GENETIC VARIATION IN A HETEROGENEOUS ENVIRONMENT. II. TEMPORAL HETEROGENEITY AND DIRECTIONAL SELECTION[1]

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ABSTRACT

The maintenance of genetic variation is investigated in a finite population where selection at an autosomal locus with two alleles varies temporally between two environments and the heterozygote has an intermediate fitness value. When there is additive gene action and equal selection in both environments, the autocorrelation between subsequent environments must be negative for more maintenance of genetic variation than for neutrality. The maximum maintenance occurs when there is equal selection in the two environments and the autocorrelation approaches -1.0 (for a stochastic model), or when there is short repeating cycle such as one related to seasons. Also comparison of the effects of stochastic variation in selection in finite and infinite populations is made by using Monte Carlo simulation. One situation was found where temporal environmental variation maintains genetic variation very effectively even in a small population and that is when there is evolution of dominance, i.e., the heterozygote is closer in fitness to the favored homozygote than the other homozygote. An important conclusion is that in a finite population genetic tracing of environmental change, particularly when there is a positive autocorrelation between environments or a long environmental cycle, leads to an increased loss of genetic variation making such a response undesirable in the long term, a result different from that in infinite populations.

HETEROGENEITY in the environment is often cited to be an important factor in maintaining both morphological and electrophoretic genetic polymorphism. LEVENE (1953), DEMPSTER (1955), and HALDANE and JAYAKAR (1963) first demonstrated theoretically how genetic variation could be maintained in an infinite population when the population existed in a heterogeneous environment (see HEDRICK, GINEVAN and EWING, 1976 for a recent review). As I have discussed previously (HEDRICK 1974), the conditions for a stable polymorphism in a diploid infinite population when environmental variation is spatial (LEVENE's model) are significantly broader than for the case when environmental variation is temporal (HALDANE and JAYAKAR's model). Furthermore, I demonstrated that only specific patterns of temporal environmental variation enhance the maintenance of genetic polymorphism in a finite popu-

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lation while other patterns of temporal environmental variation may actually reduce the amount of genetic variation, e.g., when there is a positive autocorrelation between the environments of subsequent generations.

This study also considers temporal environmental variation but where the heterozygote has a fitness between that of the two homozygotes and the direction of selection is reversed in different environments. In the present formulation, however, there is generally "marginal overdominance" (using geometric means) while in the previous paper, which considered the absolute dominance model, there was no marginal overdominance.

METHODS

The approach used to determine the relative effectiveness of different selective values in maintaining genetic variation in finite populations was outlined in detail in HEDRICK (1974). In general, different selective regimes show different abilities to retain genetic variation in finite populations. The relative effectiveness of a particular selective regime in maintaining genetic variation can be evaluated by using the retardation factor (ROBERTSON 1962; HEDRICK 1972). The retardation factor is defined as $(2N\lambda)^{-1}$ where N is the population size and λ is the rate of steady decay. If there is neutrality (no differential selection), $\lambda=1/2N$ and the retardation factor is equal to 1.0. But if $\lambda<1/2N$, the retardation factor is greater than 1.0, and the model being examined is able to maintain genetic variation in a finite population more effectively (i.e., longer) than neutrality. Therefore, the retardation factor provides an approach to compare the effectiveness of different types of selection in maintaining genetic variation in finite populations.

Two basic types of temporal environmental heterogeneity are considered: (1) a deterministic environmental sequence in which environments occur in a definite repeated cycle and (2) a stochastic model where the transition probabilities between subsequent environments are specified. The techniques used in the finite population size examples are the same as I have used before (HEDRICK 1974) but in the infinite population examples given in Table 1 a Monte Carlo simulation was used. In these infinite population runs, the sequence of environments was determined by comparing a uniform random number to the probability of transition from one environment to another. To insure the accuracy of the Monte Carlo results, 6000 runs were made of each parameter set.

The genetic model used is a general one which allows the specification of the relative fitness values in terms of different dominance levels and different selective coefficients in the two environments as follows:

	Genotype		
Environment	A_1A_1	A_1A_2	A_2A_2
1	1	$1-h_1s_1$	$1-s_1$
2	$1-s_2$	$1-h_2s_2$	1

where h_1 and h_2 indicate the degree of dominance and s_1 and s_2 are the selection coefficients in environments 1 and 2. If $h_1=h_2=0.5$, then the fitness values are additive in both environments. With additivity the model can be transformed to the one below which sets the relative fitness values of the heterozygote equal to unity rather than the genotype of highest fitness.

