

## Dominance modification in a fluctuating environment

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### SUMMARY

This paper examines the suggestion of Gale & Mackay (1979) that dominance modification will be slower in an environment with fluctuating selection coefficients than in a constant environment. The case of statistical independence between successive environments is studied. It is shown that there is an effect in the suggested direction, but that it is quantitatively slight with biologically plausible values for the parameters involved. It therefore seems unlikely that the phenomena noted by Charlesworth (1979) can be explained in these terms.

### 1. INTRODUCTION

Fisher's (1928) theory of dominance modification has usually been worked out in terms of selection for a gene which controls the degree of dominance at a locus maintained at equilibrium under mutation-selection balance (Sved & Mayo, 1970). The intensity of selection on a rare modifier of dominance is, on this model, largely independent of the selection coefficient against the mutant homozygote at the locus experiencing dominance modification. As pointed out by Charlesworth (1979), this seems to be inconsistent with the experimental findings on viability mutations in *Drosophila*; lethal mutations are much closer to recessivity than deleterious genes of small effect (Simmons & Crow, 1977). Gale & Mackay (1979) have suggested that these observations could be reconciled with the theory of dominance modification if mildly deleterious genes are subject to greater variability in the direction and intensity of selection than genes of drastic effect. They propose that temporal fluctuations in fitnesses could result in occasions when the mutant gene is neutral or at an advantage over its wild-type allele, and hence not subject to selection for recessivity.

The purpose of this note is to investigate this suggestion quantitatively by considering dominance modification in the simplest class of model of a temporally fluctuating environment: that in which the fitness of a given genotype in one generation is independent of its value in the preceding generation. One would anticipate that positively auto-correlated environments should have properties intermediate between this case and the usual case of a constant environment. The results derived here should therefore provide an extreme contrast to the case of a constant environment.

### 2. THE MODEL AND ITS ANALYSIS

We assume a single autosomal locus with two alleles  $A$  and  $a$ , in an infinitely large, randomly mating, discrete-generation population.  $A$  mutates to  $a$  with probability  $u$  per gamete per generation. In the absence of dominance modifiers, there is intermediate

dominance at this locus, so that the fitness of  $AA$ ,  $Aa$  and  $aa$  in generation  $i$  can be written as  $1$ ,  $1 - \frac{1}{2}s_i$  and  $1 - s_i$  respectively. There are temporal fluctuations in  $s_i$ , such that it has a mean of  $\langle s \rangle$  and a variance  $V_s$ . (Angle brackets are used to denote expectations.) With weak selection, as is necessary for the approximations developed below,  $\langle s \rangle$  is so small that  $V_s$  is adequately approximated by  $\langle s^2 \rangle$ . Successive values of  $s_i$  are independently distributed, and moments of third and higher order are assumed to be negligible.

Hartl (1977) has given a general treatment of mutation-selection balance in a fluctuating environment of this type, and shown that a stationary distribution of gene frequency is reached under suitable conditions; its form depends solely on  $\langle s \rangle$ ,  $V_s$  and  $u$ . The following account is based on Hartl's results. The notation employed here differs from his, and equation (3b) below corrects a minor error in his formula for the corresponding case (Hartl, 1977, p. 693), so that an outline of the derivation of the gene frequency distribution will be presented. This is then used to obtain a formula for the intensity of selection on a dominance modifier.

Let  $p_i$  and  $q_i$  be the frequencies of  $A$  and  $a$  in a generation  $i$ . Neglecting terms of order  $us_i$ , the change in frequency of  $a$  between generations  $i$  and  $i+1$  is

$$\Delta q_i = up_i - \frac{s_i p_i q_i}{2(1 - s_i q_i)}. \quad (1a)$$

Neglecting terms of order  $s_i^3$  and higher, this becomes

$$\Delta q_i \approx up_i - \frac{1}{2}s_i p_i q_i (1 + s_i q_i). \quad (1b)$$

From standard diffusion theory, the stationary distribution of gene frequency is characterized by the mean and variance of  $\Delta q$  for a given value of  $q$ , taken over the distribution of  $s_i$ , and neglecting terms of order  $s_i^3$  and higher. From equation (1b), these are respectively

