THE GENETIC STRUCTURE OF NATURAL POPULATIONS OF *DROSOPHILA MELANOGASTER*. X. DEVELOPMENTAL TIME AND VIABILITY¹

TERUMI MUKAI AND TSUNEYUKI YAMAZAKI

*Department of Genetics, North Carolina State University, Raleigh, North Carolina,
and National Institute of Genetics, Mishima, Japan*

Received May 13, 1971

IT is well known that a large amount of genetic variability with respect to fitness is maintained in equilibrium random mating populations, but the mechanism whereby this is maintained has not yet been completely clarified. This is partially due to the difficulty in the estimation of the fitness itself. Many investigators have assumed, as a first approximation, that the viability of individuals is the only component of fitness which varies, other components of fitness being constant (e.g. MORTON, CROW and MULLER 1956; WALLACE 1959; COCKERHAM and RAWLINGS 1967).

Developmental time is definitely an important component of fitness especially in populations with continuous generations. DOBZHANSKY, HOLZ and SPASSKY (1942) estimated the developmental time (from egg to adult) of homozygotes and heterozygotes with respect to the second and the fourth chromosomes of *Drosophila pseudoobscura*, and found (1) that there is variation in this parameter in natural populations and (2) that there is a slight negative correlation between viability and developmental time in the homozygous condition. Significant negative correlations ($r = -0.32$ for the second chromosomes, and -0.26 for the fourth chromosomes) were calculated by BONNIER and JONSSON (1957) using the data of DOBZHANSKY, HOLZ and SPASSKY (1942). BONNIER and JONSSON (1957) also obtained a negative correlation (-0.66 — -0.33) between developmental time and viability, using 21 wild-type strains of *D. melanogaster* of which 18 had previously been irradiated. The negative correlation between viability and *developmental time* means that more viable flies emerge earlier than less viable flies.

HIRAIZUMI (1961) reported that in *D. melanogaster* there was a positive correlation between *developmental rate* (inversely proportional to developmental time) and female fertility when the rate of development was slower than a certain level, but a negative correlation when it was faster than that level. He also attempted to relate this finding to the mechanism whereby genetic variability in fitness is maintained in natural populations.

¹ Paper number 3470 of the Journal Series of the North Carolina State University Agricultural Experiment Station, Raleigh, North Carolina, and Contribution number 825 from the National Institute of Genetics, Japan. This work was supported by Public Health Service Research Grants GM-07836 and GM-11546. The computing was supported by Public Health Service Grant FR-00011.

Using *Tribolium castaneum* and *T. confusum*, DAWSON (1966, 1967) examined the relationship between competitive ability and developmental time. He found that lines selected for faster or slower development from random mating populations manifested less competitive ability than did unselected lines, although an exceptional case appeared in later generations in selection for faster development in *T. castaneum*. DAWSON (1966) has attempted to explain the above phenomenon on the basis of genetic homeostasis (LERNER 1954): The effects of genes controlling developmental time are approximately additive, but these genes were probably pleiotropically overdominant with respect to fitness. The developmental rate is therefore maintained at an intermediate level in random mating populations, and significant genetic gains can be obtained in artificial selection for this character.

We have accumulated spontaneous mutant polygenes affecting viability in the second chromosome of *D. melanogaster*, and have estimated the occurrence rate of mutant polygenes controlling viability and the degrees of their dominance and epistasis (MUKAI 1964, 1969a,b; MUKAI and YAMAZAKI 1964, 1968). On the basis of these genetic parameters and assuming that *there is a variation only in viability among individuals with respect to fitness*, an attempt was made to predict the state of genetic equilibrium in random mating populations. These predictions seem to be consistent with the actually observed (MUKAI and MARUYAMA 1971). However, it is necessary to examine one of the basic assumptions that the viability is the same as (or proportional to) fitness. The genotypic correlations between viability and developmental time were therefore estimated for both homozygotes and heterozygotes with respect to newly arisen mutations, the same experimental data as for the estimation of the change in viability (MUKAI 1964 and later) being employed. The approximate mutation rates of polygenes affecting developmental time and their average degree of dominance were estimated to obtain supplementary information.

MATERIALS AND METHODS

Materials: Spontaneous mutations were accumulated under minimum pressure of natural selection in 104 second chromosomes derived from a single, presumably well co-adapted, normal chromosome of W160S ($+_0$). The experimental procedure has been fully described in previous papers of this series (MUKAI 1964, MUKAI, CHIGUSA and YOSHIKAWA 1964, 1965). The chromosome in Line i is designated as $+_i$ ($i = 1, 2, \dots, 104$).

