Variance component analysis for viability in an isolated population of *Drosophila melanogaster**

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SUMMARY

Using the 602 second chromosome lines extracted from the Ishigakijima population of *Drosophila melanogaster* in Japan, partial diallel cross experiments (Design II of Comstock & Robinson, 1952) were carried out, and the additive genetic variance and the dominance variance of viability were estimated. The estimated value of the additive genetic variance is 0.01754 ± 0.00608, and the dominance variance 0.00151 ± 0.00114, using a logarithmic scale. Since the value of the additive genetic variance is much larger than expected under mutation–selection balance although the dominance variance is compatible with it, we speculate that in the Ishigakijima population some type of balancing selection must be operating to maintain the genetic variability with respect to viability at a minority of loci. As candidates for such selection, overdominance, frequency-dependent selection, and diversifying selection are considered, and it is suggested that diversifying selection is the most probable candidate for increasing the additive genetic variance.

1. INTRODUCTION

A large amount of genetic variability of viability in natural populations of Drosophila has been reported by many investigators (e.g. Dobzhansky & Spassky, 1963; Mukai & Yamaguchi, 1974). It is very important from the evolutionary viewpoint to clarify the mechanism involved in the maintenance of this type of variability. Nevertheless, it has not been completely elucidated. In order to resolve this problem, Mukai *et al.* (1974) estimated the genetic variance of viability and its components for the North Carolina population of *Drosophila melanogaster* in the U.S.A., and an excess of the additive genetic variance was observed in comparison with the value expected on the basis of mutation–selection balance. Mukai (1977) and Mukai & Nagano (1983) have suggested that diversifying selection is responsible for the excess of additive genetic variance. In this work we repeated the attempt using the population of Ishigakijima, a southern island

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population in Okinawa, Japan. This island is considered to be isolated to some extent from other small island populations as well as from the major islands of Japan. Our results again suggest that, in Ishigakijima, some type of balancing selection is operating at a fraction of viability polygene loci, although the genetic variability at the majority of such loci is maintained by mutation–selection balance.

Table 1. *The numbers of second chromosomes and their karyotypes with the years of capture*

	Karyotype	
Year	*Standard*	*In(2L)t*
1976	98	98
1977	42	42
1978	70	84
1979	84	84
Total	294	308

2. MATERIALS AND METHODS

The second chromosomes used in the present experiments were extracted from a population of *Drosophila melanogaster* in Ishigakijima, Okinawa, Japan, with the mating system described by Wallace (1956) using the second chromosome balancer, *In(2LR)SM1*. In what follows we will refer to this chromosome as *Cy*, which is the dominant marker gene for that multiple inversion. The collections of flies were made from 1976 to 1979. The years when flies were captured and the number of chromosomes used are summarized in Table 1 with their karyotypes. The total number of chromosome lines employed in the present experiment was 602.

The chromosome lines were divided randomly into 39 sets of 14 lines within karyotypes and years. For each set of 14 chromosomes, a single partial diallel experiment (or a 7×7 factorial experiment) was conducted. Each set was divided into two equal subgroups, and each line of the first subgroup was mated with each line of the second to constitute a 7×7 partial diallel arrangement with 7 rows and 7 columns. Five $Cy/+_i$ females from the ith line (row) were mated to 5 $Cy/+_j$ males from the jth line (column) in two replicates. Reciprocal crosses were also made in two replicates. This design is equivalent to Design II of Comstock & Robinson (1952) with reciprocal crosses. Four days after crosses were made, all the parental flies (ten flies) were transferred to a second vial and after four more days they were discarded. The offspring were counted until the eighteenth day after the crosses (or transfers) had been made. The counts from the original and transferred vials were pooled. In the offspring, in the absence of viability differences, two phenotypes of flies segregate [$Cy(Cy/+_i$ and $Cy/+_j)$ and wild-type ($+_i/+_j$) where i and j indicate line numbers] at the expected ratio of $2:1$ since the Cy homozygotes are lethal. The viability was expressed as the logarithm of ratio, $2 \times$ (number of wild-type flies)/number of Cy flies, assuming multiplicative (independent) effects of each locus and the environment. The experiments with the $In(2L)t$-carrying chromosomes and with the standard-type chromosomes were conducted approxi-

mately at the same time. In order to test the specific interaction between the inversion-carrying and standard chromosomes, four more sets of experiments with seven standard chromosome lines as column and seven *In(2L)t* lines as row were carried out. The experimental procedure was the same as for the above 39 sets of experiments.

