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Accumulation of lethals in highly selected lines of *Drosophila melanogaster*

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Summary. Four synthetic lines of *D. melanogaster* selected for low sternopleural bristle number for 50 generations were screened for lethals on chromosome III when their mean score equalled 2.5. Each line originated from a cross between line M (previously selected for the same trait during 130 generations) and a different unselected cage population. Line M was already known to carry a recessive lethal on chromosome III affecting the selected trait, such that the bristle score of the lethal heterozygote was lower than that of the viable homozygote. Tests revealed 18 lethals, 15 of these present in at least two lines. Each line carried from 10 to 16 lethals. All lines carried groups of lethals present on the same chromosome, and at least six lethals in each line were included in such an association with a frequency of 0.18 or higher. It appears that the lethal affecting bristle score in line M has protected a segment of chromosome III from natural selection and that the remaining 14 lethals have accumulated later in that line.

Key words: Artificial selection – Selection plateau – Accumulation of lethals – Sternopleural bristle number – *Drosophila melanogaster*

Introduction

The increasing opposition of natural selection often causes a cessation of response in artificial selection experiments. In spite of genetic variation for the selected trait, a limit to selection is reached which can be characterised by an unstable equilibrium between these two forces (Al-Murrani 1974; Verghese 1974; Minvielle 1980; Nicholas and Robertson 1980).

An extreme example of this occurs when artificial selection favours the heterozygous form of a recessive lethal. In this case, selection will only change the gene frequency at this locus until all selected individuals are heterozygous for the lethal allele. At this point, the frequency of the lethal will be one-half in the selected parents and one-third in their offspring, and these values will remain unchanged for as long as the selective pressure is maintained (Hollingdale 1971). An additional consequence of selecting for lethal heterozygotes at a given locus is a reduction of the probability of losing lethal alleles at other loci that are linked in disequilibrium to the first, and therefore protected from natural selection. This will occur whether or not those alleles affect the selected trait (Madalena and Robertson 1975). Genetic drift can then raise the frequencies of such lethals up to values approaching a maximum of one-half, both in the selected and the scored individuals, as the recombination fraction between them and the artificially selected lethal tends to zero. This will cause a progressive accumulation of lethals at high frequencies in the selected line.

Continued artificial selection will therefore prevent the mean of the selected trait from returning towards its original value, but only at the expense of a continuous decline in fitness. On the other hand, relaxation of artificial selection will restore fitness, but this will be accompanied by a regression of the mean of the trait towards the value it had before selection (Lerner 1954). Experimental data on accumulation of lethals in artificially selected lines is restricted to *Drosophila*, where it has been documented on several occasions (Madalena and Robertson 1975; Yoo 1980). Also, the occurrence of lethals at high frequencies, with an effect on the selected trait, has often been reported in *Drosophila* lines that had reached a plateau after selection for a variety of traits (Al-Murrani 1974 and references therein).

The present paper describes the accumulation of lethals in four lines of *D. melanogaster* that were selected for many generations for low sternopleural bristle number, and had attained the lowest value ever reported for the trait.

Materials and methods

Four synthetic lines (MV, MCr, MDr and MPt), selected for low sternopleural bristle number, were screened for lethals.

Each of these lines originated from a cross between line M (denoted KPS[21] in López-Fanjul and Hill (1973) and previously selected for the same trait during 130 generations) and a different unselected cage population (Vallecas (V), Carboneras (Cr), Draytons (Dr) and Prat de Llobregat (Pt)). The four snynthetic lines were selected for a further 50 generations, after which the mean of the lines was the lowest reported in the literature (about 2.5 bristles). In samples from all selected lines, one generation of relaxed selection resulted in a drastic increase of the mean by about three bristles. A recessive lethal at high frequency had already been detected on chromosome III of line M, with the bristle score of the lethal heterozygote about two units (one standard deviation of the base population) below that of the viable homozygote (A. Robertson, personal communication).

Chromosomes II and III ere examined for lethals by using the Cy Ubx^{130}/Xa stock (Lindsley and Grell 1968). At generation 181 of selection, a selected sample of 15 males scoring two bristles (the lowest individual score recorded, with a class frequency of about 80% in all lines) was taken from each synthetic line, and a random sample of four second and four third chromosomes for each male was tested for lethality. The probability of a lethal carried by only one male not being detected was thus around 1/16. Lethal chromosomes were isolated and their allelic relationships tested by half-diallel crosses within males, between males within lines. and across lines. Tests were restricted to complete lethals (zero homozygote viability), incomplete lethals not being considered.