Experimental procedure: In order to estimate the mutation rates and degree of dominance and epistasis of polygenic mutations affecting viability, the homozygous viabilities of these chromosome lines as well as the heterozygous viabilities of coupling heterozygotes ($+_0/+_i$) and random heterozygotes ($+_i/+_j$) were tested in several generations (MUKAI, CHIGUSA and YOSHIKAWA 1964, 1965; MUKAI and YAMAZAKI 1964, 1968). In the estimation of viabilities, the *Cy* method of WALLACE (1956) was employed. For homozygotes, crosses were made between five $SM1(Cy)/+_i$ males and five $SM1(Cy)/+_i$ females per vial. For random heterozygotes, five $SM1(Cy)/+_i$ males and five $SM1(Cy)/+_j$ females were crossed in one vial. For the coupling heterozygotes, crosses were made between seven $+_0/+_0$ females and five $SM1(Cy)/+_i$ males per vial. $SM1(Cy)$ stands for the Second Multiple Inversion 1 with the dominant gene Curly (*Cy*). Several simultaneous replicates were carried out in all cases. Four days after the crosses were made, all flies in the vials were transferred to second vials, and five days after this

transfer all flies were eliminated from the vials. In the first three cases, phenotypically *Cy* and wild-type flies are expected to segregate with a ratio of 2 to 1. In the last case, the expected segregation ratio is 1 to 1. As described in previous papers (MUKAI 1964 and others), the viabilities of homozygotes and heterozygotes were expressed as a percentage of wild-type flies.

The number of flies in each vial was counted on the 10th, 12th, 14th, 16th, and 19th day after crosses (or transfers) were made. The results of pairs of vials (1st and 2nd) were pooled and considered as a single observation. Average developmental times were calculated for the *Cy* and wild-type flies in each observation. The difference (the average of wild-type flies—the average of the *Cy* flies) was used as an index of developmental time.

Analysis: Phenotypic and genotypic correlations between viability and developmental time were estimated. One-way analyses of variance and covariance were performed, and genotypic and phenotypic variances, and genotypic and phenotypic covariances were estimated. Using these statistics, the phenotypic and genotypic correlations were estimated. The phenotypic correlation was estimated on the basis of means of pairs of vials (*not* on the basis of single individuals). The sampling standard errors of the estimated genotypic correlations were calculated using the method described by TALLIS (1959).

In order to obtain additional information as to the relationship between viability and developmental time, the mutation rate of polygenes affecting developmental time was estimated using the method for estimating the rate of polygenic viability mutations described by MUKAI (1964). Under the assumptions that mutations are distributed on chromosomes according to a Poisson distribution and that effects at different loci are additive, the following formulae can be obtained:

$$A^2/B \leq p \quad (1)$$

$$\bar{s} \leq B/A \quad (2)$$

$$0 \leq \sigma_s^2 \leq B^2/(4A^2) \quad (3)$$

where s is the effect of a single mutation with mean $\bar{s}$ and variance σ_s^2 and p indicates the average number of mutations in the chromosomes. A stands for the change of mean developmental time and B is the increase of genotypic variance at the level of chromosomes or individuals. A and B are directly estimated from the experimental data.

The average degree of dominance of mutant polygenes affecting developmental time (h) can be estimated when there is no epistasis among loci, using the following formula (MUKAI and YAMAZAKI 1968):

$$h \doteq \frac{\text{Cov}(\text{Het and Homo})}{V(\text{Homo})} \quad (4)$$

where $\text{Cov}(\text{Het and Homo})$ stands for the genotypic covariance between heterozygote developmental time and the sum of the values of corresponding homozygotes, and $V(\text{Homo})$ indicates the genotypic variance of the sum of the homozygous values. This method could be applied only to repulsion heterozygotes which approximately satisfy the above condition.

An attempt is made to estimate the approximate average degree of dominance of mutant polygenes affecting developmental time in the *Cy* heterozygotes (*Cy*/+_{*i*}). The following mathematical model may be set up for the average of the absolute developmental time of homozygous individuals (+_{*i*}/+_{*i*}) and that of *Cy* heterozygous individuals (*Cy*/+_{*i*}) in the same vial. The former is described as X_{ij} and the latter is Y_{ij} where i stands for line number and j for replicate number within a line.

$$X_{ij} = \mu_1 + G_i + C_i + e_{1ij} \quad (5)$$

$$Y_{ij} = \mu_2 + kG_i + C_i + e_{2ij} \quad (6)$$

where μ_1 and μ_2 are the means for the homozygotes and heterozygotes over all lines, respectively; G_i is the homozygous genetic effect of mutant polygenes; k is the degree of dominance of these mutant polygenes in the *Cy* heterozygotes of mutant polygenes (it is assumed as a first approximation that k is constant over different mutant polygenes); C_i is the effect due to common environmental conditions (condition of the culture of the previous generation, effects of other

chromosomes, etc.), and e_{1ij} and e_{2ij} are the errors of homozygotes and heterozygotes, respectively. The ordinary assumptions of analysis of variance are made.