	Genotype		
Environment	A_1A_1	A_1A_2	A_2A_2
1	$1+s'_1$	1	$1-s'_1$
2	$1-s'_2$	1	$1+s'_2$

where $s'_1=\frac{1}{2}s_1/(1-\frac{1}{2}s_1)$ and $s'_2=\frac{1}{2}s_2/(1-\frac{1}{2}s_2)$.

RESULTS

Effect of environmental pattern: What effect does the pattern of subsequent environments have on the maintenance of genetic variation? If equal time is spent in both of the environments and the environmetal sequece is stochastically determined, there can be different levels of autocorrelation between subsequent environments. Different levels of autocorrelation can have a striking affect on the maintenance of genetic variation as shown in Figure 1 which gives the retardation factor for the additive model ($h_1 = h_2 = 0.5$) with equal selection ($s_1 = s_2 = 0.5$) for different levels of autocorrelation and population size.

Several important generalizations can be made about these results: (1) Only when there is a negative autocorrelation does selection cause a greater maintenance of genetic variation than neutrality, i.e., the retardation factor > 1.0. Also with a negative correlation, the retardation factor increases with increasing population size. (2) When the autocorrelation is equal to 0.0, selection has no effect in a finite population, as measured by the retardation factor. Other parameters of the stable gene frequency distribution such as the σ_q^2 and other moments are also the same as for neutrality. (For very strong selection there is a very slight difference from neutrality.) Furthermore, this result is independent of population size. (3) When there is a positive autocorrelation, then selection causes a faster elimination of variation than neutrality and as the population size becomes larger, the elimination is even faster.

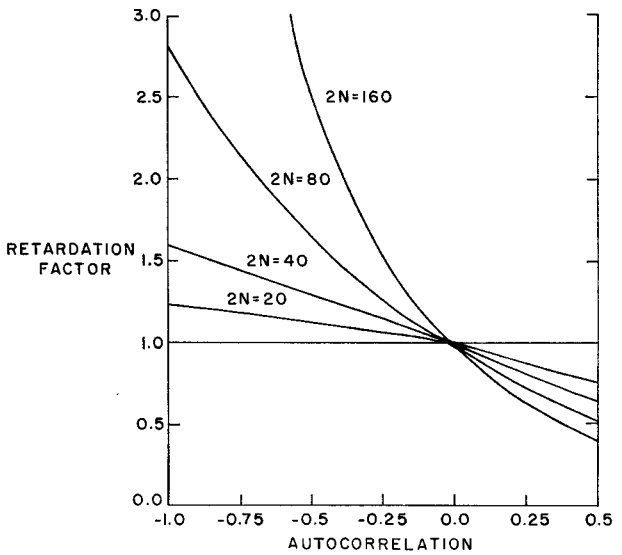

FIGURE 1.—The retardation factor for a symmetrical additive model with four different population sizes and different levels of autocorrelation between subsequent environments. The horizontal line at 1.0 indicates the value of the retardation factor when there is neutrality. The fitness of the genotypes A_1A_1, A_1A_2, and A_2A_2 in environment 1 are 1, $1-h_1s_1$ and $1-s_1$ and in environment 2 are $1-s_2$, $1-h_2s_2$ and 1. In this example $s_1 = s_2 = 0.5$ and $h_1 = h_2 = 0.5$.

The retardation factor allows one to compare the effect of selection and drift in a finite population to the effects of genetic drift in a finite population of the same size not undergoing any selection. But variation in the direction of selection by itself also causes dispersion in the gene frequency distribution in an infinite population. (See GILLESPIE 1972 and COOK and HARTL 1974 for a discussion of the effects of genetic drift versus variation in the direction of selection.) To understand the effect of stochastic selection by itself in an infinite population and compare it to the effect of stochastic selection in finite populations, the variance in the gene-frequency distribution can be used. Table 1 gives the variance in the gene-frequency distribution for three levels of autocorrelation and for three finite population sizes and an infinite population where N is the population size. The gene-frequency distribution (and its variance) for the infinite population size was obtained from the gene frequencies of 6000 Monte Carlo replicates.

The results of this simulation can be summarized in the following way: (1) the variance in the gene-frequency distribution for both the infinite and finite populations increases with higher autocorrelation, i.e., when it increases from -0.5 to 0.5. (2) The variance in the gene-frequency distribution for the finite populations declines with increasing size. This is due, of course, to the lessening effect of genetic drift in larger populations. Along with these changes, (3) the percentage of variance that is explained by the stochastic selection effects increases with higher autocorrelation and larger population size.

