IN spite of the fact that radiation-induced and spontaneous mildly deleterious mutant genes (or mutant viability polygenes) show overdominance in an otherwise homozygous genetic background (Wallace 1957, 1958, 1963; Burdick and Mukai 1958; Mukai, Chigusa and Yoshikawa 1964; Mukai, Yoshikawa and Sano 1966), the results of recent investigations have indicated that the manifestation of overdominance with respect to fitness (or viability) is rare in equilibrium populations of both Drosophila melanogaster (Greenberg and Crow 1960; Mukai and Yamazaki 1964, 1968; Temin 1966; Chigusa, Mukai and Mettler, in preparation) and Drosophila pseudoobscura (Wills 1966). This conclusion was reached from studies of the detrimental load to lethal load ratio (Greenberg and Crow 1960) and the correlation between heterozygote viabilities and the corresponding homozygote viabilities. Kimura and Crow (1964) reached the above conclusion theoretically, since the magnitude of the segregation load becomes very large if overdominance is common in equilibrium populations. However, the discovery of a large number of isozyme polymorphisms in Drosophila (Hubby and Lewontin 1966; Johnson et al. 1966; O'Brien and Macintyre 1969) has made investigators reconsider overdominance as a mechanism for maintaining genetic variability in populations. For example, Svéd, Reed and Bodmer (1967), King (1967), and Milkman (1967) have proposed genetic models in which the magnitude of genetic loads does not become extremely large even if overdominance exists. Unfortunately, these models were not set up on the basis of experimental data.

Mukai and his associates have accumulated spontaneous mutant viability polygenes in the second chromosomes of Drosophila melanogaster, and have estimated the frequency of occurrence of mutant viability polygenes and recessive lethal genes and also the degrees of dominance and epistasis. Applying these values in the present computer simulation study, both the existence of equilibrium in populations of D. melanogaster and the frequency of individuals revealing overdominance with respect to viability were predicted. The results are
discussed from the standpoint of genetic load and the mechanisms maintaining isozyme polymorphisms. The preliminary result of the present work has been published (Mukai 1968, 1969d).

SUMMARY OF THE EXPERIMENTAL RESULTS

For the sake of convenience, a summary of the experimental results previously reported will be given first. A single normal, presumably well coadapted second chromosome was taken from Dr. A. B. Burdick's W160S stock, which was extracted from an Erie, Pennsylvania population, and expanded into 104 independent chromosome lines by using the marked inversion technique. Spontaneous mutations were accumulated for many generations with as little selection as possible by the mating scheme of $SMI(Cy)/Pm$ (5 9 9) × $Pm/fi$ (one male), where $i$ indicates line number.

Firstly, the spontaneous mutation rate of viability polygenes was estimated (Mukai 1964): In generations 10, 15, 20, and 25, both the homozygous viability of each chromosome line and the genotypic variance among lines were estimated, omitting lines carrying recessive lethal and semilethal mutant genes. Using these statistics, the mutation rate (a kind of minimum estimate) was estimated to be 0.1411 per second chromosome per generation. Simultaneously, the recessive lethal mutation rate was estimated as 0.0063 per second chromosome per generation. Their ratio is 22.3. A similar experiment was conducted using three chromosomes extracted from a Madison, Wisconsin population (Mukai and Crow in preparation). The mutation rate of polygenes was estimated to be .161 and that of recessive lethals was 0.0060 per second chromosome per generation. Their ratio is 26.8.

Secondly, in generations 32, 52, 60, 78, and 85 in the first experiment (material from W160S), homozygous and heterozygous viabilities of the chromosomes of these lines (except for lethal and semilethal chromosomes) were tested, and the following results were obtained (Mukai and Yamazaki 1964, 1968; Mukai 1969a,b,c): These polygenes showed overdominance only when located in one of the originally identical normal second chromosomes (in the coupling phase) and when the number of mutant polygenes was small. However, when the number of mutant polygenes increased (when about ten mutant viability polygenes, on the average, had been accumulated), the viability of heterozygotes reached an optimum point and after that it began to decrease with the increase in the number of mutant polygenes. That is, overdominance and an optimum level of heterozygosity for the manifestation of overdominance were seen in the coupling phase. This phenomenon will be called the "coupling effect."

On the other hand, when the mutant polygenes were located heterozygously in both the originally identical normal second chromosomes (in the repulsion phase), they were not only deleterious, but their degree of dominance and its genetic variance were surprisingly high ($h = 0.43 \pm 0.008$ and $\sigma^2_h = 0.044 \pm 0.014$). By recombination tests using two different kinds of heterozygotes, these mutant polygenes were proven nonallelic. Furthermore, in repulsion heterozygotes quadratic synergistic interaction among mutant polygenes can be predicted not only on the basis of the same type of interaction discovered in homozygotes of generations 10, 15, 20, 25, 32, 52, and 60, but also from the linear relationship between homozygote and heterozygote viabilities (Mukai and Yamazaki 1964, 1968). In other words, in the repulsion phase, the average degree of dominance ($h$) of mutant polygenes is large, and there is a quadratic synergistic interaction among mutant polygenes. This phenomenon may be called the "repulsion effect." The evolutionary significance of synergistic interaction was discussed in Mukai (1969b).

ASSUMPTIONS AND METHODS

Assumptions: In the present simulation experiments, only the polygenic mutations were considered while lethals and semilethals were disregarded. The basic assumptions are: (1) Population size is infinite, and the number of loci where polygenic mutations take place is extremely large. Accordingly, the frequency of allelism of these mutant genes is effectively zero. (2)
Mutations occur on the chromosomes according to a Poisson distribution. (3) Selection is operating for viability only (or the viability is equal to the total fitness of an individual). (4) The fitness value of initial mutant-free individuals is 1.00. Specific assumptions are described for the eight experiments listed below.

Experiment A-1: (1) The mutation rate of polygenes controlling viability (which is expressed as \( M \) from now on) is 0.1411 per second chromosome per generation.

(2) The fitness values of coupling heterozygotes are determined by applying the least-squares method (assuming a cubic relationship between the number of heterozygous loci and the fitness value) to the data of Table 2 of Mukai (1969a). The following formula can be obtained:

\[
\tilde{W} = 1.0 + 0.002112X + 0.000328X^2 - 0.000170X^3
\]

(1)

where \( \tilde{W} \) is the predicted fitness and \( X \) is the number of heterozygous loci. This formula is employed for \( X = 1, \ldots, 12 \), since the predicted and observed values agree very well.