In addition, viabilities of homozygotes for the standard and *In(2L)t* chromosomes were examined simultaneously with four replicates to estimate the average degree of dominance for viability polygenes. Using these homozygous viabilities and those of the corresponding heterozygotes in the partial diallel experiment, the average degree of dominance for viability polygenes in the equilibrium population was estimated using the notation of Wright (1931). Expressing the viabilities of *AA*, *Aa* and *aa* as *1*, *1-hs* and *1-s*, the $\bar{h}$ value in the equilibrium population ($\bar{h}_E$) is estimated as follows (Mukai & Yamaguchi, 1974):

$$\bar{h}_E = \frac{\operatorname{cov}(X, Y)}{V(X)} \tag{1}$$

where Y stands for the viability of heterozygote ($+_i/+_j$) and X is the sum of the viabilities of the corresponding homozygotes ($+_i/+_i$ and $+_j/+_j$), $\operatorname{cov}(X, Y)$ is the covariance of X and Y, and $V(X)$ is the variance of X. For this experiment, 236 heterozygote crosses in the partial diallel crosses with the 1977 sample were employed. The homozygous viabilities of the constituent chromosomes of the above crosses had been larger than 0·6 of the average heterozygote viabilities in the preliminary test. Thus the chromosome carrying major genic semi-lethals were excluded from the present estimation.

Every experiment was accomplished within one year after the capture of flies. The flies were kept at 18 °C, and the experiments were conducted in the laboratory at 25 °C.

Although there was a slight difference in viability between the reciprocal crosses as described below, these were used as simultaneous replications in the present analysis. The total sum of squares in each experiment was partitioned into rows, columns, row × column interaction, and error. Considering the incomplete dominance of the *Cy* chromosome, the additive genetic variance (σ_A^2) and the dominance variance (σ_D^2) on a chromosome basis are related to σ_R^2, σ_C^2 and $\sigma_{R \times C}^2$ as follows (Mukai *et al.* 1974), where σ_R^2, σ_C^2 and $\sigma_{R \times C}^2$ are row, column and row × column components of genetic variance, respectively:

$$\sigma_A^2 \cong 4(\sigma_R^2 + \sigma_C^2 - \tfrac{1}{2}\sigma_{R \times C}^2) \tag{2}$$
$$\sigma_D^2 \cong \sigma_{R \times C}^2$$

σ_R^2, σ_C^2, and $\sigma_{R \times C}^2$ can be estimated from the mean squares and the expected mean squares shown below (Table 2).

Thus, we can estimate σ_A^2 and σ_D^2 for each experiment. Since we did experiments using 19 groups of the standard chromosomes, we were able to obtain 19 sets of estimates for σ_A^2 and σ_D^2 for the standard chromosome group. Since these estimates are independent, we estimated the pooled σ_A^2 and σ_D^2 and their standard errors. The same analyses were carried out for the experiments using only the *In(2L)t* chromosomes and for those using both types of chromosomes.

3. RESULTS AND ANALYSIS

In the beginning, the following point should be stressed. The subject of the present experiment is genetic variability of viability in natural populations. Therefore, in addition to viability, only the pleiotropic effects of viability genes on other fitness components should be considered in connection with the mechanism of maintenance of genetic variability of viability. The genes affecting only fitness components other than viability are irrelevant in the present paper.