For example, for a population size of $2N = 80$ and an autocorrelation of 0.5 after 10 generations, 84% of the variance is due to stochastic selection. On the other hand, for a smaller population size ($2N = 20$) and a negative autocor-

TABLE 1

The variance in gene frequency when selection is acting stochastically between two environments in finite populations of size N and infinite populations.

The fitness of the genotypes A_1A_1, A_1A_2, *and* A_2A_2 are 1.0, .75 and .5, .5, .75 and 1.0 in the two environments. In parentheses is the variance explained for a finite population by an infinite population having the same selection regime.

		Autocorrelation		
		-0.5	0.0	0.5
	$2N$			
Generation 10	20	.107(17%)	.119(34%)	.141(57%)
	40	.064(29%)	.081(50%)	.112(72%)
	80	.041(45%)	.061(67%)	.096(84%)
	∞	.019	.041	.081
Generation 20	20	.159(16%)	.172(34%)	.195(53%)
	40	.099(26%)	.121(48%)	.158(66%)
	80	.062(42%)	.089(65%)	.133(78%)
	∞	.026	.058	.104
Generation 40	20	.214(15%)	.223(32%)	.236(53%)
	40	.148(22%)	.173(41%)	.209(59%)
	80	.091(35%)	.127(56%)	.179(69%)
	∞	.032	.071	.124

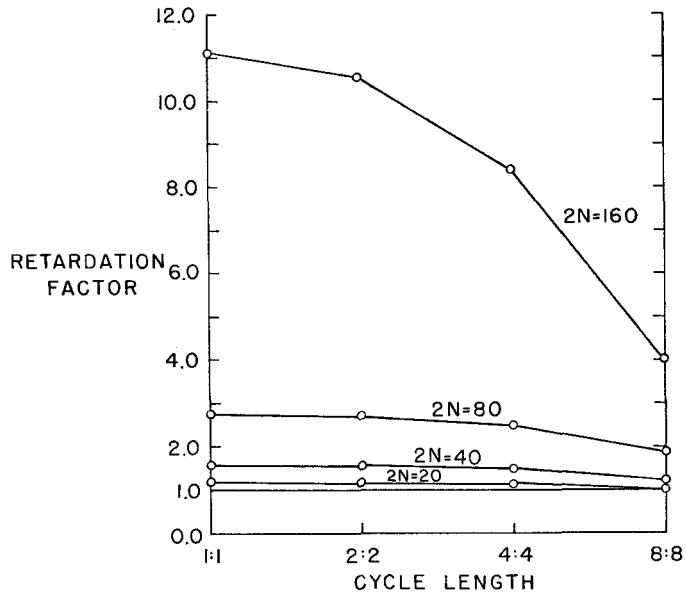

FIGURE 2.—The retardation factor for different cycle lengths and four population sizes when equal numbers of generations are spent in each environment. In this example the fitness values are the same as in Figure 1.

relation (-0.5) only 17% of the variance can be attributed to stochastic selection. The proportion of variance explained by stochastic selection declines somewhat over time, but the effects of population size and autocorrelation remain consistent.

Equal time can also be spent in each of the environments with the sequence of environments having a definite cycle. In this case, the number of consecutive generations spent in each environment may vary (varying cycle length). Figure 2 illustrates the relationship between the retardation factor and cycle length for four population sizes, again for the additive model with equal selection.

As can be seen for $2N = 20$, 40, and 80 the length of the cycle has little effect on the retardation factor. In fact for cycle lengths up to 4:4, there is virtually no difference in the retardation factor for these population sizes. However, with a long cycle length and a large population size, there is a pronounced reduction in the retardation factor. For example, with an 8:8 cycle and $2N = 160$, the retardation factor is only 35% of that for a 1:1 cycle for the same population size.