For values of \( X \) larger than 12, the following formula is applied:

\[
\tilde{W} = 1.1157 - 0.0005103X - 0.0002886X^2
\]

(2)

Formulae (1) and (2) show a fairly good continuity between \( X = 12 \) and \( X = 13 \). Using formula (2), \( \tilde{W} \) becomes negative if \( X \) is larger than 61. Thus it is assumed that \( \tilde{W} = 0 \) when \( X > 61 \), and formula (2) is employed for \( X = 13, \ldots, 61 \).

Formula (2) is obtained from the following procedure: In Figure 1 of Mukai (1969a), the formula \( \tilde{W} = 0.0520Y + 1.0639 \) (where \( Y \) is the homozygous viability of the chromosome carrying mutant polygenes in a coupling heterozygote) applied after the viabilities of coupling heterozygotes reached an optimum point. \( Y \) can be expressed in terms of the number of loci using the figures described in Table 3 of Mukai (1969b): \( \tilde{Y} = 1.0 - 0.000813X - 0.005550X^2 \). Substituting this formula for \( Y \) in the one above, formula (2) can be obtained.

(3) The fitness values of repulsion heterozygotes are determined by the following formula:

\[
\tilde{W} = 1.0 - 0.7h(0.009813X + 0.005550X^2)
\]

(3)

where \( h \) is the degree of dominance.

The procedure used to obtain formula (3) is as follows: The term in parentheses gives the magnitude of the reduction of homozygous viability when the number of mutant-carrying loci equals \( X \), as described above. There is an approximately quadratic interaction among mutant viability polygenes in repulsion heterozygotes, and the heterozygote viability can be expressed approximately by \( 1 - h(aX + bX^2) \) where \( (aX + bX^2) \) is the homozygous effect of \( X \) mutant viability polygenes. Chugusa, Mukai and Mettler (in preparation) estimated the average homozygous effect of viability polygenes from a natural population to be 0.023 (a maximum estimate), and that of newly arising individual viability polygenes is 0.027 (Mukai 1964). In the present simulation experiment, the ratio of the average homozygous effect of mutant polygenes in equilibrium populations to that of newly arising mutant polygenes is assumed to be 0.7 (less than 1.0), which is due to natural selection. Indeed, the maximum genetic variance of individual effects of newly arising mutant polygenes was estimated as 0.000180 (Mukai 1964). Thus it can be expected that the average homozygous effect of viability polygenes in equilibrium populations is less than that of newly arising viability polygenes. The factor 0.7 in formula (3) reflects this point.

Considering the effect of natural selection on the degrees of dominance, which makes the \( h \) values in equilibrium populations smaller than that of newly arising mutant polygenes, as in the case of the homozygous effects of mutant polygenes described above, the \( h \) value is assumed to be 0.1, 0.2, 0.3, and 0.4. In addition, it is assumed in formula (3) that the \( \tilde{W} \)'s are 0 if the \( X \)'s are larger than 49 for \( h = 0.1 \), 35 for \( h = 0.2 \), 28 for \( h = 0.3 \), and 24 for \( h = 0.4 \).

(4) Free recombination is assumed among mutant polygenes.

Experiment A-2: In this experiment, the basic assumptions are the same as those of experiment A-1, except for \( M \).

(1) The \( M \) is 0.2117. This is 1.5 times larger than the minimum estimate.

(2) The fitness values of coupling heterozygotes are determined by the following formulae:

\[
\tilde{W} = 1.0 + 0.001408X + 0.001035X^2 - 0.000050X^3
\]

(4)

for \( X = 1, 2, \ldots, 17 \), and \( 18 \), and

\[
\tilde{W} = 1.1157 - 0.0003402X - 0.0001283X^2
\]

(5)
for $X = 19, 20, \ldots, 91$. These formulae were obtained by the same method used in experiment A-1.

(3) The fitness values of repulsion heterozygotes are determined by the following formula:

$$\hat{W} = 1.0 - 0.7h (0.006542X + 0.002467X^2)$$  \hspace{1cm} (6)

where $h$ is assumed to be 0.1, 0.2, 0.3, and 0.4. When $h = 0.1, 0.2, 0.3,$ and 0.4, the $\hat{W}$'s are assumed to be 0 if the $X$'s are larger than 74, 52, 42, and 36, respectively.

(4) Free recombination is assumed among mutant polygenes.

**Experiment A'-1:** All assumptions are the same as those in experiment A-1, except that no recombination is assumed among mutant polygenes.

**Experiment A'-2:** All assumptions are the same as those in experiment A-2, except that no recombination is assumed.

**Experiment B'-1:** All the assumptions are the same as those in experiment B-1, except that no recombination is assumed in this experiment.

**Experiment B'-2:** All the assumptions are the same as those in experiment B-2, except that no recombination is assumed in this experiment.

The assumptions of the eight experiments described above are summarized in Table 1. A represents the coupling effect; B represents no coupling effect; prime (') stands for no recombination; no prime for free recombination; 1 means that the polygenic mutation rate is 0.1411 per second chromosome per generation; and 2 means that the rate is 0.2117 per second chromosome per generation.

**Procedure of the experiments:** The following parameter is defined: $m =$ the number of mutant genes in a homozygote or a heterozygote beyond which the individual in question becomes polygenic lethal. The actual numbers for the respective homozygotes and heterozygotes have been described above. Generation 0 starts with normal homozygotes (no mutant genes, and $W = 1.0$), and gametes are produced having no mutant genes. After that, mutations take place on the chromosomes according to a Poisson distribution on the basis of the specified mutation rates. Thus, the gametes for generation 1 have been obtained. In this stage the frequency of gametes carrying $i$ mutant polygenes is expressed by $T$, $(\sum_{i=0}^{m} T_i = 1.0)$. We may make homozygotes in an actual experiment using a marked inversion. The fitness of homozygotes carrying $i$ mutant genes is expressed as $\hat{W}O_i$.

