial heritability is 0.5 and the environmental variance equals 10 throughout

Generation	c	4 loci				20 loci			
		σ_w^2	σ_b^2	t_c	h_R^2	σ_w^2	σ_b^2	t_c	h_R^2
0	0.5 0.0	13.8	4.6	0.25	0.50	14.1	4.8	0.25	0.50
1	0.5	13.5	10.5	0.44	0.74	14.3	12.5	0.47	0.67
	0.0	13.4	10.1	0.43	0.74	13.4	10.4	0.43	0.69
2	0.5	13.0	20.2	0.60	0.75	14.6	21.8	0.60	0.77
	0.0	13.7	19.8	0.59	0.78	15.5	20.0	0.55	0.75
5	0.5	10.4	36.5	0.78	0.77	13.1	71.5	0.84	0.81
	0.0	10.7	36.1	0.77	0.74	14.5	50.5	0.77	0.77
10	0.5	9.8	41.0	0.81	0.75	11.0	115.4	0.91	0.81
	0.0	10.0	40.9	0.80	0.75	9.5	61.0	0.86	0.77
20	0.5	10.0	41.3	0.81	0.77	9.9	191.5	0.95	0.86
	0.0	10.1	41.3	0.80	0.77	9.5	68.2	0.87	0.77

SE (h_R^2) = 0.01 SE (t) = 0.01

scored and the extremes selected and mated as at generation 0, following which the replicate was discontinued.

Replicate 2 differed slightly from replicate 1 in that: flies that contributed to generation 0 were themselves reared in vials; the cycles of random mating were carried on in vials rather than in bottles, each family contributing one male and one female to those scored in the next generation; and random mating was continued for 4 generations only. The replicates were nor contemporaneous.

In both replicates, heritability was estimated from the regression of offspring on the selected mid-parental values, at generations 0, 1 and 2 and at the end of the period of relaxation. Heritability was also estimates from twice the intra-class correlation of full-sibs.

b) Results

The frequency distribution of bristle scores of individual females in replicate 2 is shown in Fig. 1 for several generations; the distributions in males and in replicate 1 were similar. The figure also shows the frequency distribution of the offspring of extreme matings. As selection proceeds the overall distribution becomes more platykurtic and the degree of overlap between the H × H and L × L distributions decreases. This lack of overlap can also be illustrated by considering the source of selected individuals. Thus in generation 1, 57% of selected flies came from matings of parents selected in the same direction (i.e. H from H × H and L from L × L), 33% from H × L or L × H matings and 10% from matings in the opposite direction (i.e. L from H × H and H from L × L). In generation 2 these values were 78%, 20% and 2% respectively. The overall increase in variance can then be attributed to the divergence between the means of progeny from the H and L matings.

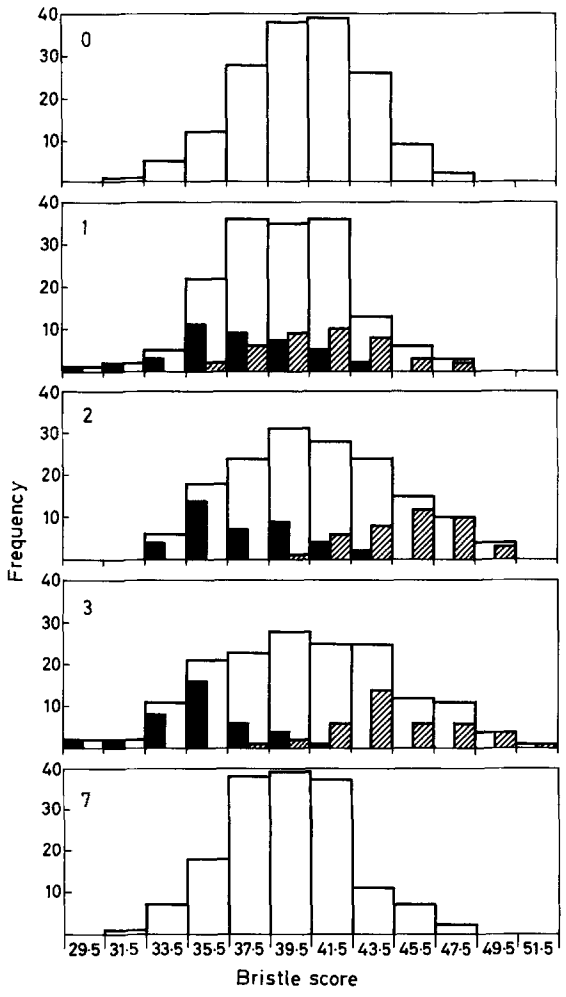

Fig. 1. Frequency distribution of bristle scores in females of replicate 2 at the start (generation 0) during selection (1, 2, 3) and after relaxation (7). Open columns refer to all progeny, solid to offspring of H × H and cross-hatched to offspring of L × L

Table 6. Estimates of heritability in *Drosophila* obtained from offspring mid-parent regressions ($b_{O\bar{P}}$), variance components within and between families (σ_w^2, σ_b^2) and twice intraclass correlation between full-sib families ($2t_c$)