An explanation for this phenomenon is given in Figure 3 where the average gene frequencies for the unfixed distributions with $2N = 160$ for the four cycle lengths in Figure 2. One can see that for the 8:8 cycle, the gene frequency fluctuates widely, ranging from 0.242 to 0.758. For the 1:1 cycle, however, the gene frequency only fluctuates from 0.463 to 0.537. With the 8:8 cycle, a large amount of fixation occurs in the generations of low and high gene frequency. On the other hand for the 1:1, 2:2, and 4:4 cycles, fixation occurs at fairly similar rates in all generations in the cycle. This explains why the

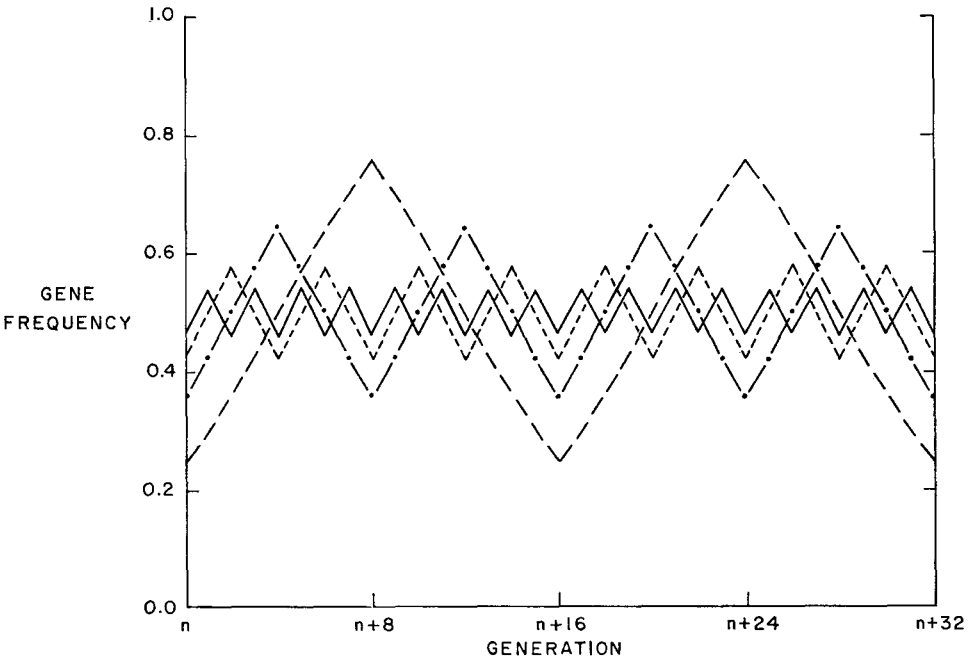

FIGURE 3.—The average gene frequency for unfixed classes of the gene frequency distribution after the steady rate of decay has been reached for $2N = 160$. The gene frequency is given for all the generations in cycles of 1:1 (solid line), 2:2 (short, broken line), 4:4 (dot-dash line) and 8:8 (long, broken line).

retardation factor is so much lower for the 8:8 cycle. With smaller population size, fixation occurs at similar rates throughout all generations, even for the 8:8 cycle because the mean gene frequency of the unfixed classes does not fluctuate as widely at these lower population sizes.

HARTL and COOK (1973) have pointed out that only when the geometric means of all the genotypes are equal is there neutrality in an infinite population. [I have found that given equal geometric means in a finite population, only when there is an environmental switch every generation (autocorrelation of -1.0) is the retardation factor equal to that for neutrality.] If the autocorrelation is greater than -1.0 or the cycle longer, then the retardation factor becomes less than one. As a result, the variation in selection that may be neutral overall in an infinite population will actually drive out variation in a finite population for most environmental patterns. The same results are also true for a haploid model where the geometric means of the genotypes are equal.

Effect of dominance: How important is the effect of dominance on the maintenance of genetic variation? The heterozygote may not be exactly intermediate between the homozygotes as assumed in the previous section. As a first approximation to relax the assumption of addivity, it can be assumed that dominance is the same in both environments, i.e., the fitness of the heterozygote is close to the fitness of the same homozygote in both environments. Since differ-

ent homozygotes are at an advantage in the two environments, equal dominance based on h values is when $h_1 = 1.0\text{-}h_2$, (Although at first thought equal dominance would seem to be when $h_1 = h_2$, this in fact constitutes a reversal of dominance in the different environments in this model.)

What level of dominance assuming equal dominance allows the greatest retention of genetic variation? Figure 4A gives the retardation factor for equal dominance when h_2 ranges from 0.0 to 0.6 for three levels of autocorrelation for $2N = 80$. (These curves are symmetric around $h_2 = 0.5$. In order to conserve space the values of h_1 from 0.6 to 1.0 are not given.) It is apparent for all three autocorrelation values, the maximum maintenance of genetic variation occurs when there is additivity, i.e., $h_1 = h_2 = 0.5$. A wide range of h values, however, maintains genetic variation more effectively than neutrality when there is a large negative autocorrelation between subsequent environments. For example, with $r = -1.0$, h_2 may be between 0.03 and 0.97 and the retardation factor is still greater than 1.0. If $h_1 = 0.0$ or 1.0 this model becomes the "absolute dominance" model (PROUT 1968, HEDRICK 1974) and although it meets the criteria for a stable polymorphism in an infinite population, it is least able to maintain genetic variation of any of the dominance levels.