$$M_{\Delta q} = uq - \frac{1}{2}\langle s \rangle pq - \frac{1}{2}V_s p q^2, \quad (2a)$$

$$V_{\Delta q} = \frac{1}{4}V_s p^2 q^2. \quad (2b)$$

The probability density function for  $q$  is then

$$\phi(q) = \frac{C}{V_{\Delta q}} \exp \left\{ 2 \int \frac{M_{\Delta q}}{V_{\Delta q}} dq \right\}, \quad (3a)$$

where  $C$  is a normalizing constant, chosen such that  $\int_0^1 \phi(q) dq = 1$ . Carrying out the integration, we obtain

$$\phi(q) = \frac{C}{V_s} p^{2(A+1)} q^{-2(A+1)} \exp - \left\{ \frac{8u}{qV_s} \right\}, \quad (3b)$$

where

$$A = (2\langle s \rangle - 4u)/V_s.$$

According to the criterion given by Hartl (1977), p. 693, the stationary distribution exists if  $2(A+1) > 1$ , i.e. if  $\langle s \rangle + \frac{1}{2}V_s > 2u$ . It is easily seen that the modal value of  $q$  is  $2u/(\langle s \rangle + \frac{1}{2}V_s)$  so that this condition is equivalent to the existence of a mode. From now on, it will be assumed that  $u$  is sufficiently small for this condition to be satisfied.

The above formula for  $\phi(q)$  can be used to obtain an expression for the intensity of selection on a dominance modifier. We use Wright's (1929, 1969) approach, which assumes a rare modifier in approximate linkage equilibrium with the selected locus. Several investigations have shown that this yields an excellent approximation to more general situations, in the constant environment case (Sved & Mayo, 1970; Karlin & Feldman, 1971). We write the fitnesses of  $AA$ ,  $Aa$  and  $aa$  with arbitrary dominance as  $1$ ,  $1 - hs_i$  and  $1 - s_i$  respectively. The increase in fitness caused to a heterozygote by modifying

the dominance coefficient  $h$  from its initial value of  $\frac{1}{2}$  to  $\frac{1}{2} - \Delta h$  is  $s_i \Delta h$ . In generation  $i$ , the frequency of heterozygotes is  $2p_i q_i$ , yielding a net change of  $2p_i q_i s_i \Delta h$ . If the dominance modifier is rare, the mean fitness of the population in generation  $i$  is approximately  $1 - s_i q_i$ , because of the assumption of initially intermediate dominance. The net fitness of carriers of the dominance modifier, relative to that for the initial population, is thus  $1 + t_i \Delta h$ , where

$$t_i = \frac{2p_i q_i s_i}{(1 - s_i q_i)}$$

so that

$$t_i \approx 2p_i q_i s_i + 2p_i q_i^2 s_i^2. \quad (4)$$

If  $s_i$  is constant at  $s$ , then from standard theory the equilibrium value of  $q$  is  $q \approx 2u/s$ , provided that  $u \ll s$ . Neglecting terms in  $q^2$ , we obtain the standard result

$$t \approx 4u. \quad (5)$$

If the environment is fluctuating, the best estimate of the net intensity of selection on the heterozygous carriers of a rare gene is given by the geometric mean of their fitnesses over the distribution of environmental states, relative to the fitnesses of individuals homozygous for the initially prevalent allele (Haldane & Jayakar, 1963; Gillespie, 1973; Hartl, 1977). In the present case, therefore, we need to obtain the geometric mean of  $1 + t_i \Delta h$ . The coefficient of selection on the dominance modifier can be expressed as the deviation of this quantity from 1, and will be written as  $t \Delta h$ .