Furthermore, the following parameters are defined, assuming G_i and C_i are not correlated:

$\sigma_{G'C}^2$ = the sum of the variance of kG_i and the variance of C_i . This estimate is referred to as D .

σ_{GC}^2 = the sum of the variance of G_i and the variance of C_i . The estimate is referred to as E .

$\sigma_{G'C,GC}$ = the covariance between $(kG_i + C_i)$ and $(G_i + C_i)$. The estimate is referred to as F .

Using the above parameters, the following formulae may be obtained:

$$\sigma_{G'C}^2 = k^2\sigma_G^2 + \sigma_C^2 \quad (7)$$

$$\sigma_{GC}^2 = \sigma_G^2 + \sigma_C^2 \quad (8)$$

$$\sigma_{G'C,GC} = k\sigma_G^2 + \sigma_C^2 \quad (9)$$

$\sigma_{G'C}^2$ and σ_{GC}^2 may be estimated as D and E , respectively, by the analysis of variance and $\sigma_{G'C,GC}$ may be estimated as F using the following relationship:

$$\sigma_{DT}^2 = \sigma_{G'C}^2 + \sigma_{GC}^2 - 2\sigma_{G'C,GC} \quad (10)$$

where σ_{DT}^2 is the genotypic variance in developmental time indices among different homozygotes, which may be estimated by the analysis of variance (see Table 1).

From formulae (7), (8), (9) and (10), the following estimating formulae can be obtained:

$$k = \frac{D-F}{F-E} \quad (11)$$

$$\hat{\sigma}_G^2 = \frac{\hat{\sigma}_{DT}^2}{(1-k)^2} \quad (12)$$

$$\hat{\sigma}_C^2 = \hat{\sigma}_{GC}^2 - \hat{\sigma}_G^2 \quad (13)$$

RESULTS AND ANALYSES

Basic results: We have estimated homozygote viabilities with or without heterozygote viabilities in several generations from generation 10 through generation 80, but only the data obtained in generation 32 and generation 60 (in which flies were counted regularly) were available for the analysis with respect to developmental time. In generation 32, data were obtained for homozygotes, coupling heterozygotes and repulsion heterozygotes, while in generation 60 data were obtained for homozygotes and coupling heterozygotes only.

Genotypic variances of developmental time and genotypic covariances between developmental time and viability were estimated. The results are presented in Table 1 together with the mean developmental times and other necessary information. Estimates of viabilities, which have been reported previously (MUKAI 1964; MUKAI and YAMAZAKI 1968), are also presented in this table.

Table 1 illustrates the following: The average developmental times of homozygotes became longer as mutations were accumulated, but those of coupling heterozygotes became shorter. This tendency is presented in Figure 1A (for homozygotes) and Figure 1B (for coupling heterozygotes). The results obtained from repulsion heterozygotes are shown together with those obtained from homozygotes. These findings are very similar to those found when viability was examined (cf. Figures 2 and 3 of MUKAI and YAMAZAKI 1968). This strongly

TABLE 1

Basic statistics and genetic parameters with respect to viability and developmental time

	Homozygote		Random heterozygote	Coupling heterozygote	
	Generation 32	Generation 60	Generation 32	Generation 32	Generation 60
Number of crosses	80	77	77	80	77
Number of observations	8	4	8	8	6
Mean					
(1) Viability	28.04	16.48	29.56	51.51	52.28
(2) Developmental time	0.487	0.958	0.435	-0.076	-0.164
Genotypic variance					
(1) Viability	5.6435	66.2132	8.2849	0.7876	2.0293
(2) Developmental time	0.042983	0.171260	0.064146	0.00179874	0.00162994
Covariance between viability and developmental time					
(1) Genotypic	-0.3634	-3.2850	-0.6497	-0.013140	-0.039413
(2) Error	-0.03049	-0.1789	-0.02142	0.088490	0.016091
Genotypic correlation between viability and developmental time	-0.738	-0.922	-0.912	-0.349	-0.685
Phenotypic correlation*	± 0.0729	± 0.0429	± 0.0355	± 0.3588	± 0.3271
between viability and developmental time	-0.331	-0.605	-0.473	0.130	-0.049

* On the basis of means of pairs of vials (not individual basis).

suggests that there is a high correlation between developmental time and viability.