Table 2. *A typical analysis of variance for a 7×7 partial diallel cross*

Source	d.f.	Sum of square	Mean square	F	EMS
Row	6	0·82509	0·13755	6·78**	$\sigma_e^2 + 4\sigma_{R \times C}^2 + 28\sigma_R^2$
Column	6	0·24392	0·04065	2·00	$\sigma_e^2 + 4\sigma_{R \times C}^2 + 28\sigma_C^2$
Row × column	36	0·73004	0·02028	1·26	$\sigma_e^2 + 4\sigma_{R \times C}^2$
Error	147	2·36958	0·01612		σ_e^2
Total	195	4·16864			

** Highly significant ($P < 0.01$).

The difference between reciprocal crosses in viability in each cell of the experiment was tested with the analysis of variance. The results are as follows:

Standard chromosome crosses $F_{910,1820} = 1.377$ ($P < 0.01$)

$In(2L)t$-carrying chromosome crosses $F_{945,1890} = 1.177$ ($P < 0.01$)

Standard-$In(2L)t$ crosses $F_{196,392} = 1.286$ ($P < 0.05$)

When significant differences between reciprocal crosses exist, it is necessary to use the quadratic analysis of reciprocal crosses in analysing the diallel experiment (Cockerham & Weir, 1977). However, as shown in the discussion, the error caused by disregarding them is negligible. Therefore, the reciprocal crosses with two simultaneous replications in each cell in the partial diallel cross experiment were used as four replicates for simplicity. Analysis of variance was applied to each diallel cross experiment, and a typical analysis of variance is shown in Table 2. Using Equation (2), the additive and dominance variances were estimated for each experiment. The estimates pooled over each karyotype group are shown in Table 3 with their 95 % confidence intervals assuming a t-distribution. Since there are no significant differences among the standard chromosome group, the $In(2L)t$ carrying chromosome group and the standard × $In(2L)t$ group, the estimates of the three groups were pooled. The results were: $\hat{\sigma}_A^2 = 0.01754 \pm 0.00608$ and $\hat{\sigma}_D^2 = 0.00151 \pm 0.00114$, and are also shown in Table 3. The pooled values are regarded as the representative values of the population in the following discussion.

The average degrees of dominance ($\bar{h}_E$) were estimated using the method described above. The numbers of heterozygote crosses were 124 and 112 for the standard chromosomes and the $In(2L)t$ chromosomes, respectively. Only the chromosomes with homozygous viability indices larger than 0·6 were chosen as the object of the investigation. In this way, the effects of major genic semi-lethals, whose h values are much smaller than those of viability polygenes, can be excluded. The estimates for the standard chromosomes and the $In(2L)t$ chromo-

somes are $0\cdot254\pm0\cdot111$ and $0\cdot186\pm0\cdot101$, respectively. These two estimates are significantly larger than 0 and also much larger than that of recessive lethals (cf. Mukai & Yamaguchi, 1974). Furthermore, the non-significant difference between these two estimates justifies the pooling of the genetic variance components of these different karyotype groups described above.

Mukai (1980) has shown that these estimates are underestimates, since the Cy chromosomes are not completely dominant over the homologous wild-type chromosomes with respect to viability. It appears that the actual $\bar{h}_E$ value is larger than $0\cdot3$ and close to additivity (cf. Mukai & Yamaguchi, 1974; Mukai & Nagano, 1983).

Table 3. *The additive and dominance variances with their 95 % confidence intervals of the second chromosomes of* Drosophila melanogaster *sampled from the Ishigakijima population*

Cross type	Additive variance	Dominance variance
Standard × Standard'	$0\cdot02245\pm0\cdot01193$	$0\cdot00226\pm0\cdot00236$
Standard × In(2L)t	$0\cdot02267\pm0\cdot01144$	$0\cdot00121\pm0\cdot00351$
In(2L)t × In(2L)t'	$0\cdot01185\pm0\cdot00675$	$0\cdot00085\pm0\cdot00109$
Pooled	$0\cdot01754\pm0\cdot00608$	$0\cdot00151\pm0\cdot00114$

In this table, ' is used to indicate the different chromosome of the same karyotype.

