THEORY OF FITNESS IN A HETEROGENEOUS ENVIRONMENT. V. OPTIMAL GENETIC SYSTEMS[1]

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FOR populations living in more or less constant environments there is a close connection between the frequencies of alleles at different loci and the direction of natural selection operating on these genes. Alleles at very low frequencies will, by and large, be those selected against but maintained by recurrent mutation. Alleles in intermediate frequencies are for the most part maintained by some form of balancing selection. This correlation between allelic frequencies and selective forces is disrupted in small populations where genetic drift will cause gene frequencies to differ from their equilibrium values, but for large populations the frequencies of alleles will, in general, be such as to maximize or nearly maximize population fitness.

When we turn to a consideration of populations in fluctuating environments, the problem is much more complex. Alleles may have low frequencies because natural selection has reduced them in past generations, but these low frequencies may be very far from the equilibrium values dictated by current selective forces. Thus gene frequencies at various loci and in various populations are correlated with past selective forces, but not necessarily with recent forces, or, worse yet, they may be negatively correlated with current selection if successive environments are themselves periodic or correlated to the proper degree.

Unfortunately, from the standpoint of the population, the fitness of the population is determined in any generation by the correspondence between the gene frequencies and selective forces at that instant. If the pattern of environmental change is such as to make past environments poor predictors of present environments, populations that have responded adaptively to past environments will be ill-adapted to present ones. Thus, it is clear that the average fitness of a population is a function of the pattern of fluctuation of the environment, on the one hand, and the way in which a population's genetic composition changes in response to the environment. While the pattern of the environment is not generally under the control of the population (it may be if the organisms' behavior allows them to modify their immediate environment adaptively), the way in which the population responds to selective forces is a function of the constants of the genetic system. Additive effects of genes, dominance, epistatic interaction, linkage, mutation rates, migration rates all are critical in determining whether the population changes quickly or slowly, whether different genotypes are differently fit, and

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thus to what extent the population has a high fitness at any time. The hypothesis has been proposed (LEVINS 1962) that the genetic parameters can be interpreted as adaptations to the statistical pattern of the environmental heterogeneity. For each such pattern of environment, there will be optimum genetic systems, that is, some values of the constants which maximize average fitness regardless of how fitness is defined. It is further argued that selection acting on the genetic system itself will change the constants toward their optimum values, so that existing populations might be expected to differ in the same directions as their optima differ.

The present study is concerned with the optimal values and adaptive significance of additive phenotypic effect and to some extent linkage, under several models of natural selection. We are asking how different patterns of environmental variation change the average fitness of a population when the genes concerned have different additive effects and different linkage relationships.

Fitness and Phenotype

The fitness of each genotype in each environment has to be specified by way of the phenotype. This can be done in two ways which are equivalent except for the units used.

1. Corresponding to each genotype there is an optimal environment. As the actual environment departs from the optimum in either direction, fitness decreases toward zero. The rate at which fitness declines, and the fitness at optimum can, of course, be different for each genotype. For instance, it is well known from the work of DOBZHANSKY and his collaborators that chromosomal heterozygotes are often less sensitive to environmental differences than are homozygotes, while the "super-vital" homozygous types are often narrow specialists. However, since our primary concern here is with adaptations to different environments rather than the genetics of homeostasis, we will assume that all genotypes have equal peak fitness and equal rates of loss of fitness with departure of the environment from the optimum but that the particular environment that is optimal differs from genotype to genotype.

Since the different phenotypes differ only in the value of the environmental variable that is optimal, the fitness of a given phenotype in a range of envrionments can be expressed as $W(S-\gamma)$ where W is a unimodel symmetric, nonnegative function of its argument $(S-\gamma)$. S is the optimal environment for the genotype in question and γ is the particular environment for which fitness is being measured. Then, in Figure 1, the two curves show the fitness of two different phenotypes, I and II, over a range of environments, γ. Here both S and γ are measured in units of environment.

2. A dual representation of this system is one in which the environment is considered fixed and S represents the phenotype that is optimal in that environment. In such a case γ represents the phenotype value of a genotype and the deviations $(S-\gamma)$ are measured in phenotype units. For this representation, the abscissa in Figure 1 is a measure of phenotype and the curves I and II are the fitnesses in two environments of a continuous range of phenotypes.