Correlation between developmental time and viability: Phenotypic and genotypic correlations between developmental time and viability were calculated; these results are presented in Table 1. All genotypic correlations were negative and significantly less than zero except for the coupling heterozygotes in generation 32. The phenotypic correlations were calculated on a single observation basis.

In order to examine negative correlations in detail, the following analysis was conducted for each of the homozygotes, coupling heterozygotes, and repulsion heterozygotes.

(1) *Homozygotes:* The control viabilities [the viability of the original homozygotes (+_o/+_o)] have been estimated to be 32.84 in generation 32, and 32.42 in generation 60 (MUKAI and YAMAZAKI 1968). The homozygotes' viability index for each line in generations 32 and 60 was standardized by taking the difference between the original viability index (or the control) and the estimated viability index; i.e., the new index is the magnitude of *reduction* of viability due to mutations. After standardization, the results obtained from the two generations were pooled and analyzed. Thus, we have 157 lines (neglecting some correlations among them). These lines were divided into 10 groups according to the order of their viabilities. Each of the first three groups includes 15 lines and any of the remaining 7 groups consists of 16 lines. The average indices of viability and

FIGURE 1.—Distribution of developmental times. A: Homozygotes in generations 32 and 60 and random heterozygotes in generation 32. B: Coupling heterozygotes in generations 32 and 60. Index of developmental time = Average developmental time (days) of homozygotes or heterozygotes minus average developmental time (days) of *Cy* heterozygotes in the same vials.

TABLE 2

The relationship between viability reduction and developmental time

Class	Homozygote†		Repulsion§		Heterozygote	
	Viability*	Developmental time†	Viability*	Developmental time†	Viability*	Developmental time†
1	0.07	0.09	2.61	0.50	—5.20	—0.16
2	2.34	0.31	3.97	0.53	—4.57	—0.17
3	3.76	0.54	4.81	0.58	—4.05	—0.19
4	4.92	0.56	6.56	0.59	—3.61	—0.13
5	6.08	0.54	—	—	—2.97	—0.13
6	7.75	0.64	—	—	—2.43	—0.10
7	12.33	0.86	—	—	—1.96	—0.10
8	17.38	1.03	—	—	—1.49	—0.10
9	21.10	1.13	—	—	—0.77	—0.08
10	25.33	1.41	—	—	+0.47	—0.05

* Viability index = Control — class average (percent index).

† Developmental time index = class average of the indices (difference from the average of *Cy* heterozygotes).

‡ Results pooled over generations 32 and 60 after standardization.

§ Result of generation 32 only.

developmental time in each group were calculated. The result is shown in Table 2 and in Figure 2. From this figure, it can be seen that there is a very close correlation between reduction of the viability index and developmental time. Indeed, the calculated correlation coefficient for these 10 pairs is 0.98.

(2) *Repulsion heterozygotes*: In random heterozygotes, if one of the homologous chromosomes carries no new mutation, the heterozygote is a coupling

FIGURE 2.—The relationships between viability reductions due to mutations and developmental times in homozygotes pooled over generations 32 and 60 after standardization, and in repulsion heterozygotes in generation 32.

heterozygote. The random heterozygotes in which both homologous chromosomes carry new different mutations have been called *repulsion heterozygotes* (MUKAI and YAMAZAKI 1968). These two types of random heterozygotes could nearly always be identified since the coupling heterozygotes showed overdominance in viability and also in developmental time (see Table 1 and Figure 1B), while the repulsion heterozygotes did not. [The average degrees of dominance (h values in the Wrightian fitness model) of mutant polygenes affecting viability and developmental time are about 0.4, see below.] The correlation between the viability of random heterozygotes and the sum of viabilities of corresponding homozygotes in generation 32 has been reported in Figure 6 of MUKAI and YAMAZAKI (1968). A very similar figure was obtained when developmental time was considered. On the basis of the distribution pattern in this figure, it was determined that 63 of the crosses resulted in repulsion heterozygotes. In order to compare the repulsion heterozygotes with homozygotes, the viabilities were standardized by taking the difference between the original viability index (or the control viability) and the estimated viability of individual heterozygotes. The 63 crosses were divided into 4 groups according to the magnitude of their viability indices. The first group consists of 15 crosses and the remaining groups each include 16 crosses. The average indices of viability and developmental time in each group were calculated. This result is presented in Table 2 and in Figure 2. From this figure, it can be seen that there is a good correlation between the reduction of viability indices and developmental time ($r = 0.94$ for the above 4 pairs). Furthermore, the line of heterozygotes overlaps that of homozygotes. Therefore, if the viabilities of homozygotes and repulsion heterozygotes are the same, their developmental times are almost the same, at least in a highly homozygous genetic background.