If the autocorrelation is set equal to -1.0, then the effects of varying dominance and population size can be examined. This can be seen in Figure 4B comparing $2N = 20$, 40 and 80 when the autocorrelation is -1.0. For even ex-

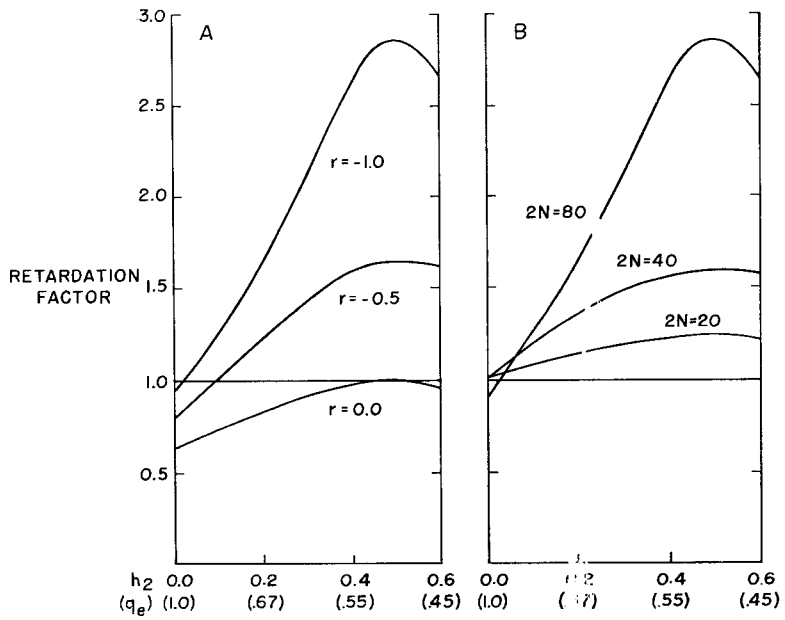

FIGURE 4.—The retardation factor when there is equal dominance, i.e., $h_1 = 1.0 - h_2$. (A) Three levels of autocorrelation ($r = -1.0, -0.5, 0.0$) are given for $2N = 80$ and (B) three population sizes (2N = 20, 40, and 80) are given for $r = -1.0$. The values of s_1 and s_2 are 0.5.

treme values of dominance, the loss of genetic variation is retarded over the situation when there is neutrality. As population size increases, the range of dominance for which the retardation factor is greater than one becomes less due to the interaction of selection and genetic drift, an effect similar to that observed by ROBERTSON (1962) for the overdominance model and HEDRICK (1974) for temporal variation and the absolute dominance model.

Dominance need not be the same in all environments and dominance may change to obviate selection pressures. If selection for dominance acts to make the heterozygote more fit in different environments even though selection may alternately favor different homozygotes, temporal variation in the direction of selection may have a substantial ability to maintain genetic varition. Figure 5 shows this for number of dominance combinations. The effect can best be understood by noticing that the open circles in Figure 5 indicate points of equal dominance ($h_1 = 1.0-h_2$) and are points on the curve for $r = -1.0$, $2N = 80$ in Figure 4. When the dominance is modified so that the heterozygote is more fit (as when h_1 is reduced for a given h_2), then the retardation factor rises strikingly. For example, when $h_1 = h_2 = 0.5$ the retardation factor is 2.820. With a change of h_2 from 0.5 to 0.3, there is approximately a fourfold increase in the retardation factor. In this situation, temporal variation in selection can have a substantial ability to maintain genetic variation.