If  $\Delta h$  is small, as may reasonably be assumed,  $1 + t \Delta h$  is adequately approximated by the arithmetic mean of  $1 + t_i \Delta h$ , so that

$$t \approx \langle t_i \rangle. \quad (6)$$

It is evident that, with statistical independence of  $s_i$  and  $s_{i-1}$ ,  $s_i$  and  $q_i$  must also be independent, once the stationary state has been reached. We can then substitute from equation (4) into equation (6) to obtain

$$t \approx 2\langle pq \rangle \langle s \rangle + 2\langle pq^2 \rangle V_s. \quad (7)$$

Using the steady-state equation (3b),  $\langle pq \rangle$  and  $\langle pq^2 \rangle$  can be obtained as  $\int_0^1 pq \phi(q) dq$  and  $\int_0^1 pq^2 \phi(q) dq$  respectively. It is useful to note that, if the mean and variance of  $q$  are written as  $\langle q \rangle$  and  $V_q$ , we have  $\langle pq \rangle = \langle q \rangle - V_q$ . Owing to the complexity of equation (3b) it is not possible to obtain algebraic formulae for  $\langle q \rangle$ ,  $V_q$  and  $\langle pq^2 \rangle$ . Numerical integration using the Clenshaw-Curtis method was therefore performed.

### 3. RESULTS AND DISCUSSION

Table 1 shows some examples of the above quantities, assuming  $u = 10^{-5}$  and a range of values of  $\langle s \rangle$  and  $V_s$ . The values of  $t$  should be compared with the value of  $4 \times 10^{-5}$  for a constant environment, given by equation (5). It will be seen that, unless  $\langle s \rangle$  is very close to zero,  $t$  is close to the constant environment value. Gale & Mackay's (1979) suggestion that fluctuating environments tend to reduce the intensity of selection for dominance modification is qualitatively borne out by these results, although the effects are slight. There is no reason to suppose that they would be much altered by taking an initial  $h$  value other than 0.5, provided it was not too close to zero.

The question arises as to whether these effects are sufficient to account for the facts discussed by Charlesworth (1979). Assuming an initial  $h$  value of 0.5, the maximum possible evolutionary change in  $h$  (to complete recessivity) is 0.5. The *Drosophila* data on mutations affecting egg-to-adult viability suggest that, on the theory of dominance

Table 1. *The intensity of selection on a dominance modifier in a fluctuating environment ( $t$ )*

$\langle s \rangle$	$V_s$	$\langle q \rangle$	Modal value of $q$	$V_q$	$t$ ( $\times 10^5$ )
0	0.001	0.1208	0.0400	0.012034	3.52
0.0001	0.0001	0.1736	0.1333	0.005059	3.31
0.0001	0.001	0.0894	0.0333	0.006718	3.64
0.001	0.001	0.0196	0.0133	0.000119	3.92
0.001	0.01	0.0140	0.0033	0.000607	3.94
0.01	0.01	0.0020	0.0013	0.000009	3.98
0.01	0.10	0.0017	0.0003	0.000033	3.99

See text for further explanation.

modification, lethals have been selected to within about 94 % of this limit, whereas genes of small effect are only about 40 % of the way to the limit (cf. Simmons & Crow, 1977). Such a difference requires at least as big a difference in the rate of selection of dominance modifiers, i.e. we need a rate of selection of modifiers of dominance of lethal mutations which is at least twice that for genes of small effect. Assume, as proposed by Gale and Mackay, that lethals are lethal in most environments, and so have negligible  $V_s$ , whereas mutations of small effect are subject to considerable fluctuations in their selection coefficients. The *Drosophila* data suggest a mean homozygous selective disadvantage of about 0.02 for viability mutations of small effect. This may be an overestimate for reasons associated with the experimental design (Simmons & Crow, 1977); on the other hand, the only component of fitness estimated in the experiments was egg-to-adult viability under standard culture conditions, which contributes to an underestimation of the net selective effects of the mutations. A value for  $\langle s \rangle$  of 0.01 is probably conservative. The results derived here therefore suggest that fluctuating environments are unlikely to have a significant effect on dominance modification of the type envisaged by Fisher. Similar remarks apply to Haldane's (1930) theory of selection for isalleles with lower  $h$ .

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