Next, random mating takes place and fertilized eggs are laid. The frequency of eggs carrying $i$ mutant polygenes in the diploid condition is expressed by $E$, $(\sum_{i=0}^{m} E_i = 1.0)$ in the B series of experiments (no coupling effect). The frequencies of fertilized eggs carrying $i$ mutant polygenes in the diploid condition are expressed by $EC_i$ for the coupling heterozygotes and $ER_i$ for the

<table>
<thead>
<tr>
<th>TABLE 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>The assumptions for the eight simulation experiments</strong></td>
</tr>
<tr>
<td>Coupling effect</td>
</tr>
<tr>
<td>Mutant rate</td>
</tr>
<tr>
<td>Free recombination</td>
</tr>
<tr>
<td>No recombination</td>
</tr>
</tbody>
</table>
repulsion heterozygotes in the A series \((\sum_{i=0}^{m} EC_i + \sum_{i=0}^{m'} ER_i = 1.0)\). The fitness values of respective genotypes are \(W_i\) for \(E_i\), \(WC_i\) for \(EC_i\), and \(WR_i\) for \(ER_i\) (\(W_o\), \(WC_o\), and \(WR_o\) are 1.00). After selection, we can obtain a population of adults. The frequency of individuals carrying \(i\) heterozygous loci is \(Z_i (\sum_{i=0}^{m} Z_i = 1.00)\). Thus, \(Z_i\) can be expressed as \(W_i E_i / \sum_{i=0}^{m} W_i E_i\) for the B series and \(Z_i = (WC_i EC_i + WR_i ER_i) / (\sum_{i=0}^{m} WC_i EC_i + \sum_{i=0}^{m'} WR_i ER_i)\) for the A series, respectively. Then meiosis occurs and gametes are formed. This process is shown diagrammatically in Figure 1. The entire cycle described above is repeated until a generation is reached where the population in question seems to have attained an approximate equilibrium.

In this generation, the following genetic parameters are obtained:

1. The average fitness of the population \(\overline{W}\)
   \[
   \overline{W} = \sum_{i=0}^{m} W_i E_i \quad \text{for the B series}
   \]
   \[
   \overline{W} = \sum_{i=0}^{m} WC_i EC_i + \sum_{i=0}^{m'} WR_i ER_i \quad \text{for the A series}
   \]

2. The average number of mutant genes per individual (second chromosome pair) \(AVNG\)
   \[
   AVNG = \sum_{i=0}^{m} Z_i \cdot i
   \]

3. The average fitness of homozygotes \(WO\). These homozygotes are assumed to be formed without selection.
   \[
   \overline{WO} = \sum_{i=0}^{m} T_i \cdot WO_i
   \]
TABLE 2

The results of experiments A-1 and A'-1

Assumptions: the mutation rate of polygenes controlling viability is 0.1411 per second chromosome per generation and overdominance occurs only in coupling heterozygotes.

<table>
<thead>
<tr>
<th>h</th>
<th>Gen.</th>
<th>$\bar{W}$</th>
<th>$\Delta\bar{W}/10$ gen.</th>
<th>$AVNG$</th>
<th>$\bar{W}_0$</th>
<th>$LO$</th>
<th>$LO_g$</th>
<th>$LE_p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Free recombination (Experiment A-1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1</td>
<td>200</td>
<td>0.866</td>
<td>-0.000205</td>
<td>16.90</td>
<td>0.625</td>
<td>0.375</td>
<td>0.279</td>
<td>0.0142</td>
</tr>
<tr>
<td>0.2</td>
<td>200</td>
<td>0.863</td>
<td>-0.000016</td>
<td>11.68</td>
<td>0.797</td>
<td>0.203</td>
<td>0.077</td>
<td>0.0004</td>
</tr>
<tr>
<td>0.3</td>
<td>200</td>
<td>0.862</td>
<td>-0.000003</td>
<td>9.34</td>
<td>0.859</td>
<td>0.141</td>
<td>0.004</td>
<td>0.0000</td>
</tr>
<tr>
<td>0.4</td>
<td>200</td>
<td>0.862</td>
<td>0.000000</td>
<td>7.94</td>
<td>0.890</td>
<td>0.109</td>
<td>-0.033</td>
<td>0.0000</td>
</tr>
<tr>
<td>(b) No recombination (Experiment A'-1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1</td>
<td>350</td>
<td>0.916</td>
<td>-0.000025</td>
<td>13.03</td>
<td>0.741</td>
<td>0.258</td>
<td>0.191</td>
<td>0.0047</td>
</tr>
<tr>
<td>0.2</td>
<td>300</td>
<td>0.906</td>
<td>-0.000002</td>
<td>9.51</td>
<td>0.846</td>
<td>0.154</td>
<td>0.067</td>
<td>0.0001</td>
</tr>
<tr>
<td>0.3</td>
<td>300</td>
<td>0.900</td>
<td>+0.000001</td>
<td>7.88</td>
<td>0.886</td>
<td>0.114</td>
<td>0.015</td>
<td>0.0000</td>
</tr>
<tr>
<td>0.4</td>
<td>300</td>
<td>0.895</td>
<td>+0.000001</td>
<td>6.87</td>
<td>0.908</td>
<td>0.092</td>
<td>-0.014</td>
<td>0.0000</td>
</tr>
</tbody>
</table>

$h = \text{the degree of dominance in repulsion heterozygotes.}$

$\bar{W} = \text{average fitness in the equilibrium population.}$

$\Delta\bar{W}/10 \text{ gen.} = \text{change in population fitness in last ten generations.}$

$AVNG = \text{average number of mutant polygenes per second chromosome pair.}$

$\bar{W}_0 = \text{average fitness of homozygotes.}$

$LO = \text{homozygous load with respect to the optimum homozygote.}$

$LO_g = \text{homozygous load with respect to } \bar{W}.$

$LE_p = \text{frequency of polygenic lethals in homozygous condition.}$

These footnotes also apply to Tables 3, 4, and 5.
PREDICTING EQUILIBRIUM

(4) Homozygous load with respect to mutant-free individuals \((LO)\)

\[
LO = 1.0 - \sum_{i=0}^{m} T_i \cdot WO_i
\]

It should be noted that the unit of \(LO\) is not the "lethal equivalent" of Morton, Crow and Muller (1956).