Table 1. Individual lethals (1 to 18) and the frequencies (%) of the corresponding within-line lethal association[a] (A to X) in the selected lines

Lethal	Line			
	MV	MPt	MCr	MDr
1	39 (A)	21 (D)	19 (F)	50 (I)
2	39 (A)	25 (K)	19 (F)	50 (I)
3	39 (A)	43 (L)	19 (F)	50 (I)
4	7 (B)	3 (E)	23 (Q)	50 (J)
5	7 (B)	3 (E)	35 (R)	50 (J)
6	7 (B)	3 (E)	8 (S)	50 (J)
7	35 (C)	32 (M)	15 (G)	–
8	35 (C)	11 (N)	15 (G)	–
9	–	18 (O)	19 (F)	50 (I)
10	–	11 (P)	19 (F)	50 (I)
11	7 (B)	–	15 (T)	50 (J)
12	39 (A)	–	8 (H)	–
13	7 (B)	–	–	8 (X)
14	7 (B)	21 (D)	–	–
15	35 (C)	–	8 (H)	–
16	–	–	8 (U)	–
17	–	–	8 (V)	–
18	–	–	8 (W)	–
Bristle score[b]	2.43	2.47	2.51	2.47

[a] SE of frequencies between 0.09 and 0.03
[b] SE of means between 0.06 and 0.04

Results

A total of six lethals were detected on chromosome II, none of them allelic across lines. Five of these lethals were at a low frequency (less than 0.13) and we found one of these in each of the MV, MDr and MPt lines and two in line MCr. The remaining lethal was found in line MDr at a frequency of 0.36 ± 0.03.

The 240 third chromosomes tested were divided among 113 different chromosomal types in the within-male tests, and 102 of these carried at least one lethal. Only 5% of the chromosomes examined were not lethal carriers. Within-line tests allowed a further grouping into 24 different lethal types (denoted by letters A to X). Finally, across-line tests revealed a minimum of 18 lethal genes (denoted by numbers 1 to 18) and 15 of these were shared by at least two lines, the remaining three being restricted to line MCr. Lethal types A through J appeared to be associations of two or more lethal genes. The general clustering pattern and the frequencies of the lethal types in the four lines as well as the line bristle score are presented in Table 1. A chromosome sampled from a selected line may carry several lethal types and therefore the frequencies of these types in a line do not have to add up to one. Of course, the sum of the frequencies of carrier and non-carrier chromosomes for any lethal type is unity.

Each line carried from 10 to 16 lethals on chromosome III, and at least six lethals in each line were included in a lethal type with a frequency of 0.18 or higher. Lethals 1 through 6 were present in all lines, and three of these (1, 2 and 3) were included in the most common lethal association in three of the four lines. As the number of lethals at high frequencies occurring together on the same chromosome is large, their frequencies are likely to be underestimated.

Strong lethal associations were present in all lines. Extreme examples are lines MV and MDr, in which all lethal chromosomes belonged to one of three types in a given line (A, B or C in line MV; I, J or X in line MDr; the frequencies of heterozygotes were 60% for AC in line MV and 80% for IJ in line MDr). Five of these six types carried several lethals.

Discussion

Our results reveal many more lethals than previously reported for lines at a selection limit (Madalena and Robertson 1975; Yoo 1980) and they are at unusually high frequencies. The selection story of our lines has a common part – pertaining to the parental line M –, and an independent one – corresponding to the four synthetics. That 15 third-chromosome lethals were shared by at least two synthetic lines strongly suggests their joint provenance from line M. Since one third-chromosome lethal affecting the selected trait was detected in

line M prior to the formation of the four synthetics, the remaining 14 lethals may have accumulated afterwards in that line, drifting to high frequency while linkage with the first, artificially selected, lethal masked them from natural selection. While these 14 lethals need not affect the selected trait, we could not estimate any such effects, because chromosomes carrying single lethals were not generally found.

Lethal associations and repulsion-linked lethal groups of considerable stability were found. Formation of synthetic lines will favour the breakdown of lethal associations occurring in line M, and the subsequent formation of new ones. This will thus increase the probability of detecting lethals already present in line M and, accordingly, the lethals in our lines far outnumber previous estimates. On the other hand, lethals appearing after the formation of synthetics are more difficult to expose, given the large number contributed by line M. Unique lethals on chromosome III were only detected in line MCr.

Our results can be explained by assuming that a single lethal affecting bristle score – the one detected in line M –, has protected a segment of chromosome III from natural selection, and other lethals have consequently accumulated there. This lethal should have a frequency between ⅓ and ½ in our sample of scored individuals. Although lethals 1, 2 and 3 are likely candidates, a more precise designation cannot be made because individual effects cannot be estimated.

Lethal induction by hybrid dysgenesis (Kidwell et al. 1977) could provide a possible explanation for the unusually large number of lethals at high frequencies observed in this experiment, as we were always dealing with synthetic lines (even line M is a synthetic formed by crossing the Kaduna and Pacific populations). If this were so, the rate of mutation in line M would have increased and the process of lethal accumulation would have been accelerated as compared to lines with a similar selection story coming from a single base population. However, associations including lethals 1 and 5 showed stability and they were at similar frequencies in the four synthetic lines 15 generations after they were first detected. This may argue against their original induction by hybrid dysgenesis. Unfortunately, all lines in this experiment were accidentally lost and no further test for the involvement of hybrid dysgenesis was possible.

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