

INFERENCES ON THE NATURE OF GENETIC VARIATION FOR VIABILITY FROM ARTIFICIAL SELECTION AND INBREEDING IN *DROSOPHILA*

A. Pérez-Figueroa, S.T. Rodríguez-Ramilo, J. Fernández and A. Caballero

Departamento de Bioquímica, Genética e Inmunología, Facultad de Ciencias,
Universidad de Vigo, 36200 Vigo, Spain

INTRODUCTION

The genetic properties of life-history traits have been investigated for a long time. On the one hand, a number of estimates of heritability and inbreeding depression are available for reproductive traits in a variety of species (Lynch and Walsh, 1998). On the other, estimates of mutational parameters, such as mutational variances and rates and effects of deleterious mutations, are also available for such traits (Lynch *et al.*, 1999 ; García-Dorado *et al.*, 1999). These two sorts of information can be combined, assuming a simple genetic model, to obtain information on the genetic architecture of life-history traits. We carried out an experiment of artificial selection and inbreeding with a natural population of *Drosophila melanogaster*, and obtained estimates of selection response and inbreeding depression for egg-to-adult viability. Using a range of mutational parameters and assuming a simple deleterious mutation-selection balance model of variation, we simulated the experimental conditions and compared the simulated results with the empirical observations. Our results suggest that a model assuming mutation-selection balance can explain the frequency of genes affecting viability in the natural population, but contrasting models of mutation cannot be discarded.

MATERIAL AND METHODS

Base population, culture conditions and trait scored. More than 300 pregnant females were captured in a wine cellar in Vigo (Spain). These females were put into glass vials with 10 ml medium added, and a male and a female progeny were collected from each vial. For the next two generations matings were made at random avoiding full-sib matings, with a male and a female offspring contributed by each couple. After these two generations the experiment of inbreeding and selection was started. Flies were reared in the standard medium formula of this laboratory (brewer's yeast-agar-sucrose). All cultures were incubated at $25\pm 1^\circ\text{C}$ and maintained under continuous lighting. Flies were handled at room temperature under CO_2 anaesthesia. The trait considered was egg-to-adult viability, which was evaluated as follows. Four-day-old virgin females were individually mated to males of the same age in vials. After two days, both parents were transferred to a new vial with fresh medium to which food colouring was added. Oviposition was allowed for 24 hours. 30 eggs were transferred to a fresh vial and allowed to develop into adults. The trait measured was the proportion of adults emerged from the 30 eggs laid.

Selection and inbreeding procedure. A series of treatments were carried out: **SN:** Selected non-inbred. 40 males and 40 females were mated at random in vials avoiding full-sib mating. The viability of their offspring was evaluated and the 25% families with the largest viability (4

males and 4 females of each of the top 10 vials) were selected as parents for the next generation. **CN**: Control non-inbred. As SN, except that selection of parents was at random. **SI**: Selected inbred. The same procedure as in SN was followed except that 75% of matings (30 out of 40) were between full-sibs. **CI** : Control inbred. The same as in SI except that selection of parents was at random. Each treatment was carried out for five generations and replicated three times. Inbreeding coefficients were obtained from the pedigree, which was recorded for the whole experiment. Inbreeding depression was estimated as $[\ln(v_0) - \ln(v_t)] / F_t$, where v_t and F_t are the mean viability and mean inbreeding coefficient at generation t .

Mutational parameters and simulations. We carried out simulations resembling the experimental conditions. An ancestral population was first set up in which gene frequencies were at mutation-selection balance following equation (6.2.6) of Crow and Kimura (1970). Fitness was controlled by a large number of biallelic loci with variable effects in homozygosis, s , and dominance coefficients, h . Fitness action was assumed to be multiplicative among loci. Deleterious mutations were assumed to appear at a rate λ per haploid genome and generation and were sampled from a gamma distribution with shape parameter β and mean effect $E(s)$. The dominance coefficient of mutations, h , was obtained from a uniform distribution between 0 and $\exp(-ks)$, where k is a constant allowing the mean dominance coefficient, $E(h)$, to be the desired one. A range of models were used in the simulations as follows: Model A ($\lambda = 0.5$, $E(s) = 0.02$). Model B ($\lambda = 0.1$, $E(s) = 0.05$). Model C ($\lambda = 0.015$, $E(s) = 0.2$). Therefore, model A assumed many mutations of small effect and model C assumed few mutations of large effect. These are the two contrasting models proposed in the literature for spontaneous mutations affecting viability in *Drosophila*. Model B was chosen as an intermediate situation. The parameter β was chosen so that the mutational variance explained by each model was 0.0006, a value experimentally observed (García-Dorado *et al.*, 1999). The mean dominance coefficient was allowed to take values $E(h) = 0.15, 0.2, 0.3$ and 0.4 . In all cases, lethal mutations were also considered, appearing at a rate 0.015 per generation and dominance $h = 0.02$ (Simmons and Crow, 1977). Simulations were replicated 3000 times and 2.5% and 97.5% percentiles were taken to contrast results from different models and observations.

RESULTS AND DISCUSSION

Experimental results. Figure 1A shows the average viability of the lines deviated from the control non-inbred population to remove unexplained environmental effects. Figure 1B shows the average coefficient of inbreeding in each case. All plotted lines are the average of the three replicates, as the agreement between replicates was very high in all cases.