(5) Homozygous load with respect to the average fitness of the population \((LO_s)\)

\[
LO_s = \frac{LO}{\bar{W}}
\]

(6) The frequency of homozygous lethals due to mutant polygenes \((LE_p)\)

\[
LE_p = \sum_{i=0}^{\infty} T_i - \sum_{i=0}^{m} T_i = 1.0 - \sum_{i=0}^{m} T_i
\]

RESULTS AND ANALYSES

The numbers of generations needed for the populations to reach equilibrium differed from experiment to experiment owing to the difference in assumptions (mutation rates, recombination, coupling effect, and the degrees of dominance). Table 2 shows the results of experiments A-1 and A'-1 (assuming \(M = 0.1411\) and coupling effect). Table 2 lists the degrees of dominance in the repulsion phase, the number of generations for which simulation experiments were conducted, the reduction of \(\bar{W}\) per last ten generations, the average number of mutant genes per individual (second chromosome pair), the average fitness values of homozygotes, homozygous loads, standardized homozygous loads with respect to respective \(\bar{W}\)'s, and the frequencies of polygenic lethals (homozygotes). In Table 3, the same results are tabulated for experiments A-2 and A'-2 (assuming \(M = 0.2117\) and coupling effect). The results of experiments B-1 and B'-1 and of experiments B-2 and B'-2 are presented in Tables 4 and 5, respectively.

We have found some evidence that \(\bar{W}\) is fluctuating in experiments A'-1, A'-2, and B'-2, but the amount of fluctuation seems negligible.

From these tables the following findings are apparent:

(1) The average number of mutant genes per individual is increased in every case with an increase in the mutation rate, and accordingly, \(\bar{W}\) is decreased. The frequency of polygenic lethal homozygotes also increases with an increase in the mutation rate, although their frequencies are always very low.

(2) The \(\bar{W}\)'s are almost independent of the degrees of dominance within an experiment, even when the coupling effect is involved. This is the same as in the case of multiplicative gene action with no coupling effect (Haldane 1937; Muller 1950). The average number of mutant genes per individual is decreased with an increase in the degree of dominance, and accordingly, the average fitness of homozygotes increases. The frequency of polygenic lethal homozygotes decreases with an increase in the degree of dominance.

(3) The effect of linkage on the above genetic parameters differs depending on whether or not the coupling effect exists. This conclusion will be discussed in detail below.

As is shown in Tables 2 and 3, the effect of the mutation rate on \(\bar{W}\) is significant even in the case where the coupling effect is assumed. In practice, it might be impossible to assume that \(M\) is larger than 0.2117 (excluding neutral and
TABLE 3

The results of experiments A-2 and A'-2

Assumptions: the mutation rate of polygenes controlling viability is 0.2117 per second chromosome per generation and overdominance occurs only in coupling heterozygotes.

<table>
<thead>
<tr>
<th>h</th>
<th>Gen.</th>
<th>$\bar{W}$</th>
<th>$\Delta W/10$ gen.</th>
<th>$\Delta W\times 100$</th>
<th>$\bar{W}_0$</th>
<th>$L_0$</th>
<th>$L_{0g}$</th>
<th>$L_{Ep}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Free recombination (Experiment A-2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1</td>
<td>300</td>
<td>0.814</td>
<td>-0.000021</td>
<td>30.51</td>
<td>0.495</td>
<td>0.504</td>
<td>0.391</td>
<td>0.0419</td>
</tr>
<tr>
<td>0.2</td>
<td>300</td>
<td>0.810</td>
<td>-0.000000</td>
<td>21.27</td>
<td>0.728</td>
<td>0.271</td>
<td>0.101</td>
<td>0.0007</td>
</tr>
<tr>
<td>0.3</td>
<td>200</td>
<td>0.807</td>
<td>-0.000010</td>
<td>17.14</td>
<td>0.812</td>
<td>0.188</td>
<td>-0.006</td>
<td>0.0000</td>
</tr>
<tr>
<td>0.4</td>
<td>200</td>
<td>0.804</td>
<td>-0.000002</td>
<td>14.67</td>
<td>0.854</td>
<td>0.146</td>
<td>-0.062</td>
<td>0.0000</td>
</tr>
<tr>
<td>(b) No recombination (Experiment A'-2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1</td>
<td>400</td>
<td>0.865</td>
<td>-0.000347</td>
<td>25.46</td>
<td>0.620</td>
<td>0.379</td>
<td>0.283</td>
<td>0.0150</td>
</tr>
<tr>
<td>0.2</td>
<td>400</td>
<td>0.855</td>
<td>+0.000051</td>
<td>18.15</td>
<td>0.786</td>
<td>0.241</td>
<td>0.081</td>
<td>0.0002</td>
</tr>
<tr>
<td>0.3</td>
<td>400</td>
<td>0.847</td>
<td>-0.000009</td>
<td>14.92</td>
<td>0.845</td>
<td>0.154</td>
<td>0.002</td>
<td>0.0000</td>
</tr>
<tr>
<td>0.4</td>
<td>400</td>
<td>0.842</td>
<td>+0.000001</td>
<td>12.95</td>
<td>0.878</td>
<td>0.122</td>
<td>-0.042</td>
<td>0.0000</td>
</tr>
</tbody>
</table>
TABLE 4

The results of experiments B-1 and B'-1
Assumptions: the mutation rate of polygenes controlling viability is 0.1411 per second chromosome per generation and overdominance occurs in neither coupling nor repulsion heterozygotes