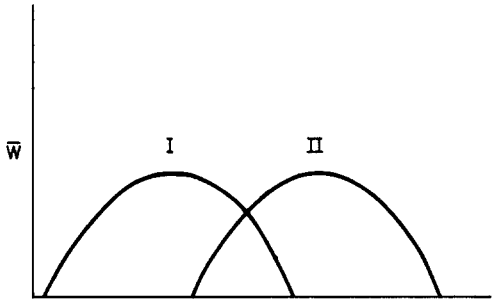

FIGURE 1.—Relation between fitness, on the ordinate, and environment or phenotype, on the abscissa. In one model, curves I and II represent two different phenotypes and the abscissa is in environmental units. In the dual representation, I and II are different environments and the abscissa is in phenotypic units.

Among the possible models of $W(S-\gamma)$ the quadratic deviation model is the simplest with the essential qualities. Here

$$W(S-\gamma) = \begin{cases} 1-(S-\gamma)^2/H & \geqslant 0 \\ 0 & \text{otherwise.} \end{cases}$$

where H is a measure of homeostasis, a large H reducing the sensitivity of the genotype to environmental change and therefore the effective environmental variance. For most of this paper we are not concerned with homeostasis and set $H = 1$ for convenience.

Any fitness model which is symmetric about its peak will have a quadratic deviation model as its first approximation. In the previous paper (1964), it was shown that for a unimodally distributed S the quadratic deviation model has the same qualitative results as a more general W, while a bimodally distributed S is essentially the 2-niche model of the first paper (1962). The mathematical convenience of the quadratic deviation model is of course that the expected value of the fitness depends only on the means, variances, and covariances of the environmental variable and the gene frequency. Therefore, it has been used by a number of authors (FISHER 1930; WRIGHT 1935; LEWONTIN 1964) in analyzing populations.

More complicated functions for $W(S-\gamma)$ introduce higher moments of the variables, but the qualitative results remain.

Methods and Approach

What we wish to do in this paper is to determine the effect of different values of genetic parameters such as gene effect and recombination fraction on the average fitness of a population through time. The average fitness $\bar{W}$, of a population segregating at a single locus is defined by

$$\bar{W} = W_{11}\,x^2 + 2W_{12}\,x(1-x) + W_{22}\,(1-x)^2 \qquad (1)$$

where W_{11}, W_{12} and W_{22} are the fitnesses (relative probabilities of leaving offspring) of the three genotypes AA, Aa, and aa, and where x is the frequency of

the gene A. Thus, if we know the gene frequency in each generation and the fitnesses we can evaluate (1) for $\overline{W}$ and average these values through time. When environment is constant (W_{ij}'s are constant) we can make use of the equation for gene frequency change

$$\Delta x = \frac{x(1-x)}{2\overline{W}} \frac{d\overline{W}}{dx} \tag{2}$$

to solve for the gene frequency x in every generation starting with any arbitrary gene frequency x_0. These values, x, when substituted into (1) give the required value of $\overline{W}$.

Our problem is more complex, however. The fitnesses are varying each generation with some secular as well as random component to the variation. For any particular sequence of fitnesses through time we can determine Δx in each generation and find the average fitness over time. But we are concerned not with particular sequences of environments, but with general descriptions of environmental change. Thus, we would like to be able to specify the distribution of gene frequencies over time, the probability that a gene frequency will take a particular value, when the statistical characteristics of the environment are given. Such characteristics are the mean selection coefficient, its variance through time and the serial autocorrelation between successive environments, among other things. If we can specify the gene frequency distribution, it is then a simple matter to calculate the average fitness from equation 1.

If the environment is a "pure noise" random variable with no autocorrelation (implying no secular trend), the methods of diffusion equations give the distribution of gene frequencies through time (KIMURA 1955), and, using such distributions of x together with equation 1, average values of $\overline{W}$ can be found. The most interesting problems arise, however, when successive environments are correlated, but no simple solutions are possible in such cases, and so I have resorted to a Monte Carlo simulation scheme.