The response to selection was very small for the selected non-inbred (SN) lines, giving a realised heritability of 0.043 ± 0.037 . This denotes that alleles increasing viability should be at very high frequencies in the wild population. The control inbred (CI) lines suffered inbreeding depression particularly in the first two generations. This was estimated as 1.3% decrease in mean per 1% increase in inbreeding, a value slightly larger than usually obtained for this trait (Lynch and Walsh, 1998).

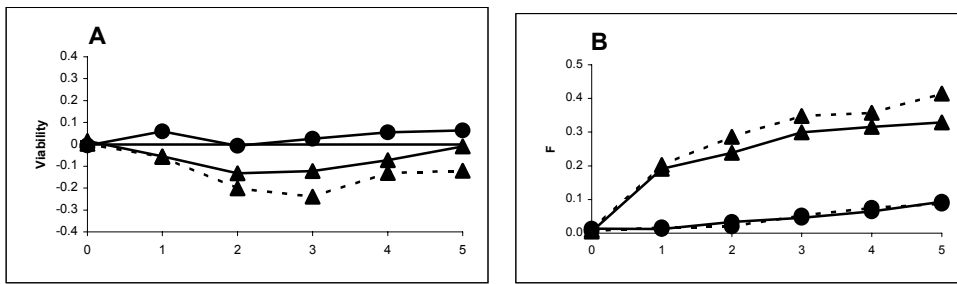


Figure 1. (A) Average viability, deviated from the viability of CN, and (B) average inbreeding coefficient for CN (broken line with circles), SN (continuous line with circles), CI (broken line with triangles) and SI (continuous line with triangles)

The selected inbred (SI) lines showed inbreeding depression in the first generation at a similar rate as the CI lines, but there was a recovery towards the control non-inbred value, denoting purging selection. The realised heritability for these lines when deviated from the inbred control line was 0.092 ± 0.004 .

Simulation results. The behaviour of the simulations was in remarkable agreement with the observed results. An example of simulation is depicted in Figure 2. The results suggest that a simple model assuming mutation-selection balance in an infinite population can explain the frequency of genes controlling viability in a wild population.

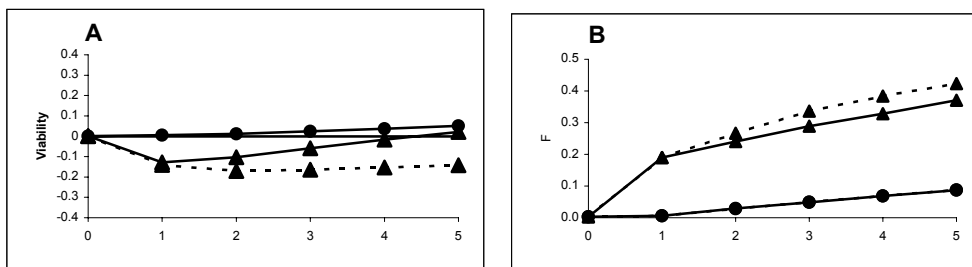


Figure 2. (A) Average viability, deviated from the viability of CN, and (B) average inbreeding coefficient from simulations for model E ($\lambda = 0.015$, $E(s) = 0.2$) with $E(h) = 0.15$ (see Figure 1 for the definition of lines)

The results from the different simulation models were compared with the empirical observations with the objective of finding what sort of models could explain all observations. Interestingly, all models could satisfactorily explain the levels of inbreeding in the CN, SN (not shown) and CI lines (see Table 1), as well as the selection response observed in the SN and SI lines (Table 1). The only clear discrepancies between models occurred with the magnitude of the inbreeding depression as well as with the inbreeding coefficient of the SI lines (Table 1). For some models the selected inbred lines did not recover the levels of the CN lines and the inbreeding coefficient was restrained. Overall, a model of many mutations of small effect (model A) with large average dominance (0.4) or a model of few mutations of

large effect (model C) with small average dominance (0.15) were able to explain all observations. This is unfortunate because these precise models of mutations are being currently debated as alternatives for viability in *Drosophila* (Lynch *et al.*, 1999; García-Dorado *et al.*, 1999).

Table 1. Comparison of empirical and simulated values

Model (E[h])	Inbreeding Depression ^A	F for CI at gen. 5 ^B	F for SI at gen. 5 ^C	Response of SN ^D	Response of SI ^E
Observed	1.3	0.414	0.328	0.009	0.017
A (0.15)	3.1	0.423	0.287	0.007	0.029
A (0.2)	3.0	0.423	0.290	0.007	0.027
A (0.3)	2.7	0.423	0.300	0.006	0.023
A (0.4)	1.6	0.422	0.332	0.005	0.016
B (0.15)	2.6	0.422	0.285	0.010	0.039
B (0.2)	2.5	0.422	0.290	0.010	0.036
B (0.3)	1.9	0.423	0.310	0.009	0.032
B (0.4)	0.9	0.423	0.383	0.009	0.024
C (0.15)	1.3	0.423	0.371	0.009	0.035
C (0.2)	1.0	0.424	0.401	0.009	0.030
C (0.3)	0.7	0.423	0.420	0.009	0.023
C (0.4)	0.6	0.423	0.420	0.009	0.021

^AInbreeding depression for the first two generations in the CI line; ^{B,C}Average inbreeding coefficient at generation five for the CI and SI line, respectively; ^{D,E}Average response per generation to selection for the SN and SI lines, respectively, relative to their corresponding controls. Bold face values denote non-significance departures from observed values.

In conclusion, the results indicate that a simple model of mutation-selection balance in an infinite population can explain the results of inbreeding and selection experimentally obtained. However, contrasting models of mutation proposed in the literature cannot be distinguished, as they were able to explain satisfactorily all observations.

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