<table>
<thead>
<tr>
<th>h</th>
<th>Gen.</th>
<th>W̄</th>
<th>ΔW/10 gen.</th>
<th>AVNG</th>
<th>W₀</th>
<th>L₀</th>
<th>L₀ₕ</th>
<th>Lₚ</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Free recombination (Experiment B-1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1</td>
<td>200</td>
<td>0.866</td>
<td>-0.000193</td>
<td>16.91</td>
<td>0.624</td>
<td>0.376</td>
<td>0.280</td>
<td>0.0143</td>
</tr>
<tr>
<td>0.2</td>
<td>200</td>
<td>0.862</td>
<td>-0.000014</td>
<td>11.73</td>
<td>0.795</td>
<td>0.204</td>
<td>0.077</td>
<td>0.0004</td>
</tr>
<tr>
<td>0.3</td>
<td>200</td>
<td>0.859</td>
<td>-0.000001</td>
<td>9.42</td>
<td>0.856</td>
<td>0.143</td>
<td>0.003</td>
<td>0.0000</td>
</tr>
<tr>
<td>0.4</td>
<td>200</td>
<td>0.856</td>
<td>0.000000</td>
<td>8.05</td>
<td>0.888</td>
<td>0.112</td>
<td>-0.037</td>
<td>0.0000</td>
</tr>
<tr>
<td>(b) No recombination (Experiment B'-1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1</td>
<td>500</td>
<td>0.834</td>
<td>-0.000246</td>
<td>19.11</td>
<td>0.544</td>
<td>0.456</td>
<td>0.348</td>
<td>0.0196</td>
</tr>
<tr>
<td>0.2</td>
<td>350</td>
<td>0.830</td>
<td>-0.000555</td>
<td>13.29</td>
<td>0.755</td>
<td>0.245</td>
<td>0.091</td>
<td>0.0002</td>
</tr>
<tr>
<td>0.3</td>
<td>350</td>
<td>0.825</td>
<td>-0.000319</td>
<td>10.75</td>
<td>0.828</td>
<td>0.172</td>
<td>-0.003</td>
<td>0.0000</td>
</tr>
<tr>
<td>0.4</td>
<td>350</td>
<td>0.823</td>
<td>-0.000196</td>
<td>9.21</td>
<td>0.866</td>
<td>0.134</td>
<td>-0.053</td>
<td>0.0000</td>
</tr>
</tbody>
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TABLE 5
The results of experiments B-2 and B'-2
Assumptions: the mutation rate of polygenes controlling viability is 0.2117 per second chromosome per generation and overdominance occurs in neither coupling nor repulsion heterozygotes

<table>
<thead>
<tr>
<th>h</th>
<th>Gen.</th>
<th>( \bar{w} )</th>
<th>( \Delta \bar{w}/10 \text{ gen.} )</th>
<th>AVNG</th>
<th>( \bar{w}_0 )</th>
<th>LO</th>
<th>L0g</th>
<th>LEp</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Free recombination (Experiment B-2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1</td>
<td>250</td>
<td>0.814</td>
<td>-0.000122</td>
<td>30.52</td>
<td>0.495</td>
<td>0.505</td>
<td>0.392</td>
<td>0.0419</td>
</tr>
<tr>
<td>0.2</td>
<td>250</td>
<td>0.810</td>
<td>-0.000007</td>
<td>21.27</td>
<td>0.728</td>
<td>0.271</td>
<td>0.101</td>
<td>0.0007</td>
</tr>
<tr>
<td>0.3</td>
<td>200</td>
<td>0.807</td>
<td>-0.000011</td>
<td>17.14</td>
<td>0.811</td>
<td>0.188</td>
<td>-0.006</td>
<td>0.0000</td>
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<tr>
<td>0.4</td>
<td>200</td>
<td>0.804</td>
<td>-0.000002</td>
<td>14.68</td>
<td>0.854</td>
<td>0.146</td>
<td>-0.062</td>
<td>0.0000</td>
</tr>
<tr>
<td>(b) No recombination (Experiment B'-2)</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td>0.1</td>
<td>650</td>
<td>0.744</td>
<td>-0.001242</td>
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<td>0.675</td>
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<tr>
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<td>-0.001065</td>
<td>25.79</td>
<td>0.630</td>
<td>0.370</td>
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</tr>
<tr>
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<td>550</td>
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<td>-0.000269</td>
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<td>0.760</td>
<td>0.239</td>
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<tr>
<td>0.4</td>
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<td>0.758</td>
<td>+0.000054</td>
<td>16.65</td>
<td>0.824</td>
<td>0.176</td>
<td>-0.087</td>
<td>0.0000</td>
</tr>
</tbody>
</table>
effectively neutral mutations). Assuming the coupling effect and no recombination, a random genetic load becomes approximately 0.22 where $M = 0.2117$, following the original definition of random genetic load by Crow (1958) $[(W_{opt} - \bar{W})/W_{opt}]$, where $W_{opt}$ is the fitness of the optimum genotype. In the present case $W_{opt} = 1.0854$. Assuming $M = 0.1411 - 0.2117$, the degree of dominance in repulsion heterozygotes is estimated. Figure 2 shows the relationship between the homozygous loads with respect to the average fitness of the population ($LO_x$) and the degrees of dominance in repulsion heterozygotes ($h$). Using the Madison, Wisconsin population and Dr. Wallace’s cage population, Temin (1966) estimated the average viability of nonlethal homozygotes to be 0.863 in comparison with the average viability of random heterozygotes for second chromosomes of D. melanogaster. Thus the homozygous load is 0.173 (unit is not lethal equivalent). Chigusa, Mukai and Mettler (in preparation) have reported that the $LO_x$ (excluding the effect of lethals) of the Raleigh, North Carolina population of D. melanogaster was 0.327 including semilethals, and 0.234
excluding semilethals. Thus it may reasonably be assumed that the $LO_s$ due to polygenes or mildly deleterious genes is approximately $0.15-0.25$ in the second chromosomes in this species. If we estimate the $h$ value corresponding to the above $LO_s$ in Figure 2, it becomes $0.08-0.19$. This estimate is only slightly smaller than the one obtained using the formulae of Kimura and Maruyama (1966) under the assumption that there is no coupling effect [$h = 0.1-0.2$, Mukai (1969b)]. The estimated $\overline{h}$ value of $0.17$ from the natural population (Chigusa, Mukai and Mettler, in preparation) and the predicted $\overline{h}$ value of $0.17-0.27$ (Mukai (1969c) overlap the range of the present estimates. Wills' (1966) estimate of $0.18-0.30$ is slightly larger than the present estimates. However, these differences can easily be explained by the differences in populations, species, and experimental technique or the method of estimation. In general, it is concluded that the present predicted $\overline{h}$ values agree very well with the actual estimates from the populations and with the other predicted values.

From a different viewpoint, if we assume that $\overline{h}$ is $0.17$, then the mutation rate should be close to $0.2117$, assuming $LO_s$ (excluding the effects of lethals and semilethals) $= 0.15-0.25$.