There is no question that, in general, environments are serially correlated to a greater or lesser degree. It is well known, for example, that in continental temperate regions a weather predictor can be correct more than 70% of the time by simply predicting that tomorrow's weather will be the same as today's. The serial autocorrelation grows weaker as the time interval between points grows greater so that the correlation between days one month apart is very low and that between days a year apart is essentially zero. The correlation between successive two-day periods would be .49, and for successive weeks or months would decline further. Thus short generations would permit environments with higher autocorrelation. This autocorrelation is completely independent of any cyclic changes in the environment. A process of this kind can be generated in the following way:

Let S_t = value of some environmental variable at some moment or during some time interval
S_{t-1} = value of the same variable at the equivalent moment or interval in the previous generation, year, month, etc.
$\bar{S}$ = average value of the variable over all *serially equivalent* moments or intervals
ε = a random variable with zero mean and variance, σ_ε^2 and K_1, K_2 = arbitrary weights

Then the deviation of S_t from $\bar{S}$ can be related to the deviation of S_{t-1} from $\bar{S}$ by the relation

$$S_t - \bar{S} = K_1 (S_{t-1} - \bar{S}) + K_2 \varepsilon \tag{3}$$

Provided that K_1 is less than unity, it can be shown that after a sufficiently long time, t, S_t has a stable distribution with a finite variance

$$\sigma_s^2 = \frac{K_2^2}{1 - K_1^2} \sigma_\epsilon^2$$

and that the ordinary product-moment correlation between S_t and S_{t-1}, ρ, is, in fact, K_1.

In this paper I have investigated the effect of the autocorrelated process given in expression 3 with $K_2 = \sqrt{1 - K_1^2}$ so that the environmental variance, σ_S^2, is equal to σ_ϵ^2, and the correlation between successive generations is K_1. By varying K_1 and σ_ϵ^2, it is then possible to control the pattern of environment over time. I have examined the effect of this variation on the fitness of a population segregating at two loci each with two alleles. The loci are considered identical in their phenotypic effect. Table 1 shows the relation between fitness and phenotype at each locus according to the quadratic optimum model discussed above. The course of events in such a population subject to the correlated fluctuations in environment is followed by simulating the process with a digital computer as follows.

The computer is started with some arbitrary gene frequency (usually .5) at each locus, and some arbitrary initial value of S (usually zero). The computer generates a random value of ε by generating a uniformly distributed pseudo-random variable between 0 and 1 (BOFINGER and BOFINGER 1958) and then using that variable as the argument in a uniformly spaced table of the inverse normal distribution. The value from the table is multiplied by a constant to adjust the variance of ε. From the current value of ε_t equation 3 yields S_t which, when substituted in the relations in Table 1, gives the fitnesses, W_{ij}. These in turn when substituted into (1) give the current value of $\bar{W}$ and when used in (2) give the next generation gene frequency. This procedure is repeated sequentially, beginning with the current value of S_t and the gene frequencies, for 100 generations and the average $\bar{W}$ is calculated. Such a sequence of 100 generations constitutes one replication and each parameter set is replicated ten times. Computations were performed on the IBM 7070/7074 Computer at the University of Rochester.

An alternative model for the environment is based on seasonal change. Here the environment is allowed to alternate every n generations between S and $-S$.

TABLE 1

Quadratic deviation model for one locus

Genotype	Frequency	Phenotype	Fitness
AA	x^2	a	$1-(S-a)^2>0$, zero otherwise
AA'	$2x(1-x)$	0	$1-S^2 \quad >0$, zero otherwise
$A'A'$	$(1-x)^2$	$-a$	$1-(S+a)^2>0$, zero otherwise

This may seem highly simplified compared to the familiar sinusoidal graphs of monthly temperature or rainfall. However these graphs are based on averages over many years data. In any one year the change over from winter to spring weather patterns is rather abrupt although the time of change varies. Thus a sinusoidal model is not necessarily more realistic. In this model, when the environment changes every n generations the autocorrelation is $(n-2)/n$ so that there will be a positive autocorrelation only when the period exceeds four generations.