(3) *Coupling heterozygotes*: The expected viability of coupling heterozygotes is 50.0. The control viabilities have been estimated to be 49.91 in generation 32 and 48.62 in generation 60. As in the cases of homozygotes and repulsion heterozygotes, the viability indices of all lines in generations 32 and 60 were standardized as described above. The same analysis as that for homozygotes was carried out, pooling the results of the two generations. There were 10 groups, each consisting of 15 or 16 lines. The result is presented in Table 2 and Figure 3. There is in general a strong correlation between the decrement of viability indices and developmental time ($r = 0.94$ for the above 10 pairs). It seems at face value that the developmental time becomes shorter and shorter as the viability increases until group 8 (class 3 in Table 2), but after that it becomes longer with an increase in viability. In order to examine whether or not this tendency is statistically significant, the mean developmental time of groups 9 and 10 (classes 1 and 2 in Table 2) was compared with that of group 8. There was no significant difference between these groups ($t_{df=43} = 0.29$, $0.50 < P$). The present data does not, therefore, indicate that developmental time increases if the viability is above a certain point.

In conclusion, it can be said that there is a strong negative correlation between viability and developmental time in homozygotes, coupling heterozygotes, and repulsion heterozygotes.

FIGURE 3.—The relationship between viability reductions due to mutations and developmental times in coupling heterozygotes.

Estimation of the rate of polygenic mutations affecting developmental time: Formulae (1), (2) and (3) require additivity among loci. In the early generations, this requirement may be nearly satisfied. An approximate linear relationship was observed between the reduction of homozygote viabilities and generation number until generation 32. After that a synergistic interaction was observed (MUKAI 1969b). Only results obtained from homozygotes in generation 32 were therefore employed for the estimation of mutation rates.

A regression method was employed for the estimation of the developmental time of the original new-mutant-free homozygote in the environment of generation 32. A quadratic regression sufficiently expresses the relationship between viability and developmental time. This might indicate that either developmental time or viability violates the assumption of additivity in the estimation of mutation rates in generation 32. As this effect was probably very slight, some compromising was done. Using the above quadratic relationship, the developmental time of the original homozygotes (or control) whose homozygous viability has been estimated to be 32.84, was estimated to be 0.066.

$$\text{Thus, } A = 0.487 - 0.066 = 0.421$$

$$B = 0.04298$$

$$\hat{p} \geq \frac{A^2}{B} = 4.2980 \text{ or } 0.134 \text{ per generation}$$

$$\sigma_s^2 \leq \frac{B^2}{4A^2} = 0.002607$$

$$\bar{s} \leq \frac{0.04298}{0.4209} = 0.102$$

Note that the mutation rate is almost the same as that of mutant viability polygenes (0.14/2nd chromosome/generation, MUKAI 1964). The effect of single mutations is relatively small, the maximum delay per mutant in the homozygous conditions being about 2.5 hr.

Estimation of the average degree of dominance of mutant polygenes affecting developmental time: We used only the repulsion heterozygotes in random heterozygotes. Using the 63 repulsion heterozygotes and the corresponding homozygotes in generation 32, the genotypic covariance between the developmental times of repulsion heterozygotes and the sums of the values of homozygote constituents of the repulsion heterozygotes, and the genotypic variance of the sums of the values of the homozygote constituents of repulsion heterozygotes were estimated by an analysis of covariance and an analysis of variance, respectively. The estimated components of variance and covariance are presented in Table 3. The average degree of dominance can be estimated using formula (4). This gave a result of 0.35 ± 0.20 which is significantly larger than zero at the 5% level (one tail test) and very close to the average degree of dominance of viability mutant polygenes.