The frequency distributions of gametes having different numbers of mutant polygenes were examined. Figure 3 shows the distributions of gametes just be-

![Figure 3](image-url)
Therefore, the formation of zygotes where $M = 0.1411$ and $h = 0.1$. Very similar distributions are obtained for various combinations of $M$ and $h$. The average number of mutant polygenes per gamete before mutations occur can be obtained by dividing the average number of mutant polygenes (which is shown in Tables 2-5) by 2. From Figure 3, the following findings can be obtained for the case of $M = 0.1411$ and $h = 0.1$: (1) When free recombination takes place, all the second chromosomes carry at least one mutant gene (average number of mutant genes per gamete = 8.59). Therefore, there is no chance for the manifestation of overdominance even in the A series (coupling effect is assumed). Accordingly, there is no difference between corresponding A and B experiments. (2) In the A series, when recombination does not take place, the average number of mutant polygenes decreases (6.66) in comparison with the corresponding experiment where free recombination takes place (8.59). This is due to linkage disequilibrium. However, for the B series, the number increases (9.69) in comparison with the corresponding experiment (8.59). As a result, when recombination does not take place, the number of mutant polygenes in the A series is smaller than that for the corresponding experiment in the B series. For $M = 0.1411$ in the A series, the frequencies of gametes which do not carry any newly arising polygenic mutants are 0.0201, 0.0364, 0.0504 and 0.0637 where $h = 0.1, 0.2, 0.3,$ and $0.4$, respectively. The corresponding figures for $M = 0.2117$ are 0.0011 ($h = 0.1$), 0.0039 ($h = 0.2$), 0.0069 ($h = 0.3$), and 0.0102 ($h = 0.4$). Thus it can be concluded that the frequency of gametes carrying no mutant polygenes in an equilibrium population increases with an increase in the degree of dominance in the repulsion phase, and decreases with an increase in the mutation rate. The frequencies of these gametes are directly related to the frequencies of individuals manifesting overdominance. This will be discussed below.

Thus it appears that the coupling effect decreases the number of mutant polygenes with linkage, but that a synergistic interaction without the coupling effect rather increases the numbers of mutant polygenes per gamete with linkage. The distribution patterns of the number of heterozygous loci per zygote are very similar to those of Figure 2.

Figure 4 presents the distributions of the fitness values for the case where $M = 0.1411$ and $h = 0.1$. In experiment A'-1 (the coupling effect is assumed), the distribution is rather bimodal in the right-hand side, and this is definitely caused by the coupling effect which is strictly defined in the present work. That is, if one of the homologous chromosomes has only one mutant gene (the other carries many mutant genes), this heterozygote is classified as a repulsion heterozygote in the present simulation experiments. Practically, the situation might not be decided as strictly as the above, and even if a very small number of mutant genes with extremely small homozygous effects is carried in one of the homologous chromosomes (the other containing many), the overdominance might be seen in some cases. Furthermore, environmental effects might smooth the distribution. Figure 4 clearly shows the contribution of coupling heterozygotes to increasing the average fitness of the population when linkage exists.

The average fitness values and the average numbers of mutant polygenes per
individual of the respective populations can be seen in Tables 2, 3, 4, and 5. The following findings can be obtained from these tables, and can also be directly predicted from the results of the gamete studies described above: (1) In the case where the coupling effect does not exist, the average number of mutant polygenes per individual increases with linkage, and consequently the average fitness decreases in comparison with the case of free recombination. For the case where $M = 0.1411$ and $h = 0.1$, the number of mutant polygenes is 19.11 and $W$ is 0.834 for no recombination, or 16.91 and 0.866, respectively, for free recombination. (2) The situation is completely reversed where there is a coupling effect. That is, the average number of mutant polygenes per individual decreases with linkage, and accordingly, the average fitness increases as compared with the case of free recombination. Where $M = 0.1411$ and $h = 0.1$, the number of mutant polygenes is 13.03 and $W$ is 0.916 for no recombination, or 16.90 and 0.866, respectively, for free recombination. It should be noted here that the coupling effect is manifested only when linkage exists (in the case of free recombination, the frequency of gametes carrying no mutant polygenes is effectively zero and no overdominance is manifested). It should also be noted that the frequency of individuals showing overdominance is only 4.7% in the equilibrium population where $M = 0.1411$ and $h = 0.1$. For reference, the frequencies of coupling heterozygotes are tabulated for various combinations of $M$ and $h$ in Table 6. From this

**Figure 4.**—Distributions of fitness values for the case where $M = 0.1411$ and $h = 0.1$. 

![Graph showing distributions of fitness values](image)
The frequencies of coupling heterozygotes in equilibrium populations when no recombination is assumed

<table>
<thead>
<tr>
<th>Degree of dominance (h)</th>
<th>Mutation rate (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.2117</td>
</tr>
<tr>
<td></td>
<td>0.1411</td>
</tr>
<tr>
<td>0.1</td>
<td>0.0020</td>
</tr>
<tr>
<td></td>
<td>0.0456</td>
</tr>
<tr>
<td>0.2</td>
<td>0.0095</td>
</tr>
<tr>
<td></td>
<td>0.0809</td>
</tr>
<tr>
<td>0.3</td>
<td>0.0167</td>
</tr>
<tr>
<td></td>
<td>0.1104</td>
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<tr>
<td>0.4</td>
<td>0.0251</td>
</tr>
<tr>
<td></td>
<td>0.1376</td>
</tr>
</tbody>
</table>

* In the repulsion heterozygotes.

In the repulsion heterozygotes, the following can be seen: (1) The frequency of coupling heterozygotes increases with an increase in the degree of dominance in repulsion heterozygotes, and (2) it decreases with an increase in the mutation rate. It is most significant that in spite of the fact that the frequency of coupling heterozygotes is low, its effect on the $W$ is very large when linkage exists [the amount of increase in $W$ is about 0.07 when $M = 0.1411$ and about 0.10 when $M = 0.2117$ (cf. Tables 2 and 3)].

It may be necessary to consider the evolutionary significance of overdominance with optimum heterozygosity in coupling heterozygotes. The generality of overdominance has been questioned because it causes too much random genetic load (segregation load) (Kimura and Crow 1964). Overdominance becomes significant when in combination with optimum heterozygosity and linkage; although the frequency of individuals manifesting it in equilibrium populations is low, since population fitness increases without increasing genetic load. For example, when $M = 0.1411$ and $h = 0.1$, the random genetic load is 0.166 and $W = 0.834$ when no recombination and no coupling effect occur. On the other hand, where the coupling effect and no recombination ($M = 0.1411$ and $h = 0.1$) are assumed, the random genetic load is 0.155 with respect to the optimum genotype ($W_{opt} = 1.0839$), and $W = 0.916$.