4. DISCUSSION

(i) *Excess additive variance*

We observed that the additive genetic variance of viability is much larger than its dominance variance in the Ishigakijima population of *Drosophila melanogaster*. From this result it can be deduced that viability polygenes are partially recessive at the locus level and that the epistatic variance (after the log transformation) is small compared to the additive genetic variance (see Mukai *et al.* 1974). Now we will inquire into this model in detail. We assume only two alleles, A and a at each locus for simplicity, and use the viability model (cf. Wright, 1931) described above. Under the mutation–selection balance hypothesis, the equilibrium gene frequency of the allele a (q) is approximately expressed as $q \cong u/chs$, where u and chs are the mutation rate from allele A to allele a and the reduction of the fitness of heterozygote Aa, respectively (Mukai *et al.* 1974). Thus, the ratio of the additive genetic variance (σ_A^2) to the inbreeding depression (or homozygous load relative to the average viability of random heterozygotes) at the chromosomal level [$L_{I(R)}$] can be expressed as:

$$\sigma_A^2/L_{I(R)} \cong 2E[ush/c]/E[u(1-2h)/c] = 2E(sh)/[E(1/h)-2], \qquad (3)$$

where the expectations are taken all over the relevant loci and no correlation between u/c and sh is assumed. For the parameters in Equation (3) other than σ_A^2, the following estimates have been reported:

$$L_{I(R)} \cong 0\cdot24 \quad \text{(Mukai } et\ al. \text{ 1980)},$$
$$E[sh] \cong 0\cdot015 \quad \text{and} \quad E[1/h] \cong 3\cdot7 \quad \text{(Mukai, 1969)}.$$

8

Using these estimates and $\hat{\sigma}_A^2$ obtained, the left and the right sides of Equation (3) can be calculated as follows:

$$\frac{\sigma_A^2}{L_{I(R)}} = \frac{0.018}{0.24} = 0.075 \quad \text{and} \quad \frac{2E[sh]}{E[1/h]-2} = 0.018.$$

The estimate of the left side of Equation (3) is much larger than that of the right side. This discrepancy cannot be due to the inflation of σ_A^2 by random genetic drift since the expected departure of σ_A^2 from that of an infinite population was calculated to be negligible assuming the effective population number of this population to be 4500 (Yamaguchi *et al.* 1980). We cannot, therefore, explain the high value of $\hat{\sigma}_A^2$ as due only to the incompletely dominant mutants in genetic equilibrium. The same conclusion was reached for the Raleigh, N.C. (U.S.A.) population by Mukai *et al.* (1974).

Now we will examine the case where the gene frequencies in natural populations are not the values determined by fitness proportional to the observed viability. If $(1-2h)q$ is small compared with h, then,

$$\sigma_A^2 \cong nE[2pqh^2s^2] = 2n\{E[pq]E[h^2s^2] + \text{cov}[pq, h^2s^2]\}$$
$$L_{I(R)} = nE[pq(1-2h)s] = n\{E[pq]E[(1-2h)s] + \text{cov}[pq, (1-2h)s]\}.$$

Thus, the ratio becomes as follows:

$$\frac{\sigma_A^2}{L_{I(R)}} = \frac{2\{E[pq]E[h^2s^2] + \text{cov}[pq, h^2s^2]\}}{\{E[pq]E[(1-2h)s] + \text{cov}[pq, (1-2h)s]\}}.$$

As this ratio is insensitive to a change in pq, its excess may be attributed to the covariance terms. In the equilibrium population with incomplete dominance, $\text{cov}[pq, h^2s^2]$ is negative. Therefore, the excess means that the $\text{cov}[pq, h^2s^2]$ approaches 0 or even becomes positive. In this case it can be said that there is a trend such that hs is large for polymorphic loci. Such a situation can be expected in the following case: the viability changes in different environments in such a way that in one environment (for example, in our laboratory) one allele is superior and, in another environment, it becomes inferior. This type of selection is known as diversifying selection (Dobzhansky, 1970) and is able to maintain polymorphism of allele under certain conditions (Levene, 1953; Gillespie & Langley, 1974). This hypothesis accords well with biological intuition, since Ishigakijima island is located in the subtropics and it is highly probable that there are many niches for fruit flies.