Optimum Phenotypic Effect

In the two locus model we have used, each locus contributes $\pm a$ to the phenotype (Table 1). Thus, a large value of a represents a major gene while if $a = 0$ the locus has effectively disappeared. The first question is, what is the optimum value of a? In previous analytical investigations (LEVINS 1964), it was shown that the optimal value of a is different from zero when the autocorrelation of the environment exceeds about 0.8. Therefore we calculated the mean $\overline{W}$ for environments with different autocorrelations, ρ, and mean environment $\bar{S} = 0$. Figure 2 shows the relation between the average fitness and the additive phenotypic effect a for several values of ρ. We see that for the smaller values of ρ there is no intermediate value of a that is optimum. For populations living in such environments the highest average fitness is maintained by modifying the phenotypic effect until there is no effect of segregation at all. For $\rho \geqslant .8$, however, there is an

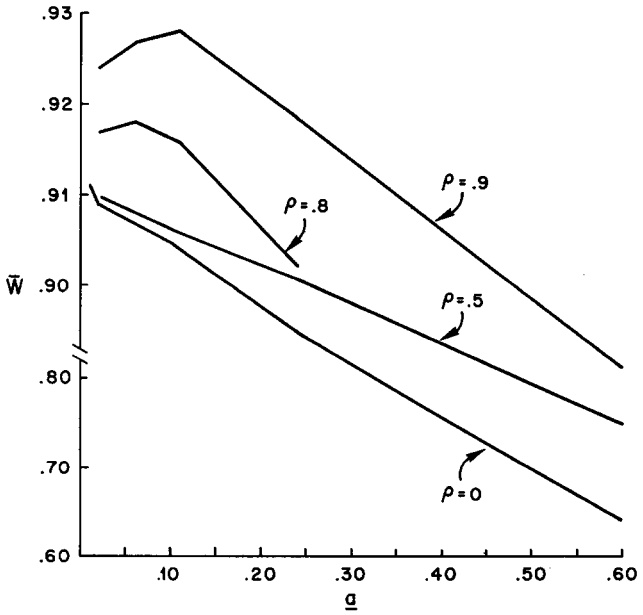

FIGURE 2.—The relation between $\overline{W}$ and gene effect, a, for different degrees of environmental autocorrelation. The scale of $\overline{W}$ is compressed below .90.

optimum a different from zero. The value of this optimum increases as ρ increases. Finally, whatever the phenotypic effect of the locus, an increase in autocorrelation results in an increase in mean fitness.

For a more detailed examination of the relation between W and the genetic parameters, fitness can be broken down into several components:

$$\bar{W}_t = 1 - (S_t - M_t)^2 - \text{VAPHE}_t \quad (4)$$

where M_t is the mean phenotype of the population and VAPHE is the phenotypic variance in generation t. In our particular case the phenotypic variance is entirely genetic. Taking the expectation of $\bar{W}$ over time we get:

$$E(\bar{W}) = 1 - \sigma_S^2 - (\bar{S} - \bar{M})^2 - \sigma_M^2 - E(\text{VAPHE}) + 2\,\text{COV}(S,M) \quad (5)$$

For a given set of environmental parameters, σ_S^2 and S are fixed whereas the other terms depend on the genetic parameters. In our program, σ_M^2, COV(S,M) VAPHE, SQDIF (defined as $(\bar{S} - \bar{M})^2$ for each 100 reps) and the correlation between S and M were calculated.

Since the scale used in the model is arbitrary, the biologically meaningful comparisons are optimum a and VAPHE compared to variance of the environment and the proportion of the total fitness lost due to fluctuation that is restored by responding to selection. When there is no fluctuation, the optimum a is zero and fitness equals 1. As the fluctuations increase but with a held at zero, fitness declines roughly by σ_S^2 (but not exactly, since for extreme environments fitness reaches zero and no negative values are allowed). Let $E(\bar{W}_0)$ be the mean fitness for $a = 0$. Then $1 - E(\bar{W}_0)$ is the loss of fitness due to fluctuation. For each environmental pattern there is some optimum a, with mean fitness $E(\bar{W}_a)$. Thus the fitness restored by the optimal system is $E(\bar{W}_a) - E(\bar{W}_0)$ and the proportion of fitness restored is $[E(\bar{W}_a) - E(\bar{W}_0)]/[1 - E(\bar{W}_0)]$.

TABLE 2

Optimum phenotypic effects

Model	ρ	σ_S^2	Optimum a	VAPHE at optimum a	Proportion fitness loss restored
Normal random environment					
1 locus	0.8	any	0	0	0
1 locus	0.8	0.1	.06	.002	.02
1 locus	.9	0.05	.06	.002	. .
1 locus	0.9	0.1	.12	.005	.07
1 locus	0.99	0.1	.20	.012	.34
1 locus	0.9	0.2	.20	.007	.10
Periodic environment					
S = ± .9 every 20 generations	0.9	.081	.9	.04	.87
S = ± .6 every 100 generations	0.98	.36	.6	.007	.94
S = ± .9 every 100 generations	.98	.81	.9	. .	.96

Table 2 shows the phenotypic variance and the fitness loss restored by responding to selection for a number of models. In the first group of models the environment, S, is generated by the method already described involving the normal distribution. For the second set, S is not a random but a strictly periodic function. If S varies cyclically with the value $+K$ for n generations followed by $-K$ for n generations, it is simple to show that the serial autocorrelation $\rho = (n-2)/n$.