In conclusion, the following are predicted for the second chromosomes of an equilibrium population: the polygenic mutation rate is 0.14–0.21 per second chromosome per generation; the degree of dominance in the repulsion phase is 0.08–0.19; the frequency of coupling heterozygotes which show overdominance is probably less than four percent; the average number of polygenic heterozygous loci per second chromosome is 13–26 (excluding neutral genes); and the magnitude of random genetic load is 0.15–0.22 with respect to the optimum genotypes and is 0.09–0.15 with respect to initial mutant-free individuals.

Finally, the following things should be noted: (1) In the present experiment the effect of coadaptation as a whole is not considered, though overdominance in the coupling phase in particular might be one of the outcomes of coadaptation. This phenomenon is said to have developed through natural selection (Dobzhansky 1950). Thus it may be that the predicted values are slightly biased. (2) Complete linkage and free recombination were assumed in the present ex-
periment, but the actual situation is between them. If the amount of recombination should begin increasing from zero toward free recombination, then the linkage disequilibrium which was established in the case of complete linkage might tend to disappear rapidly. (3) In a finite population, the frequency of homozygously highly viable chromosomes will increase. Accordingly, the expected frequency of individuals manifesting overdominance might increase in the population when the conditions for the manifestation of coupling overdominance are fulfilled.

**DISCUSSION**

**Peculiarity of the coupling-repulsion effect of newly arising mutations:** We are aware that a coupling-repulsion effect for randomly occurring mutant genes which are far apart on the chromosome may not be expected on the basis of the present knowledge of molecular genetics. However, a very similar phenomenon, which Dobzhansky (1959) has called the “organization effect,” was discovered using materials sampled from natural populations. Levitan (1955) reported an interaction similar to the coupling-repulsion effect at the level of inversions. He discovered a nonrandom association of inversions in the left and right arms of the second chromosomes of *D. robusta*. The same type of possible position effect has been discovered in the *X* chromosome of *D. robusta* (Levitan 1958), in the fourth chromosome of *D. guaramunu* (Levitan and Salzano 1959), in the *X* and second chromosomes of *D. paramelanica* (Stalker 1960), and in the fourth chromosome of *D. pavani* (Brncic 1961). Similar phenomena were discovered at a genic level with respect to sternopleural chaeta number and lethality (Gibson and Thoday 1962) and the manifestation of extra-sexcomb (Hannah-Alava 1964) in *D. melanogaster*. The *F₂* breakdown of heterosis expressed by *F₁* individuals of interpopulational crosses [*D. pseudoobscura*, Brncic (1954); *D. melanogaster* and other species of Drosophila, Wallace and Vetukhiv (1955)] is of the same nature. Wallace and Dobzhansky (1962) examined the viability of chromosomes when homozygous and when heterozygous with marked chromosomes in *D. melanogaster* and *D. pseudoobscura*. The result indicates that the heterozygotes generally exceed in viability the corresponding homozygotes. This is particularly true in the upper part of the viability range, where the viabilities of the heterozygotes and homozygotes diverge. This divergence might be related to the optimum heterozygosity principle. All the above experimental results are consistent with the coupling-repulsion effect.

Mukai (1970) has not claimed overdominance of viability polygenes or mildly deleterious genes as a generality for coupling heterozygotes. He feels that the necessary conditions for its manifestation are that the homozygous viability of the original chromosome should be normal and that the genes in the chromosome must be coadapted (Wallace and Vetukhiv 1955). Mukai, Yoshikawa and Sano (1966) showed for newly arisen polygenic mutations that the manifestation of overdominance depends upon the genetic backgrounds. Falk (1961) could not show overdominance due to X-ray-induced mutations, probably because at least one of the above requirements was not satisfied (Wallace 1963).
The Classical hypothesis and the Balance hypothesis: The mechanisms for maintaining genetic variability in populations have been defined in two different hypotheses which Dobzhansky (1955) has termed the Classical hypothesis and the Balance hypothesis. The former hypothesis assumes that genetic variability can be maintained mainly by a balance between mutation and selection pressures. The latter assumes that genetic variability at most loci is determined by balanced selective forces including overdominance. Some investigators supporting this hypothesis presumed the generality of overdominance in equilibrium populations (Wallace 1958).

It has been thought that the experimental result obtained by Wallace (1958) best supports the Balance hypothesis: He clearly showed that mutations (mainly polygenic) induced in the second chromosome of D. melanogaster by 500 R x rays were overdominant in the coupling heterozygotes in the present terminology. Wallace (1958) tentatively concluded that individuals of his experimental population were heterozygous, on the average, at 50% or more of all loci. However, Kimura and Crow (1964) suggested that too much genetic load would be created under the above condition. If the coupling-repulsion effect and optimum heterozygosity exist as general phenomena in well coadapted populations of D. melanogaster, it is possible to increase the average fitness of a population significantly by only less than 4% of the total individuals which manifest overdominance without increasing random genetic load or without rejecting Wallace's experimental result.

On the other hand, if we base our discussion on the Classical hypothesis, the following conclusion would be reached. Under multiplicative or independent gene action, if we assume that the mutation rate of viability polygenes is 0.14 per second chromosome per generation, the magnitude of the predicted mutation load probably becomes too large, i.e., about 0.56 in females and 0.77 in males (Kimura 1961; Mukai 1969b). The magnitude of the mutation load is approximately the same as the total mutation rate per gamete under the condition of quadratic synergistic interaction (Kimura 1961; Kimura and Maruyama 1966). In a previous paper of this series, we have reported that there is a quadratic synergistic interaction among mutant polygenes (Mukai 1969b).

Natural selection has probably determined the linkage intensity in order to increase the adaptability and fitness of the species. For some species a high recombination value might be beneficial and for another species the opposite situation might be true, depending upon the nature of reproduction of the species and their environmental conditions (Stebbins 1958). Even within species, variation of recombination values due to inversions can be seen between marginal and central populations of D. robusta (Carson 1958). There have been several reports of significant decreases in recombination value per nucleotide pair with the evolution of organisms; ranked in order from highest to lowest reported recombination values, the organisms are: phage T4, E. coli, Aspergillus, Drosophila, and mouse (Pontercorvo 1958; Hayes 1964; Nei 1968). This ranking might correspond to the evolution of greater complexity in the structure of chromosomes. During a relatively short period of evolution, the average recombina-
tion value per unit of physical length of the chromosome might also have been
decreased at least in the genus Drosophila. No crossing over in males is one of the
evidences for this speculation. NEI (1967) has mathematically shown that a
modifier which decreases the recombination value between two genes would be
selectively advantageous if epistasis exists between the two genes in question,
although this statement is not always universally true (experiment B vs. experi-
ment B').