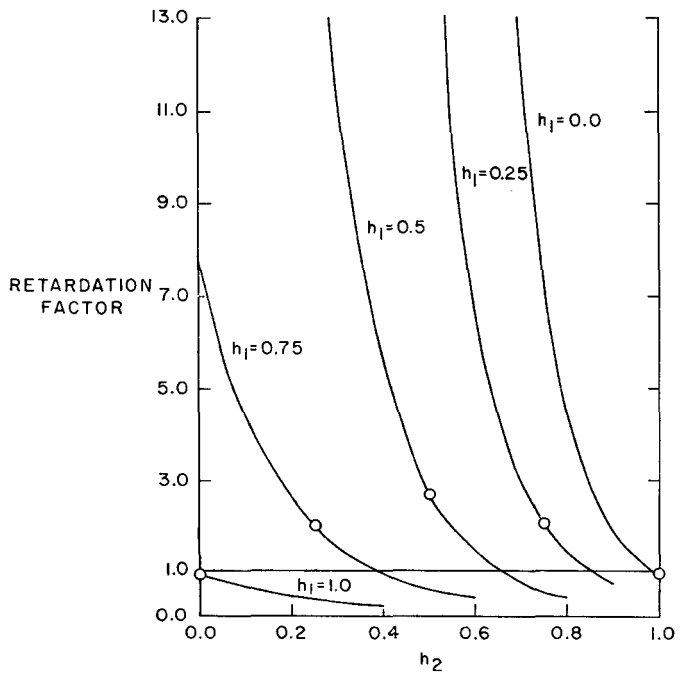

FIGURE 5.—The retardation factor for various combinations of dominance. The circles indicate examples of equal dominance ($h_1 = 1.0-h_2$). The autocorrelation is -1.0, $2N = 80$. and $s_1 = s_2 = 0.5$.

Effect of unequal selection: The assumption of equal magnitudes of selection in both environments ($s_1 = s_2$) may not hold for many natural populations. The effects of different magnitudes of selection can be examined by keeping selection constant in one environment and varying the selection intensity in the other environment. Figure 6A gives the retardation factor when s_1 is set equal to 0.5, $h_1 = h_2 = 0.5$, and s_2 is variable. Here it is apparent even with an autocorrelation of -1.0, the region where selection retards fixation more than neutrality is very narrow, i.e., s_2 must be between 0.43 and 0.58. This is a somewhat narrower range than that for stability in an infinite population for which s_2 must be between 0.4 and $\frac{2}{3}$ (these points are indicated as circles in Figure 6). Note also that the curves are slightly asymmetrical with the maximum when s_2 is slightly greater than 0.5. This results from an asymmetry in the gene frequency change and equilibrium. For example, when $s_2 = 0.6$, there is not a gene frequency equilibrium but when $s_2 = 0.4$ the gene frequency equilibrium is 0.09.

As the population size becomes larger (compare $2N = 20$, 40 and 80 in Figure 6B for $r = -1.0$) the curve becomes more peaked and the range of s_2 which gives a retardation factor greater than 1.0 becomes smaller. It is apparent that the effect of an increase in population size when selection is variable is also similar to that found for overdominance.

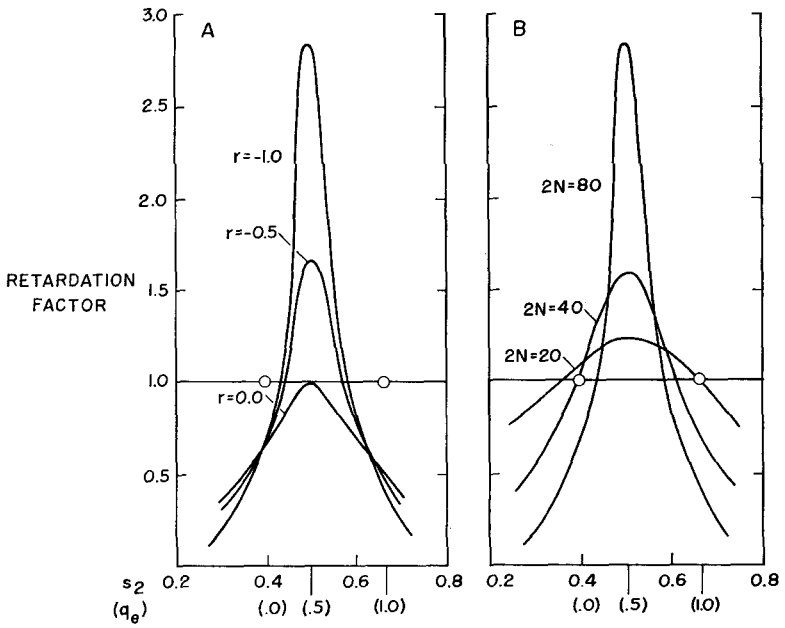

FIGURE 6.—The retardation factor when the selection coefficient, s_2, is allowed to vary. (A) Three levels of autocorrelation ($r = -1.0$, -0.5, and 0.0) are given for $sN = 80$ and (B) three population sizes ($sN = 20$, 40, and 80) are given for $r = 1.0$. The value of s_1 is 0.5 and $h_1 = h_2 = 0.5$. The circles indicate the limits for a stable polymorphism in an infinite population.