Despite differences among the models, the optimum a is roughly of the same order of magnitude as the variance of the environment and VAPHE is 2 to 10% of that variance. The fitness restored by the optimal a is small compared to the fitness differences among genotypes, so that natural selection on a toward the establishment of the optimum will be considerably slower than the fluctuations in gene frequency except when the autocorrelation is very strong. However, even selective advantages on the order of .02 can still result in changes in a over periods which are short compared to the life of the species.

Expression 5 allows us to examine in some detail the components determining the average fitness under different conditions and so to understand the existence of an optimum value of a different from zero.

As a increases, the population becomes more sensitive to selection so that the variance of the gene frequency increases. Since the mean phenotype is

$$M = a(2x-1) \tag{6}$$

its variance is $4a^2\sigma_x^2$ which increases more rapidly than the second power of a VAPHE increases also, since a given degree of genetic heterogeneity produces more phenotypic variance. However, its increase is less rapid than that of σ_M^2. VAPHE is given by

$$\text{VAPHE} = 2a^2\, x(1-x) \tag{7}$$

so that its average value is

$$E(\text{VAPHE}) = 2a^2\, \bar{x}(1-\bar{x}) - 2a^2\, \sigma_x^2 \tag{8}$$

Hence the greater the variance in gene frequency, the more of the time the population is relatively homogeneous (displaced from the frequency of .5 at which VAPHE is greatest). The combined effect of VAPHE and σ_M^2 is to reduce fitness by $2a^2\bar{x}(1-\bar{x}) + 2a^2\sigma_x^2$.

SQDIF has the expected value over all possible series of 100 generations.

$$E(\text{SQDIF}) = \sigma_S^2 + \sigma_M^2 + 2\,\text{COV}(\bar{S},\bar{M}) + [E(\bar{S})-E(\bar{M})]^2 \tag{9}$$

The difference between the means of the replicate means will be very small. However, since successive values of S and of M are correlated, the variances of the replicate means are still large. For example, with an autocorrelation of 0.9, the variance of the mean of 100 generations would be about 0.19 times the variance of a single value. The covariance of $\bar{S}$ and $\bar{M}$ measures the effectiveness of selection over the 100 generations and would be positive even when there is no autocorrelation. When there is autocorrelation, part of it appears in $\text{COV}(S,M)$ and part enters SDQIF through the $\text{COV}(\bar{S},\bar{M})$. Over an indefinitely long period, SQDIF should vanish. It is included only as a bookkeeping device for finite replications.