It should be noted that the degrees of dominance (h) at the loci where diversifying selection is operating are close to 0.5. The reason is as follows. In a northern Japanese population (Aomori) of Drosophila, the additive genetic variance is approximately $\frac{1}{6}$ of the southern (Ishigakijima) population, but the homozygous load of the former relative to the average viability of the population is approximately equal to the latter (Aomori vs. Ishigakijima = 0.243:0.243), and the genetic variability of viability in this population can be explained by the mutation–selection balance (Mukai *et al.* 1982). If $h = 0.5$, the inbreeding depression becomes 0. Using this information, it is speculated that diversifying selection is not operating at many loci. If diversifying selection is working at many loci, the

gene frequencies at these loci must be increased. Thus, the contribution of these loci to the estimate of the average h_E using the regression method (Mukai & Yamaguchi, 1974) becomes large. Contrary to this expectation, the estimate of $\bar{h}_E$ for the present equilibrium population ($\bar{h}_E = 0.18$–0.26) is smaller than the estimate for newly arisen mutant viability polygenes ($\bar{h}_N = 0.43$), and the former is very close to the expected value under the mutation–selection balance ($\bar{h}_E = 0.17$–0.27) (Mukai, 1969). Under this model $\bar{h}_E$ is expected to be the harmonic mean of h_N values (Morton, Crow & Muller, 1956).

In the estimation of relative viability, the phenotypically wild-type homozygote and heterozygote flies compete only with phenotypically *Cy* flies at a frequency of 2/3. Using this property, Mukai *et al.* (1982) and Mukai, Kusakabe & Tachida (1983) examined the possibility of frequency-dependent selection for viability polygenes. Although the present experimental results can be explained by this type of selection for the additive and dominance variances if the average frequency of alleles (p_0) that are of the same types as those on the *Cy* chromosome is approximately 0.87 in the Ishigakijima population, this estimate ($\hat{p}_0$) is inconsistent with the average degree of dominance. The same findings were obtained in the other three populations analysed. Thus, it is concluded that frequency-dependent selection cannot explain the excess additive genetic variance.

(ii) *Viability and fitness*

In the previous section, we assume that the reduction in viability also causes the reduction in fitness. The assumption requires positive correlation between fitness and viability at the locus level. There have been some investigations of the correlation between these two characters (Marinkovic, 1967; Watanabe & Ohnishi, 1975; Simmons, Preston & Engels, 1980). When natural populations were analysed, the correlation between the two characters (in the first two studies, the two characters are viability and fertility) is very low and not significantly different from zero in every case. These findings appear to contradict our assumption. However, it should be pointed out that the measurements of these authors are carried out at the chromosome level. This does not always mean that viability and fitness at the genic level are not correlated. For example, if there is a major-genic mutation on a chromosome which affects only fertility, the correlation between viability and fitness will be greatly diminished at the chromosome level. This does not matter in our discussion as long as linkage equilibrium has been attained, since we are concerned only with the viability polygenes and selection occurring between the alleles at the same loci. It cannot be answered decisively at present whether this is the case or not, but there is strong suggestive evidence for the assumption of positive correlation between the two characters in question at the locus level.

Following the discussion of Greenberg & Crow (1960), we can reach the conclusion that the mutant viability polygenes must be selected out at the same rate as the lethal genes, which are known to be deleterious for both viability and fertility in heterozygous conditions. The reason is that the detrimental load to lethal load ratio of a typical equilibrium population, which is determined by the gene frequencies and their effects on viability, is approximately equal to that of

newly arisen mutations with respect to viability. A mildly deleterious gene (or a viability polygene) is known to be deleterious for viability in heterozygous conditions to the same degree as a lethal gene on average (Mukai & Yamazaki, 1968). If so, mildly deleterious genes should be deleterious for fertility in heterozygous conditions (Mukai, 1977; Mukai & Nagano, 1983). Furthermore, it has been pointed out from the calculation of homozygous load (Mukai *et al.* 1972; Mukai & Yamaguchi, 1974) that mutant viability polygenes should be eliminated by their deleterious effect on fertility as well as by their deleterious effect on viability in heterozygous conditions since the mutation rate of viability polygenes is very high (Mukai, 1964). These are not direct verifications of our assumption, but strongly support it. Furthermore, the same type of experiment as the present one using the northern population (the Aomori population) (Mukai *et al.* 1982) tells us that the additive genetic variance can be well explained by the positive correlation between the two characters in question. The reason is as follows. The additive genetic variance of that population is 0·00276, and the inbred load 0·243, from which the $[\sigma_A^2/L_{I(R)}]$ ratio (see the previous section) becomes 0·011, which is close to the expected value 0·018. Thus, the mutant viability polygenes also appear to be deleterious to fitness in these cases. The present result shows that the $[\sigma_A^2/L_{I(R)}]$ value is much larger than that expected from the incomplete dominance of mutant genes in the Ishigakijima population. However, we do not think that this is caused by the absence of the correlation between fitness and viability at the genic level. On the contrary, we think that fitness and viability are essentially correlated at the genic level, but through the change in environmental conditions, the viability in the laboratory is not always the same as that in nature. That is to say, diversifying selection is going on in nature, and it may be considered that the laboratory condition is one aspect of variable environmental conditions in nature. The fact that there are some populations (e.g. the Aomori population) in which the variation can be well explained by the positive correlation of the two characters seems to support the positive correlation hypothesis.