All the above estimates were obtained assuming in addition that the average k value ($\bar{k}$) is zero. This assumption was examined. The $\sigma_{g'g}^2$ and σ_{gg}^2 were estimated by the analysis of variance: $\hat{\sigma}_{g'g}^2 = 0.04340 \pm 0.00925$ and $\hat{\sigma}_{gg}^2 = 0.08797 \pm 0.01806$. From these values, $\hat{\sigma}_{DT}^2 = 0.04298 \pm 0.00142$, and formula (10), $\sigma_{g'g,gg}$ can be estimated to be 0.04420. Thus, k , σ_g^2 , and σ_c^2 can be estimated using formulae (11), (12), and (13). The results are:

$$\hat{k} = 0.0182$$

$$\hat{\sigma}_g^2 = 0.04458$$

$$\hat{\sigma}_c^2 = 0.04339$$

The average k value would be very small and of the order of the average degree

TABLE 3

Relationship between the developmental times of heterozygotes and the sums of the corresponding homozygotes

The genotypic variance of heterozygotes	0.00370 $\pm$ 0.00262
The genotypic variance of the sums of the corresponding homozygotes	0.01563 $\pm$ 0.00655
The genotypic covariance between the heterozygotes and the sums of the corresponding homozygotes	0.00544 $\pm$ 0.00300
The average degree of dominance ($\bar{k}$)	0.35 $\pm$ 0.20

of dominance of lethal genes (cf. YOSHIKAWA and MUKAI 1970). The above most important assumption in the present investigation is therefore at least approximately justified.

It should be noted here that the degree of dominance of mutant polygenes affecting developmental time is different due to the genetic background ($\bar{h} \doteq 0.35$ and $\bar{k} \doteq 0.018$) as in the case of viability (c.f. MUKAI and YAMAZAKI 1968; WALLACE and DOBZHANSKY 1962). This phenomenon should be tested in more detail together with the "coupling and repulsion" effect in future experiments.

DISCUSSION

Experimental and analytical methods: The female parents were allowed to lay eggs for four or five days. Thus, the eggs of the flies that emerged on the same day were not always laid on the same day. This difficulty in the estimation of developmental time can be removed by considering the difference between non-*Cy* and *Cy* flies [cf. formula (12)]. It can be shown mathematically that the developmental time index employed in the present analysis is the unbiased estimate if there is no aging effect in the segregation of + and *Cy* chromosomes in the formation of gametes, and if there is no variation in competitive effect due to the day of emergence.

In the present analysis, it has been assumed that the *Cy* chromosome when in the heterozygous condition completely suppresses the effect of mutant polygenes which occur in any wild normal chromosome. In the present experiment, this has been shown to be nearly true, as it is in the case of viability (WALLACE and DOBZHANSKY 1962). Although the k value was estimated to be very small, its effects on the various estimates obtained in the present investigation were considered.

In a single locus model, an effect of a mutant in a homozygous condition is s and the degree of dominance of the mutant over its wild-type allele is h in a homozygous genetic background. The changes in developmental time of mutant homozygotes and random heterozygotes from the control are $s(1-k)$ and $s(h-k/2)$. To the extent that h and k do not show an appreciable amount of genetic variation over different mutants, the genetic correlations between developmental time and viability estimated in the present investigation will be very close to the unbiased estimate. The same is true of the estimate of mutation rate, but the maximum estimate of the average effect of single mutations will be an underestimate by the factor of approximately $(1-\bar{k})$ where $\bar{k}$ is the average of k 's.

Note that the estimate of $\bar{h}$ (the average of h 's) is not appreciably affected by $\bar{k}$ if $\bar{h}$ is close to 0.5. The regression coefficient of the heterozygote developmental time on the sum of the corresponding homozygotes can be expressed as $(h-k/2)/(1-k)$ on a single locus basis. On an overall locus basis this regression coefficient was estimated to be 0.35. The ratio of the average change in the developmental times of repulsion heterozygotes to that in the sums of the corresponding homozygotes can be expressed as:

$$(1 - \bar{k}) / (2\bar{h} - \bar{k}) \quad (14)$$

Using the 63 repulsion heterozygotes, the former was estimated to be 0.484 (0.551 - 0.066), and the latter 0.480 (0.546 - 0.066). The ratio is about 1.0. Thus, from formula (5), $\bar{h} = 0.5$, which is close to the 0.35 estimated above, and $\bar{k}$ can take any value.

Developmental time and fitness: We have found that genotypic correlations between developmental time and viability were negative (all significant except in the case of coupling heterozygotes in generation 32). These results agree with those of DOBZHANSKY, HOLZ and SPASSKY (1942) and BONNIER and JONSSON (1957). The rate of polygenic mutations affecting developmental time was estimated to be approximately 0.13/2nd chromosome/generation. This is almost the same as that of polygenic mutations affecting viability (about 0.14/second chromosome/generation, MUKAI 1964). These two findings indicate that, in a homozygous genetic background, most of the differences in developmental times among homozygous lines or among heterozygous crosses are pleiotropically controlled by the mutant polygenes affecting viability.