The overall effect of these three components is to reduce the fitness of the

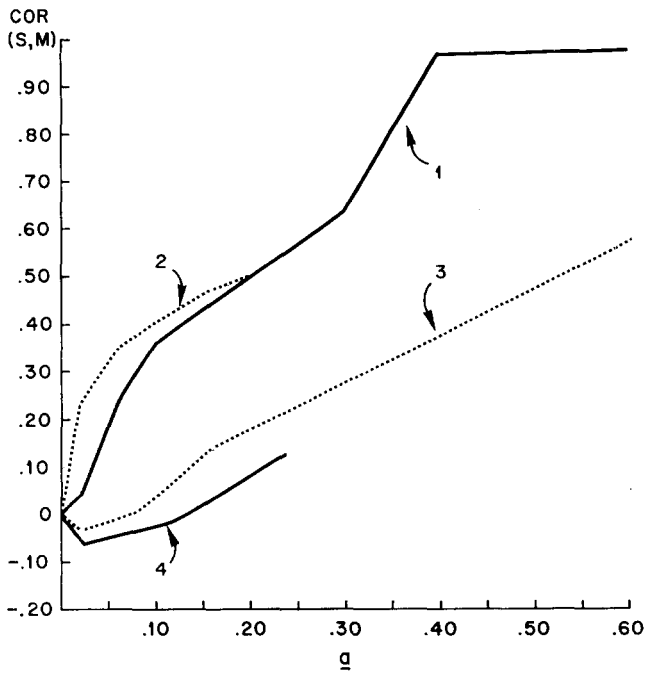

FIGURE 3.—Relation between environment-phenotype correlation and gene effect, a, for a variety of environmental situations. **1:** periodic environment, period 100, amplitude .9; **2:** random environment, $\rho = .99$, $\sigma_S^2 = .1$; **3:** random environment, $\rho = 90$, $\sigma_S^2 = .1$; **4:** random environment, $\rho = .80$, $\sigma_S^2 = .1$.

population as a increases. However, this may be offset by an increased covariance term provided the autocorrelation is sufficiently great. In Figure 3 we show the relation between a and correlation of S and M. Table 3 shows the components of fitness for several models and values of a.

The response to selection is not the only way in which genetic diversity may be advantageous. If the environment has a bimodal distribution with the modes sufficiently far apart, the optimal a will be equal to the mode even in the absence of autocorrelation. In this case it is advantageous to have a fixed genetic composition which does not change with selection. In the periodic environments in which the environment alternated between S and $-S$, this occurred when S exceeded .5 so that a genotype which had fitness 1 in one environment was lethal in the other. This aspect of the problem was studied analytically in LEVINS (1962) and will not be discussed further here.

The Role of Linkage

When we study two loci, each with two alleles, the genetic composition is defined by the frequencies of the gametic types *AB,Ab, aBab*. The equation for change is given by LEWONTIN and KOJIMA (1960) as

$$\Delta x_{AB} = [X_{AB}\,(MF_{AB} - \bar{W}) - RDW_{AaBb}]/\bar{W} \qquad (10)$$

TABLE 3

Components of fitness

Model	a	$\bar{W}$	VAPHE	VAR (M)	SQDIF	COV
Normal random environment						
$\sigma_S^2 = .1,\ \rho = .9$	.06	.9265	.0014	.0002	.0088	—.0001
	.12	.9280	.0046	.0017	.0037	+.0005
	.24	.9194	.0150	.0112	.0009	+.0047
	.60	.8140	....	.0976	.0078	+.0460
$\sigma_S^2 = .1,\ \rho = .99$	.06	.9603	.0015	.0020	.0239	+.0006
	.12	.9672	.0050	.0013	.0151	+.0019
	.20	.9679	.0124	.0047	.0065	+.0044
$\sigma_S^2 = .2,\ \rho = .9$	.06	.8575	.0010	.0006	.0155	+.0002
	.12	.8579	.0030	.0039	.0079	.0018
	.20	.8590	.0071	.0128	.0030	.0069
Periodic environment						
$S = \pm .33$ every 20 generations	.02	.8901	.0002	0	.0001	0
	.06	.8889	.0018	.0001	0	—.0002
$S = \pm .9$ every 20 generations	.10	.3201	.0009	.0084	.0003	+.0696
	.60	.8124	.0187	.3258	.0003	.4405
	.90	.8933	.0408	.7358	.0003	.6624

where D is the measure of linkage disequilibrium, defined by

$$D = f_{AB}f_{ab} - f_{Ab}f_{aB}. \tag{11}$$

Here, f_{ij} is the frequency of the corresponding gamete, R is the frequency of recombination, and MF_{AB} is the marginal fitness of the AB gamete. Thus, a negative D implies excess of repulsion gametes (with total phenotypic effect small, or zero when the two loci have equal effects).

In all cases there was an excess of repulsion (negative D). This is what we would expect when we consider that a pair of repulsion gametes have an average fitness $1-\sigma_S^2-\sigma_M^2/4 + \mathrm{COV}(S,M)$ while a pair of coupling gametes have an average fitness of $1-\sigma_S^2-\sigma_M^2/4 + \mathrm{COV}(S,M) - a^2$. The excess of repulsion has the effect of reducing the genetic variance, so that tighter linkage reduces both VAPHE and σ_M^2. In Table 4 and Figure 4 we show the relationship among components of fitness and linkage for some typical cases.