Joint effects of dominance and unequal selection: Can dominance and selection interact synergistically? If amount of selection is not the same in the two environments, then this might be compensated for by greater dominance in the environment with lower selection pressure. Figure 7 gives the retardation factor when $h_1 = 1 - h_2$ and s_2 is variable. As expected, dominance is able to compensate for different amounts of selection, but the effect is quite small. For example, with $h_1 = 0.5$ and s_2 is below 0.43, the retardation factor is less than one. With compensating dominance such as $h_1 = 0.1$, the retardation factor goes below 1.0 when s_2 is less than 0.38. The compensating effect is present, but it appears to be minimal.

DISCUSSION

From the results of this study it is clear that temporal variation in the direction of selection is able to effectively maintain genetic variation in a finite population in a limited number of situations. As for the absolute dominance model (HEDRICK 1974), a negative autocorrelation between subsequent environments or a strict cyclic model was most effective in maintaining genetic variation when the heterozygote is intermediate. In fact a spring-fall cycle such as that which occurs in a bivoltine insect, with selection acting in opposite directions in the two environments, maintains genetic variation very effectively. In comparing different autocorrelation levels, it appears that for a large popula-

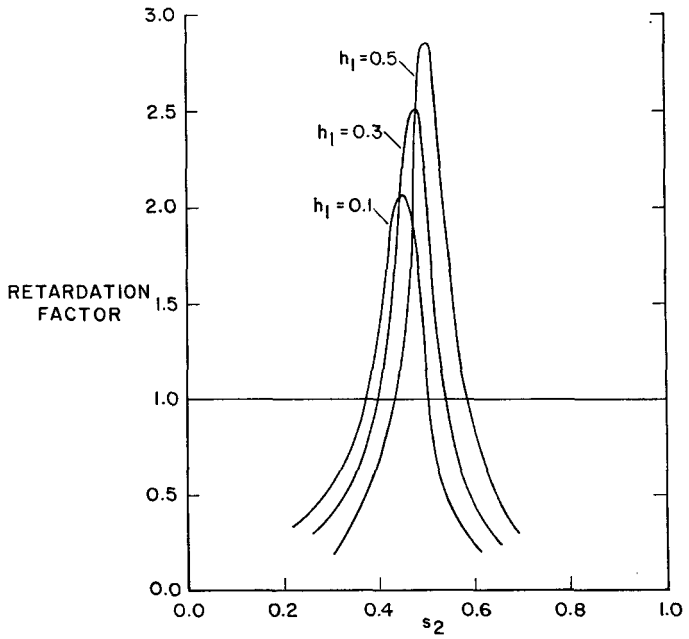

FIGURE 7.—The retardation factor when s_2 and h_1 are varied. In this example $sN = 80$, $r = -1.0$, and $h_1 = 1.0 - h_2$.

tion size, a retardation factor curve as is in Figure 1, would be nearly vertical. This means that any small amount of negative autocorrelation in a large population would increase the maintenance of genetic variation. The converse being that any small amount of positive autocorrelation would cause an increased rate of elimination of variation. This is particularly important because many environments show positive autocorrelations of environments of subsequent generations (e.g., BRYANT 1974). Another important finding is that when the autocorrelation is 0.0 and selection in both environments is equal and additive, the retardation factor and the moments of the stable gene-frequency distribution are the same as for neutrality.

Other parameters which are not related to the stable gene-frequency distribution do, however, differ as a function of the initial gene frequency. For example, the probability of fixation is not equal to the initial gene frequency (except when $q_0 = 0.5$) when there is variable selection. It is higher for initial gene frequencies below 0.5 and lower for those about this level (shown by JENSEN 1973 and KARLIN and LEVIKSON 1974 for other models). Also the time to fixation is not the same as neutrality but is shorter for the selection model when the initial gene frequency is near 0.5 and longer for the selection model when the initial gene frequency is near 0.0 or 1.0 KARLIN and LEVIKSON (1974) and COOK and HARTL (1975) observed a similar phenomenon using different models.