Generation of offspring	Replicate 1				Replicate 2			
	$b_{O\bar{P}}$	σ_w^2	σ_b^2	$2t_c$	$b_{O\bar{P}}$	σ_w^2	σ_b^2	$2t_c$
0[a]						7.4	1.0	0.24
1	0.38	5.9	3.7	0.77	0.35	4.5	3.5	0.88
2	0.54	6.9	7.0	1.00	0.72	7.3	7.8	1.03
3	0.74	10.0	16.5	1.25	0.64	7.5	9.5	1.11
7[a]						6.7	2.0	0.46
8					0.44	7.3	4.7	0.78
10	0.47	11.1	5.0	0.62				

[a] Estimates of the intraclass correlation before selection at generation 0 and after the generations of random mating

$SE(b_{O\bar{P}} = 0.07$ $SE(2t_c) = 0.12$

Estimates of heritability by regression of offspring on mid-parent and intra-class correlations between full-sib families together with the corresponding variance components are given in Table 6. There is a conspicuous increase in the offspring-parent regression followed by a decline after random mating. The heritability estimate based on the intraclass correlation is biased upwards relative to the regression estimate. In replicate 2, the estimate based on intra-class correlation at the end of the period of relaxation is in close agreement with that obtained subsequently from regression.

The expected decline in variance due to drift in replicate 1 during the 6 cycles of random mating, using estimates of the ratio of effective to actual numbers reported by Crow and Morton (1955), is about 6%. In replicate 2 where flies were kept in vials during the four cycles of relaxation and each family contributed equally to the next generation (and thus eliminating any effect of natural selection operating between fami-

lies) the expected decline in variance due to drift is about 2%. In both replicates the observed decline in variance is well in excess of that expected from drift alone.

Most of the environmental variance in this character can be attributed to "developmental error" (Clayton et al. 1957). The within-fly variance was calculated in each generation in both replicates and it remained virtually unchanged throughout the selection experiment at about 4 square units.

4 Discussion

The theoretical study was intended to extend Bulmer's (1971) results to take account of finite population size and number of loci. The analysis of models of finite numbers of loci and the simulation results support his assumptions for infinite number of loci that most of the changes in genotypic variance in disruptive selection experiments of short duration are due to the build-up of positive linkage disequilibrium. In small populations however, in contrast with results obtained using deterministic theory, the tighter the linkage among the loci affecting the trait the smaller the amount of disequilibrium produced as selection proceeds. Another way of saying the same thing is to view the experiment as a two way selection experiment in which case we conclude that with tight linkage the divergence between means of offspring from extreme matings is reduced and hence the overall genotypic variance increases less than when there is free recombination.

The experiment with *Drosophila* provides evidence of the build-up of disequilibrium during selection. This is reflected by the increase in the offspring mid-parent regression as selection starts operating followed by a decline at the end of the period of relaxation, with, during the whole period, little change in mean score. This is further substantiated by the positive bias of heritability estimates based on intra-class correlations (Table 6). The rate of breakdown of disequilibrium during random mating is proportional to the recombination fraction among the loci involved. In the experiment, the heritability did not appear to revert back completely to its original value in either replicate. This may have been due to sampling error of the estimate, but theory does predict that gene frequency changes, although small, would tend to move gene frequencies towards 0.5 and thus increase the variance; and more importantly, not all the disequilibrium produced by selection will have broken down during random mating. In fact, the variance is expected to decline initially rather rapidly due to the breakdown of disequilibria between genes on different chromosomes followed by a slower decline from genes on the same chromosome.

Table 7. Estimates of heritability from (i) *Drosophila* by offspring mid-parent regression (b); (ii) Monte Carlo simulation from both the ratio of genotypic to phenotypic variance (VG/VP), and offspring parent regression (b); using a model of 10 identical loci on each of 3 chromosomes with recombination fraction 0.1 between adjacent loci and initial gene frequencies 0.5, with 16 selected out of 160 scored in each sex, as for the *Drosophila*

Generation of parents	*Drosophila*	Monte Carlo	
	b*	VG/VP	b**
Selection			
0	0.37[a]	0.37	0.38
1	0.65[a]	0.44	0.58
2	0.68[a]	0.56	0.67
Random mating			
7	0.44	0.43	0.45
9	0.47	0.42	0.44

* SE(b) = 0.05 ** SE(b) = 0.02
[a] Replicates pooled

Disruptive selection leads to non-normality in the underlying genotypic distribution and consequently offspring mid-parent regressions become nonlinear, as we illustrated in the section on Monte Carlo simulation. This is further illustrated in Table 7 which shows observed mid-parent regressions of the *Drosophila* experiment together with the observed ratios of genotypic and phenotypic variance and observed realized heritabilities obtained from Monte Carlo simulations. (The *Drosophila* data are classified by the generation of the parent to correspond with the simulation results shown earlier.) The regression from the *Drosophila* experiment and from the simulation are in reasonable agreement, but estimates based on regression do not agree with the ratio, due to the non-linearity.

Whith the selection intensities practised here, the subpopulations diverge fairly quickly such that most of the high selected individuals are chosen from the offspring of H × H matings. If facilities were available for further work, it would be useful to check whether, with weaker selection, the variance also changes as predicted by theory and reaches a stable value without fixation of the extreme gametes.

In an analysis of possible selective forces that maintain sexual reproduction and genetic recombination in nature, Maynard Smith (1979) concluded that both normalizing and disruptive selection tend to reduce recombination. For disruptive selection this appears to be true for infinite populations but if population size is finite, the population divergence is reduced with tight linkage as for directional selection.

It therefore seems reasonable to conclude that disruptive selection of sufficient intensity as to lead to population divergence favours recombination rather than tight linkage.

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