When there is no autocorrelation in the environment, so that any response to selection is harmful, closer linkage is favorable at all values of a. The linkage disequilibrium reduces the effect of increasing a so that the decline of W with a is slower than for a single locus. However, when the environment is highly autocorrelated a certain response to selection is advantageous. Therefore, when a is small a maximum of recombination is desirable, releasing more genetic variance. But when a is large the total genetic variance may be excessive and tighter linkage is beneficial.

The same total additive phenotypic effect may be divided among several loci. In Table 5 we show the effects of different divisions of the same total a between

TABLE 4

Effect of recombination on components of fitness, $\sigma_S^2 = .1$ for normal random environment

ρ	a	R	$\overline{W}$	VAPHE	M	COV	D
0	.06	0	.90717	.00301	.00011	—.00039	—.0340
		.1	.90674	.00340	.00014	—.00041	—.0064
		.3	.90667	.00346	.00015	—.00042	—.0023
		.5	.90666	.00347	.00015	—.00042	—.0014
	.30	0	.89898	.01077	.00143	+.00007	—.2189
		.1	.85453	.05100	.00620	—.00087	—.1035
		.3	.83056	.07126	.01068	—.00125	—.0439
		.5	.82380	.07690	.01208	—.00134	—.0272
.9	.06	0	.92749	.00275	.00062	—.00009	—.0186
		.1	.92754	.00293	.00070	—.00003	—.0038
		.3	.92755	.00295	.00072	—.00003	—.0014
		.5	.92756	.00296	.00072	—.00003	—.0009
	.12	0	.92646	.00841	.00315	+.00137	—.0559
		.1	.92568	.01033	.00476	+.00240	—.0119
		.3	.92548	.01060	.00506	+.00255	—.0045
		.5	.92542	.01066	.00514	+.00256	—.0028
	.30	0	.92063	.01991	.00991	+.00878	—.1816
		.1	.90165	.05423	.03038	.02452	—.0686
		.3	.89055	.06572	.03927	.02912	—.0288
		.5	.88728	.06877	.04197	.03037	—.01797

R = recombination, ρ = autocorrelation of the environment, a = phenotypic effect of a single locus.

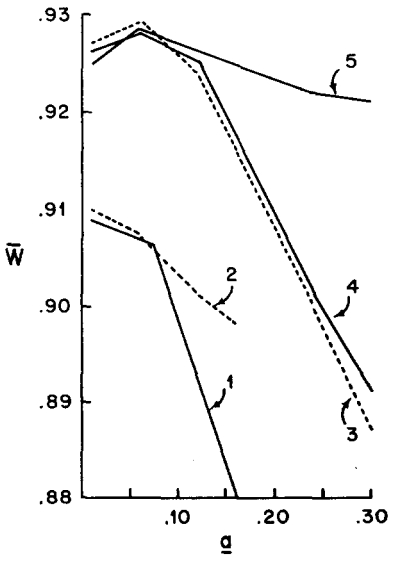

FIGURE 4.—Relation between mean fitness, $\overline{W}$, and gene effect, a, for various values of recombination and environmental autocorrelation. **1**: $R = .5$ $\rho = 0$; **2**: $R = 0$, $\rho = 0$; **3**: $R = .5$, $\rho = .9$; **4**: $R = .3$, $\rho = .9$; **5**: $R = 0$, $\rho = .9$.

TABLE 5

Components of fitness for two loci and normal random environment
$a_1 + a_2 = .12$, VAR $(s) = .1$, $\rho = .9$

a_1	a_2	W	VAPHE	M	SQDIF	COV
.12	0	.9279	.0040	.0014	.0044	+.0003
.09	.03	.9278	.0033	.0009	.0053	+.0001
.07	.05	.9276	.0030	.0007	.0058	0
.06	.06	.9275	.0026	.0006	.0060	—.0001

two loci. It is apparent that the optimal arrangement is one in which the effect is concentrated at one locus. The reason for this is that in these models VAPHE. the total genetic variance, is increased by the introduction of some epistatic variance as well as additive so that the response to selection is smaller compared to the VAPHE. The price paid for each unit response to selection is greater than in a single locus.

DISCUSSION

It has long been known in qualitative terms that a response to selection increases the fitness of populations. This is not universally true however. Whether or not the response is beneficial depends on the other components of fitness (especially homeostasis) and the pattern of the environment (especially its variability and autocorrelation). The effect of good individual homeostasis is to reduce the effective variance of the environment, σ_S^2/H, and therefore to make it less likely that selection will be advantageous.

