GENETIC LOAD, GENETIC VARIANCE AND NATURAL
SELECTION IN *DROSOPHILA MELANOGASTER* POPULATIONS

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SUMMARY

Four natural populations of *D.melanogaster* were analyzed for genetic variability of viability on the basis of the combination of homozygous genetic load and additive genetic variance. It was found that there is a north-to-south cline in the ratio of additive variance to homozygous load and that the dominance variance was nearly zero. The results suggest that genetic variability has been maintained by mutation-selection balance in the northernmost population but some form of balancing selection other than overdominance must be operating in the southern populations. The operation of diversifying selection due to genotype $\times$ environment interaction

KEYWORDS: Homozygous load; Additive genetic variance; Dominance variance; diversifying selection; Overdominance

is suggested.

1. Introduction

In general, a large amount of genetic variability has been maintained in any equilibrium random mating population of organisms. Viability of the individual, one of the important components of fitness, is not an exceptional case. Usually, two types of measures of genetic variability have been used: (1) genetic load and (2) genetic variance. The latter can be partitioned into additive, dominance and epistatic components. The epistatic variance for viability is generally very small. Therefore, it is not considered in this report. The genetic load as the first degree statistics was defined by Crow (1958) as follows: the proportion by which the fitness of the average genotype in the population is reduced in comparison to the best genotype. We use viability instead of fitness in the present study.

The purpose of this investigation was to analyze the mechanisms involved in the maintenance of genetic variability of viability by using information from measures of genetic load

and genetic variance simultaneously.

2. Theoretical Basis

The fitness model of WRIGHT (1931) was employed: There are two alleles, A and a at one locus. The gene frequency of the former is p and the latter q ($p+q=1.0$). The relative viabilities and the frequencies in a random mating population can be expressed as :

Genotype	AA	Aa	aa
Frequency	p^2	$2pq$	q^2
Viability	1	$1-hs$	$1-s$

where s is the selection coefficient against aa and h is the degree of dominance.

Genetic load: Genetic load in an equilibrium random mating population (random genetic load) (L_R) can be expressed as follows (HALDANE 1937) when h and s are positive:

$$L_R = 2pqhs + q^2s \quad \dots\dots(1)$$

In an equilibrium population, $\hat{q}$ can be expressed as $\hat{q} \approx \mu/chs$ where c is a factor which makes chs selection coefficient of Aa for fitness as a whole. Since $\hat{q}$ is much smaller than 1, L_R turns out to be:

$$L_R = 2\mu/c \quad \dots\dots\dots(1')$$

Homozygous load (L_I) is defined as the reduction of the average homozygote viability in comparison with the optimum genotype. The value in an equilibrium population can be expressed as:

$$L_I = qs = \mu/ch \quad \dots\dots\dots(2)$$

Homozygous load relative to the average of the random mating population $L_{I(R)}$ becomes as follows:

$$L_{I(R)} = \mu/ch - 2\mu/c = \frac{\mu}{c} \left(\frac{1}{h} - 2 \right) \quad \dots\dots\dots(3)$$

Homozygous and random genetic loads were also calculated in the case of overdominance, but these quantities are not described here because overdominance is seldom manifested in *Drosophila melanogaster* populations as will be shown later.

Genetic variance: Using the above notations, the total genetic variance (σ_g^2), additive genetic variance (σ_a^2) and dominance variance (σ_d^2) can be expressed as follows:

$$\sigma_g^2 = pq[2(1-2pq)h^2 - 4q^2h + q(1+q)]s^2 \quad \dots\dots\dots(4)$$

$$\sigma_a^2 = 2pq[(p-q)h + q]^2 s^2 \quad \dots\dots\dots(5)$$

$$\sigma_d^2 = p^2 q^2 (2h-1)^2 s^2 \quad \dots\dots\dots(6)$$

When these quantities are expressed on a chromosome basis, σ_G^2 , σ_A^2 , and σ_D^2 will be used respec-

tively in the present report.

Ratio of additive variance (σ_A^2) to homozygous load relative to the average heterozygote viability $[L_{I(R)}]$: If genetic variability is maintained in an equilibrium population by mutation-selection balance, additive genetic variance of viability turns out to be approximately $\sigma_A^2 \cong 2(\frac{\bar{u}}{c})\Sigma hs$ disregarding slight possible correlation between c and hs , since $q \ll 1$. Thus,

$$\sigma_{A/L_{I(R)}}^2 \cong \frac{2\overline{hs}}{\frac{1}{\bar{h}} - 2} \dots\dots\dots (7)$$

where $\overline{hs}$ and $\bar{h}$ are the arithmetic and harmonic means of hs and h , respectively. This quantity becomes useful to test whether or not balancing selection is common.

3. Materials and Methods

Materials: Fruit flies (*D.melanogaster*) sampled from 4 populations were employed in the present experiment : Aomori, Japan (46.60°N), Raleigh, N.C., U.S.A. (35.77°N), Orlando-Lake Placid, Florida, U.S.A. (27.17°N) and Ishigakijima, Japan (23.30°N).