(iii) *Reciprocal crosses*

As described in the results, there were significant differences in viability between the reciprocal crosses, but in the analysis of variance we disregarded these differences. It is therefore necessary to evaluate briefly the error caused by this approach.

Let r be half the reciprocal difference. In this notation, the viability of an offspring of one cross and that of its reciprocal cross can be expressed as $g + r + e_i$ and $g - r + e_j$, where g and e's are the genotypic value and error terms, respectively. With this model, the expected mean square for error in the two-way analysis of variance used above becomes $\sigma_e^2 + \frac{4}{3}r^2$, while the other expected mean squares are not changed from those in Table 2. Thus, only $\sigma_{R \times C}^2$ [dominance variance, see (2)] is underestimated by $\frac{1}{3}r^2$ and both σ_R^2 and σ_C^2 are estimated correctly; $\frac{1}{3}r^2$ can be estimated using the value of standard chromosome crosses, where the largest F-value ($F = 1·38$) was found, as follows. The expected F-ratio of reciprocal crosses is calculated to be $(\sigma_e^2 + 4r^2)/\sigma_e^2$ and the estimate for σ_e^2 of the crosses is 0·020.

Therefore, $\frac{1}{3}r^2$ is estimated to be 0·00063 (= 0·38 × 0·020/12). Using this correction, we obtain 0·00289 as an estimate for the dominance variance. The decrease in the additive genetic variance caused by this correction is $2 \times 0.00063 = 0.00126$ [see (1)]. Thus, the effects of reciprocal differences can be said to be negligible and the conclusion obtained in the previous section need not be changed.

(iv) *Hybrid dysgenesis*

There is a possibility that the excess additive genetic variance is due to hybrid dysgenesis induced on wild-type chromosomes (P or Q type) in the cytoplasm of the *Cy/Pm* stock (M-type) (cf. Kidwell, Kidwell & Sved, 1977; Cardellino & Mukai, 1975; Yamaguchi & Mukai, 1974; Kidwell, 1979). However, it was found that the effects of newly induced mutations in and after the process of establishment of chromosome lines are negligible, since the means and mean squares in the analysis of variances in the different sets of experiments did not decrease or increase following the advance of experiments. Some of the reasons for this phenomenon are (1) that the chromosome lines after their establishment were maintained at 18 °C, at which mutation rate is low; and (2) that natural selection appears to have eliminated mutations easily from the lines. However, the effects of mutations induced in the second generation in the isolation of the chromosomes were confounded with the genetic variance in the population, since only a single male ($Cy/+$ or $Pm/+$) was used in each line in that generation.

(v) *Conclusion*

It may be said in conclusion that some type of balancing selection is operating at some fraction of the polygenic loci affecting viability in the Ishigakijima population, although the genetic variation is maintained by mutation–selection balance at the majority of such loci (cf. Mukai & Yamaguchi, 1974). Since overdominance has been clearly ruled out in the present experiment, the other two kinds of balancing selection – frequency-dependent selection and diversifying selection – are candidates for the maintenance mechanism of the excess variability. However, the possibility of frequency-dependent selection may be very low as described above, and diversifying selection is most probably responsible for the excess of the additive genetic variance.

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