A highly variable and autocorrelated environment is necessary for the response to selection to be beneficial. Thus organisms with short generations will have more highly autocorrelated environments and will be more likely to depend on the response to selection for their adaptation. For both reasons fluctuating polymorphism is more likely to be important to insects than to mammals, and for the second reason more likely in Diptera than in the longer lived Lepidoptera or Orthoptera.

The brief investigation of multiple loci indicated that a system with all its phenotypic variability concentrated at one locus could respond more effectively to selection than one in which the additive variance is spread over several loci.

The degree of response to selection in a population was controlled in our model by the average phenotypic effect a. But although a is treated as a constant in the equations of changing gene frequency, it depends on the rest of the genotype and is subject to evolutionary change through the seletcion of modifiers. If the autocorrelation of the environment is too low or the level of individual homeostasis too high, the optimum value of a will be 0. The selection will work to modify the developmental pathways which link up with the locus in question in such a way that all genotypes at this locus will have the same phenotype. At this point the locus has disappeared at the level of gross phenotype although it may persist as a segregating isoallelic system at the enzymatic level.

The response to selection in a fluctuating environment is not the only adaptive advantage of genetic variance within populations. In the first paper of this series, it was shown that if the environmental heterogeneity is large compared to the individual homeostasis, and independently of any autocorrelation, a stable polymorphism is advantageous as "mixed strategy". These two kinds of adaptive polymorphism can be distinguished in several ways:

In mixed strategy polymorphism the optimal genetic variance for fitness is about equal to the variance of the environment on the same scale, whereas in response-to-selection polymorphism it is at least an order of magnitude lower. In mixed strategy polymorphism the genetic variance is largely epistatic and stable whereas in response-to-selection polymorphism it is largely additive and easily altered. Therefore, in species with a predominantly mixed strategy type of polymorphism local populations are likely to differ in epistatic blocks of genes. Therefore, crosses between populations would be expected to produce F_2 breakdown. In response-to-selection polymorphism the differences between local populations will be more additive and the recombinants will be intermediate on the average. Finally, the reduced fitness resulting from the F_2 breakdown in mixed strategy polymorphism creates a selective advantage to anything which reduces crossing. Isolating mechanisms would appear frequently in such species, and we would expect to see large clusters of similar species. In contrast, response-to-selection polymorphism would lead to large, widespread, and taxonomically distinct species with little tendency to speciate. With respect to Drosophila, this permits us to recognize three modes of adaptation: (1) The *D. melanogaster* mode—broad niche, high individual homeostasis, low levels of polymorphism, genetic variance mostly additive, little F_2 breakdown, and little tendency to speciate. (2) The *D. willistoni* mode—broad niche, low individual homeostasis, high levels of polymorphism, variance more epistatic, higher F_2 breakdown, and strong tendencies toward speciation. (3) The *D. prosaltans* mode—narrow niche, poor individual homeostasis, low polymorphism.

The predicted correlates within the adaptive system permit experimental testing of the theory.

SUMMARY

In the optimum quadratic deviation model in an unstable environment, an increase in the phenotypic effect of a locus reduces fitness by increasing the variance of the mean phenotype and the average variance within the population. It also can increase fitness by increasing the correlation between the mean phenotype and the optimum, which is an environmental variable, provided the autocorrelation of the environment exceeds about 0.8.

There is an optimal phenotypic effect a, different from zero, if the environment is sufficiently predictable. This optimum increases with the autocorrelation of the environment and with its variance but decreases with the homeostasis (environmental tolerance) of the individual. Thus species which are very sensitive to environmental change will depend more on genetic change to adapt. In any case, the average phenotypic variance of an optimal population is roughly 2 to 10% of the environmental variance.

The response to selection may restore a significant proportion of the fitness lost due to environmental fluctuation. For a normal random environment, the proportion of fitness restored is smaller than for environments that alternate periodically between discrete alternatives. Even a restoration of 2% would create enough selection pressure to move the population toward optimum on a time scale which is still short compared to the life of the species.

Linkage reduces the response to selection and the average variance because there is an excess of repulsion over coupling gametes. Thus tight linkage is advantageous when the total phenotypic effects of the loci are above optimum, and disadvantageous when they are below optimum.

Testable predictions are made relating the response to selection to other aspects of the adaptive system and species structure.

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