Methods: Using the multiple inversion technique [the *Cy-Pm* method (cf. WALLACE 1956)] many

second chromosome lines were established from each of the above populations in the form of $Cy/+_i \times Cy/+_i$ where Cy is the dominant marker gene included in $In(2LR)SM1$.

Homozygous genetic load was estimated on the basis of the average homozygote ($+_i/+_i$) and heterozygote ($+_i/+_j$) viabilities. The homozygous viability of $+_i/+_i$ was estimated by making crosses between $Cy/+_i$ males and females. In the offspring, phenotypically Cy and wild-type flies segregate in the expected ratio of 2:1 since Cy homozygotes are lethal. Viability index (v) was expressed by:

$$v = 2a/(b+1) \quad \dots\dots\dots (8)$$

where a and b are the numbers of phenotypically Cy and wild-type flies, and the one in the denominator is added as a correction for the bias introduced when ratios are averaged (see HALDANE 1956). The heterozygote viability was estimated in the same way.

Homozygous loads were estimated by the method devised by GREENBERG and CROW (1960). Homozygous lethal load (L) and detrimental load (D) were estimated assuming multiplicative gene

action as follows:

$$D = \ln(A/C), \text{ and } L = \ln(C/B) \quad \dots\dots\dots (9)$$

where A is the average viability of heterozygotes, B is the average viability of all homozygotes, and C is the average viability of non-lethal homozygotes. It should be noted that, using the above formulae, D estimates $L_{I(R)}$ due to non-lethal deleterious genes but L estimates homozygous load due to lethal genes with respect to the optimum genotype.

The components of genetic variance were estimated by 7×7 factorial experiments using 14 independent lines extracted from the same population. Four simultaneous replications were conducted. The experiments were repeated many times with different chromosome lines.

The variance components of Row, Column, and Row $\times$ Column interaction (σ_R^2 , σ_C^2 , and $\sigma_{R \times C}^2$, respectively) were estimated from the analysis of variance for the factorial experiments. Considering that the *Cy* chromosome does not always completely suppress the effect of its homologous wild-type chromosome, the additive and dominance variances were estimated by the following formu-

lae:

$$\hat{\sigma}_A^2 \cong 4(\sigma_R^2 + \sigma_C^2 - \frac{1}{2}\sigma_{R \times C}^2) \quad \dots\dots\dots (10)$$

$$\hat{\sigma}_D^2 \cong \sigma_{R \times C}^2 \quad \dots\dots\dots (11)$$

4. Results and Analyses

Experimental results: The estimates of σ_A^2 , σ_D^2 , D or $L_{I(R)}$ due to non-lethal deleterious genes $\sigma_A^2/L_{I(R)}$ are tabulated in Table 1 for the 4 populations investigated. The latitudes of these populations are also given.

Analyses and conclusions: If overdominance is manifested at a locus, the equilibrium gene frequency of a is expressed as $\hat{q} = h/(2h-1)$. Then, the additive variance becomes 0 and all the genetic variance becomes dominance variance. Its magnitude can be expressed as $\sigma_D^2 = [(h-1)hs]^2 / (2h-1)^2$. On the contrary, if equilibrium gene frequency is determined by mutation-selection balance ($\hat{q} \cong \mu/chs$), and if h is close to 0.5 rather than 0, the dominance variance becomes nearly 0 and almost all the genetic variance becomes additive variance (MUKAI et al. 1974). Since the estimates of dominance variance were nearly 0, it is clear that overdominance is not

Table 1

Homozygous loads and the components of genetic variance for viability in four natural populations of *Drosophila melanogaster*

Population	Ishigaki-jima	Orlando	Raleigh	Aomori
Latitude	24.30°N	27.17°N	35.77°N	40.60°N
$\hat{\sigma}_A^2$	0.0175 ±0.0061	0.0227 ±0.0042	0.0096 ±0.0025	0.0027 ±0.0010
$\hat{L}_{I(R)}$ or $\hat{D}$	0.243	0.403	0.334	0.243
$\hat{\sigma}_A^2 / \hat{L}_{I(R)}$	0.072	0.056	0.029	0.010

$\hat{\sigma}_A^2$: additive variance; $\hat{L}_{I(R)}$ or $\hat{D}$: homozygous load due to non-lethal deleterious genes.

manifested in natural populations of this species.

If mutation-selection balance is a general rule, the value of $\sigma_A^2/\hat{L}_{I(R)}$ should become approximately 0.010 because, in the other experiment, $\bar{h}s$ and $\tilde{h}$ have been estimated to be approximately 0.015 and 0.25, respectively (see MUKAI 1978). Thus, only the genetic variability of the Aomori population can be explained by mutation-selection balance. In the other populations, some form of balancing selection other than overdominance is expected to be operating. Since the operation of frequency-dependent selection was already rejected by our experiment, the most probable candidate is diversifying selection due to genotype $\times$ environment interaction. A north-to-south cline of $\hat{\sigma}_A^2/\hat{L}_{I(R)}$ values supports this speculation.

It should be noted that the excess of genetic variance appears to be caused by mutations in non-coding regions but not by those at structural loci and the present finding is not inconsistent with the neutral theory of molecular evolution (KIMURA 1968).

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