By varying selection values, autocorrelation and levels of dominance, I have shown that a parameter combination of an autocorrelation of -1.0, equal selection intensities in both environments, and additivity (given the restriction of equal dominance, $h_1 = 1.0-h_2$) is the most effective parameter set for maintaining genetic variation for temporal environmental variation. When the restriction of equal dominance is relaxed, however, it was found that some h_1 and h_2 combinations can be much more effective in maintaining genetic variation. This may be a biologically important situation since evolution of dominance favoring the homozygote with the highest fitness has been documented (e.g., KETTLEWELL 1965).

An extreme example of this type is a kind of balanced lethal system as suggested by LEVINS (1962). He hypothesized that one homozygote was lethal in environment 1 and the other in environment 2 with the heterozygotes as fit as the surviving homozygotes in both environments. A biological example of this type selection could be imagined in annual plants (ANTONOVICS pers. comm.). Assume that genetic variation at a locus affects plant height in an additive manner but that the effects are reversed in wet and dry habitats. However, for a maximum number of sound seed (fitness) the plants need only to be medium height. A model for this balancing type of selection is given below with the height phenotypes in parantheses.

		Genotype	
Environment	A_1A_1	A_1A_2	A_2A_2
1 (wet)	1 (tall)	1 (medium)	$1-s_1$ (short)
2 (dry)	$1-s_2$ (short)	1 (medium)	1 (tall)

The selective values used in this study are quite high. Even so the ability of temporal selection to maintain genetic variation in most cases is not much greater than neutrality. It should also be noted that the amount of retardation for symmetric selection, additivity and an autocorrelaion of -1.0, is approximated fairly well by the geometric means of the fitness over environments. If the geometric means are standardized so that the mean fitness of the heterozygote is 1.0, then for the example where fitness are 1.0, 0.75, and 0.5, 0.75 and 1.0, the geometric relative fitnesses become 0.9428, 1.0, and 0.9428. This example is then nearly equivalent in maintaining genetic variation to an overdominant model where $s_1 + s_2 = 0.1144$ and $q_e = 0.5$. If you wish to generalize to larger population sizes, by using the relationship $N(s_1 + s_2)$ for an overdominant model, the effect of any combination can be estimated (ROBERTSON 1962). When there are different levels of dominance or unequal selection, this approximation does not hold as well and the geometric mean tends to underestimate the ability of varying directional selection to maintain genetic variation.

The conditions for a stable polymorphism with temporal variation in fitness were originally given by HALDANE and JAYAKAR (1963). They showed that in an infinite population the geometric mean of the heterozygote must be greater than the geometric means of the homozygotes and they state that a "mere series of changes in the direction of selection may be enough to secure polymorphism." GILLESPIE (1973) also showed that these conditions are independent of the autocovariance (autocorrelation) of the environments. The present results show that there is a quite remarkable difference between the conditions for polymorphism in an infinite population and the maintenance of genetic variation in a finite population. A number of situations, e.g., positive autocorrelation between environment and long sequences in a single environment which meet the conditions for polymorphism in an infinite population are less effective than neutrality in a finite population. This results from the great fluctuations in gene frequency that by chance (in a stochastic model) or periodically (in a cyclic model) bring the gene frequency near 0.0 or 1.0 where the probability of the loss of genetic variation by drift is greatly enhanced. In finite populations as demonstrated here, the environmental pattern is critical to understanding the effect of variable selection. It appears then that geometric mean fitness will not tell the whole story in finite populations concerning the maintenance of genetic variation (see also COOK and HARTL 1975; BRYANT 1976).

BRYANT (1973, 1976) has refocused attention on the ability of a population to genetically track an environment. LEVINS (1962) said concerning this problem "there is some threshold value of the correlation between environments of successive generations (or the period if there is cyclic variation), beyond which response to selection is advantageous." Both BRYANT and LEVINS are discussing an infinite population or at least one large enough that the chance loss of genetic variation due to drift is quite small. Furthermore, they are concerned about maximizing the mean fitness of the population. As demonstrated in Figures 1 and 2, however, a positive correlation between subsequent environments or a

long cycle when finite population size is important may lead to the loss of the actual variation which allows genetic tracking. In other words the conclusions concerning genetic tracking of an environment in an infinite population are contrary to what is found for finite populations. Having a long cycle in an infinite population allows the relative fitness to become very high at the end of the cycle or a series of generations in the same environment. However, the extreme gene frequency which gives the high fitness in an infinite population actually causes an increase in the probability of fixation and loss in a finite population.

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