We have found coupling-repulsion effects on viability (MUKAI and YAMAZAKI 1964, 1968). These effects are also manifested when developmental time is considered (Figure 1B). The developmental time in the coupling heterozygotes is shorter in generation 60 than in generation 32 (a tendency opposite to that found in homozygotes). On the other hand, the average degree of dominance is 0.35 in repulsion heterozygotes, so that there is approximate additivity within loci. This similarity is consistent with the pleiotropism hypothesis described above.

If such pleiotropy as the above also exists between viability and other fitness components (this probability is high; cf. TEMIN 1966), then we can expect that the magnitude of mutation load becomes much smaller than twice the sum of the respective mutation rates (cf. HALDANE 1937) even if mutation rates of polygenes affecting individual fitness components are high.

A tendency similar to that found by HIRAZUMI (1961) with respect to developmental rate and female fecundity was seen in the coupling heterozygotes of generation 60, but not significantly so. In Figure 3, the shortest developmental time was reached when the viability index was about 54. An analysis of a Raleigh, North Carolina population gave an average viability of random heterozygotes of about 46.0-47.0 (MUKAI, unpublished) and the frequency of individuals showing a viability index larger than 54.0 was very low (8.2% in 1969 and 2.6% in 1970). Thus, it appears that even if there is an optimal level of viability for the manifestation of the minimum developmental time, it is much beyond the population mean of viability and, accordingly, it may not be an effective means of maintaining genetic variability of fitness in random mating populations.

The present finding that developmental time is mainly controlled by a pleiotropic effect of viability polygenes agrees with an assumption of DAWSON (1966). However, another finding that the genetic parameters associated with the expression of these polygenes for both characters are quite similar, is inconsistent with his second assumption (these polygenes are overdominant with respect to fitness), if we consider that the viability is a main component of fitness. Furthermore, although the average degree of dominance of newly arisen mutant polygenes

affecting developmental time was estimated to be 0.35, the degree of dominance might become much smaller in equilibrium populations because of the action of natural selection as in the case of viability polygenes (MUKAI 1969c), or by the accumulation of modifiers. These two possibilities should be examined in future experiments. Thus, it may be difficult to apply DAWSON's hypothesis to *D. melanogaster* populations.

In conclusion, it may be said that the assumption usually made in studies of population dynamics that viability is proportional to the sum of fitness components is not seriously violated as far as developmental time is concerned.

The authors are grateful to Mrs. DIANNE CUTHBERTSON for her efficient help in processing the data, and to Dr. J. S. JONES for correcting the English.

SUMMARY

Using newly arisen polygenic mutations which were accumulated in co-isogenic normal second chromosomes, the relationship between developmental time and viability was examined using the data of generations 32 and 60. (cf. MUKAI and YAMAZAKI 1968). About 1.76 million individuals were counted and the following findings were obtained:—1. The minimum rate of polygenic mutations affecting developmental time was estimated to be 0.13/second chromosome/generation, which is very close to that of polygenic mutations controlling viability (0.14/second chromosome/generation). The average delay of developmental time due to a single polygenic mutation in a homozygous condition was about 2.5 hr at 25°C.—2. As in the case of viability, a coupling-repulsion effect was detected. In the coupling heterozygotes (in which mutant polygenes are located in only one of the originally identical normal homologous chromosomes), developmental time was shorter than with the control (or original) homozygotes, while in the repulsion heterozygotes (in which mutant polygenes are located in both of the originally identical homologous chromosomes), the average degree of dominance of mutant polygenes affecting developmental time was estimated to be 0.35 ± 0.20 . The average degree of dominance of mutant polygenes in the *Cy* heterozygotes ($\bar{k}$) was estimated to be approximately zero ($\bar{k} \doteq 0.018$). This degree of dominance is also the same as that found in examining viability polygenes.—3. There was a high negative genetic correlation between developmental time and viability for all homozygotes (-0.74 ± 0.073 in generation 32, and -0.92 ± 0.043 in generation 60), coupling heterozygotes (-0.35 ± 0.36 in generation 32, and -0.69 ± 0.33 in generation 60), and repulsion heterozygotes (-0.91 ± 0.036 in generation 32).—It appears, therefore, (1) that most of the change in developmental time due to polygenic mutations is controlled by pleiotropic effects of mutant viability polygenes and (2) that the assumption that viability is proportional to fitness is not seriously violated as far as developmental time is concerned.