It has become clear from the present simulation experiment that under the
condition that only quadratic synergistic interaction exists, the average fitness
of the population is decreased if the recombination value becomes smaller. Thus
the synergistic interaction is significant for decreasing the mutation load, but
it might be incompatible with the reduction of recombination values in this
species. The present simulation experiment suggests that if overdominance and
optimum heterozygosity in the coupling phase exist (even at a very low fre-
quency) in addition to synergistic interaction in the repulsion phase, the above
inconsistency can be removed. Furthermore, the predicted equilibrium population
is very close to the actual population with respect to genetic load (homozy-
gous load with respect to the average fitness of the population). Indeed, overdom-
inance, optimum heterozygosity, and decreased recombination seem to have de-
veloped in close relation to each other.

On the basis of the above consideration, it appears that the difficulties of the
Classical and Balance hypotheses can be overcome by the coupling effect without
denying any of the experimental results of WALLACE (1958 and later), GREEN-
BERG and CROW (1969), TEMIN (1966), WILLS (1966), and others. In fact, WAL-
LACE (1958) and others examined the heterozygous effect in the coupling con-
dition in an otherwise homozygous genetic background and detected overdom-
inance, while GREENBERG and CROW (1960), TEMIN (1966), and WILLS (1966)
could not detect overdominance when analyzing natural and/or experimental
populations where the frequency of coupling heterozygotes was probably very
low.

Isozyme polymorphism: On the basis of their experimental results, LEWONTIN
and HUBBY (1966) calculated the average heterozygosity of an individual to be
about 12% in Drosophila pseudoobscura. Similar magnitudes of heterozygosity
were detected in D. ananassae (JOHNSON et al. 1966) and in D. melanogaster
(O'BRIEN and MACINTYRE, 1969). These phenomena are apparently contradic-
tory to one of the findings in the present study, that is, that genetic variability
with respect to viability in the second chromosomes of D. melanogaster can be
explained, on the average, by only 13–26 heterozygous loci (the number of genes
only having homozygous and heterozygous effects on viability).

LEWONTIN and HUBBY (1966) first stated that all these polymorphisms can-
not be maintained by overdominance since it would cause too much genetic load.
SVED, REED and BODMER (1967) and others have proposed a “threshold model”
of overdominance (the fitness values of individuals with more than a certain
number of heterozygous loci are nearly equal) to help explain the polymor-
phisms without necessarily creating an extreme segregation load. If isozyme
genes are the same as viability polygenes (they have definitely assumed so), this "threshold model" may be rejected since we have experimentally found an optimum heterozygosity in coupling heterozygotes (Mukai 1969a). Crow (1968) criticized the "threshold model" on the grounds that it is impossible to avoid excessive drastic inbreeding under this model without being inconsistent with the actual data. Truncation selection proposed by King (1967) and Milkman (1967), in which a certain proportion of individuals with the lowest survival values are selected out of the population by natural selection appears attractive, but so far there is no experimental evidence supporting truncation selection.

Crow (1968) has suggested that isozyme loci are generally not strongly selected, and that they may be maintained at intermediate frequencies by mutation pressure or by slight heterozygote advantage. On the basis of the substitution load due to nucleotide substitution, Kimura (1968) has proposed that most of the amino acid substitution of proteins in human populations is due not to natural selection, but to neutral mutations and genetic drift of gene frequency. Supporting evidence was published in Kimura (1969) and King and Jukes (1969). MacIntyre and Wright (1966) demonstrated that esterase-6 alleles are almost selectively neutral when in a homozygous genetic background. Ohta and Kimura (1969) have shown mathematically that apparent overdominance of intrinsically neutral alleles may arise due to the presence of tightly linked overdominant or ordinary dominant loci if the population size is small.

Prakash, Lewontin and Hubby (1969), rejecting the neutrality hypothesis, argued that isozyme polymorphisms might have been maintained by a kind of balancing selection since the frequencies of some specific genes are very similar over many isolated populations of D pseudoobscura, although the balancing factors have not been detected.

In the present series of papers, we have operationally defined "viability polygenes" as the means of decreasing homozygous viability slightly (Mukai 1964). If isozyme genes decrease the homozygous viability slightly, they can be classified as viability polygenes, but it is very difficult to determine what percent of viability polygenes are directly involved in isozyme formations. The above apparent contradiction (numerous isozyme polymorphisms vs. few heterozygous polygenic loci) can be explained only if the isozyme variation does not make a significant contribution to the genetic load in equilibrium and nearly equilibrium populations. This means that most, but not necessarily all, segregating isozyme loci involve neutral or nearly neutral isozyme genes at least in equilibrium or nearly equilibrium populations. The general mechanism for the maintenance of isozyme polymorphisms is still unknown.

We are grateful to Dr. J. Felsenstein for his constructive criticisms.

SUMMARY

A simulation experiment was conducted in order to predict the state of an equilibrium population on the basis of genetic parameters reported in papers of the present series (polygenic mutation rate = 0.1411–0.2117 per second chromo-
some per generation; overdominance and optimum heterozygosity in the coupling phase, and a high degree of dominance and synergistic interaction in the repulsion phase). On the criterion that the predicted and the observed homozygous genetic loads are the same, the following conclusions are reached: (1) The average degree of dominance in repulsion heterozygotes is 0.08–0.19. (2) The frequency of coupling heterozygotes which show overdominance is less than four percent. (3) The average number of polygenic heterozygous loci per second chromosome is 13–26 (excluding neutral genes). (4) The magnitude of the random genetic load is 0.15–0.22 with respect to the optimum genotype, and 0.09–0.15 with respect to originally mutant-free individuals. On the basis of the findings obtained in the present simulation, the Classical and the Balance hypotheses are discussed. Furthermore, near-neutrality of most isozyme genes in equilibrium populations is suggested.

LITERATURE CITED


PREDICTING EQUILIBRIUM


MUKAI, T. and J. F. CROW, 1971 Mutation rate and dominance of genes affecting viability in Drosophila melanogaster (to be submitted to Genetics).