LITERATURE CITED

- BONNIER, G. and U. B. JONSSON, 1957 Rate of development of viability mutants in *Drosophila melanogaster*. *Evolution* **11**: 271–279.

- COCKERHAM, C. C. and J. O. RAWLINGS, 1967 Apparent heterosis of a neutral gene with inbreeding. *Ciência e Cultura* **19**: 89-94.
- DOBZHANSKY, TH., A. M. HOLZ and B. SPASSKY, 1942 Genetics of natural populations. VIII. Concealed variability in the second and the fourth chromosomes of *Drosophila pseudoobscura* and its bearing on the problem of heterosis. *Genetics* **27**: 463-490.
- DAWSON, P. S., 1966 Developmental rate and competitive ability in *Tribolium*. *Evolution* **20**: 104-116. —, 1967 Developmental rate and competitive ability in *Tribolium*. II. Changes in competitive ability following further selection for developmental rate. *Evolution* **21**: 292-298.
- HALDANE, J. B. S., 1937 The effect of variation of fitness. *Am. Naturalist* **71**: 337-349.
- HIRAZUMI, Y., 1961 Negative correlation between rate of development and female fertility in *Drosophila melanogaster*. *Genetics* **46**: 615-624.
- LERNER, I. M., 1954 *Genetic homeostasis*. Oliver and Boyd, Edinburgh.
- MORTON, N. E., J. F. CROW and H. J. MULLER, 1956 An estimate of the mutational damage in man from data consanguineous marriages. *Proc. Natl. Acad. Sci. U. S.* **42**: 855-863.
- MUKAI, T., 1964 The genetic structure of natural populations of *Drosophila melanogaster*. I. Spontaneous mutation rate of polygenes controlling viability. *Genetics* **50**: 1-19. —, 1969a The genetic structure of natural populations of *Drosophila melanogaster*. VI. Further studies on the optimum heterozygosity hypothesis. *Genetics* **61**: 479-495. —, 1969b The genetic structure of natural populations of *Drosophila melanogaster*. VII. Synergistic interaction of spontaneous mutant polygenes controlling viability. *Genetics* **61**: 749-761. —, 1969c The genetic structure of natural populations of *Drosophila melanogaster*. VIII. Natural selection on the degree of dominance of viability polygenes. *Genetics* **63**: 467-478.
- MUKAI, T., S. CHIGUSA and I. YOSHIKAWA, 1964 The genetic structure of natural populations of *Drosophila melanogaster*. II. Overdominance of spontaneous mutant polygenes controlling viability in homozygous genetic background. *Genetics* **50**: 711-715. —, 1965 The genetic structure of natural populations of *Drosophila melanogaster*. III. Dominance effect of spontaneous mutant polygenes controlling viability in heterozygous genetic backgrounds. *Genetics* **52**: 493-501.
- MUKAI, T. and T. MARUYAMA, 1971 The genetic structure of natural populations of *Drosophila melanogaster*. IX. A prediction of genetic equilibrium. *Genetics* **68**: 105-126.
- MUKAI, T. and T. YAMAZAKI, 1964 Position effect of spontaneous mutant polygenes controlling viability in *Drosophila melanogaster*. *Proc. Japan Acad.* **40**: 840-845. —, 1968 The genetic structure of natural populations of *Drosophila melanogaster*. V. Coupling-repulsion effect of spontaneous mutant polygenes controlling viability. *Genetics* **59**: 513-539.
- TALLIS, G. M., 1959 Sampling errors of genetic correlation coefficients calculated from analyses of variance and covariance. *Australian J. Stat.* **1**: 35-43.
- TEMIN, R. G., 1966 Homozygous viability and fertility loads in *Drosophila melanogaster*. *Genetics* **53**: 27-46.
- WALLACE, B., 1956 Studies on irradiated populations of *Drosophila melanogaster*. *J. Genet.* **54**: 280-293. —, 1959 The role of heterozygosity in *Drosophila* populations. *Proc. Xth Intern. Congr. Genet.* **1**: 403-419.
- WALLACE, B. and TH. DOBZHANSKY, 1962 Experimental proof of balanced genetic loads in *Drosophila*. *Genetics* **47**: 1027-1042.
- YOSHIKAWA, I. and T. MUKAI, 1970 Heterozygous effects on viability of spontaneous lethal genes in *Drosophila melanogaster*. *Japan J. Genet.* **45**: 443-455.