PARTIAL SELFING AND LINKAGE:
THE EFFECT OF A HETEROTIC LOCUS ON A NEUTRAL LOCUS

CURTIS STROBECK

Department of Genetics, University of Alberta, Edmonton, Alberta

ABSTRACT

Equilibria are determined for the two-locus model in a partially selfing population when one locus is neutral and the other locus is heterotic. At an equilibrium point, the frequency of heterozygotes at the neutral locus is greater than that expected from one-locus theory, even if the heterotic locus is on a different chromosome. Thus, the neutral locus also appears to be heterotic. The magnitude of this effect is determined for several different proportions of selfing and amounts of recombination.

IT is tacitly assumed in the theory of neutral alleles that all loci are neutral or at least that the relevant behavior of the neutral locus is unaffected by selected loci. The correctness or incorrectness of this assumption can in part be determined by the construction of a two-locus model in which one locus is neutral and the other locus is selected. For example, in an infinite, random-mating population the frequencies of the genotypes at a neutral locus are in Hardy-Weinberg proportions even if it is linked to a heterotic locus (provided there is some recombination between the two loci). Therefore, if the expected Hardy-Weinberg proportions from one-locus theory are used to determine the presence or absence of selection, the neutral locus in the two-locus model does indeed appear to be neutral. However, this is not true in a finite population where there is apparent selection at the neutral locus (associative overdominance) due to randomly generated linkage disequilibrium (OHTA and KIMURA 1970).

In this paper, the equilibrium points of the two-locus model with partial selfing are determined when one locus is neutral and the other is overdominant. It is shown that at an equilibrium point the frequency of heterozygotes at the neutral locus is greater than that expected from one-locus theory even if the neutral locus is not on the same chromosome as the selected locus. Therefore there appears to be selection at the neutral locus in the two-locus model, and the apparent selection coefficients are estimated by again using one-locus theory. The magnitude of this effect for different amounts of selfing and recombination are studied in some detail.

The results reported here are suggested by several previous papers on both completely selfing and partially selfing populations. In a completely selfing population, BARTLETT and HALDANE (1935) showed that the rate to homozygosity for

a neutral locus is decreased when it is linked to a balanced lethal. This certainly can be interpreted as saying that there appears to be apparent overdominance at the neutral locus. In a partially selfing population with two neutral loci, the frequency of double heterozygotes is greater than the product of the two marginal frequencies of the heterozygotes, $f(AaBb) > f(Aa) \times f(Bb)$, at equilibrium (BENNETT and BINET 1956; WEIR and COCKERHAM 1973). Since the conditional frequency of the Bb genotype when associated with the genotype Aa is greater than the marginal frequency of Bb, selection for the genotype Aa would result in an increase in the frequency of the genotype Bb. Therefore, if there is overdominance at the neutral locus. This is developed more formally in COCKERHAM and RAWLINGS (1967) with a one-locus model and in OHTA and COCKERHAM (1974), using a two-locus model with deleterious mutants occurring at one locus.

THEORY

One-locus theory: In this section, the one-locus theory of selection in a partially selfing population with two alleles (WORKMAN and JAIN 1966; KIMURA and OHTA 1971) is quickly reviewed. Let the gametic frequencies of the two alleles, A and a, be noted by x_1 and x_2 and the genotypic frequencies of AA, Aa, and aa, by u_1, u_2, and u_3, respectively. If the relative fitness values of the three genotypes AA, Aa, and aa are denoted by $1-t_1$, 1, and $1-t_2$ and the proportion of selfing by S, then the equations for the three genotypes in the next generation before selection has occurred are

$$
\begin{aligned}
u_1' &= x_1^2(1-S) + [u_1(1-t_1) + (u_2/4]S/W \\
u_2' &= 2x_1x_2(1-S) + (u_2/2)S/W \\
u_3' &= x_2^2(1-S) + [u_3(1-t_2) + (u_2/4)]S/W
\end{aligned}
\tag{1}
$$

where

$$
\begin{aligned}
Wx_1 &= u_1(1-t_1) + (u_2/2) \\
Wx_2 &= u_3(1-t_2) + (u_2/2) \\
W &= 1 - u_1t_1 - u_3t_2 .
\end{aligned}
$$

Providing that t_1 and t_2 are not zero, the equilibrium is

$$
\hat{u}_1 = \hat{x}_1^2 + \hat{x}_1\hat{x}_2 f \qquad \hat{u}_2 = 2\hat{x}_1\hat{x}_2(1-f) \qquad \hat{u}_3 = \hat{x}_2^2 + \hat{x}_1\hat{x}_2 f
$$

$$
\hat{x}_1 = \frac{t_2 - t_1 f}{(t_1+t_2)(1-f)} \qquad \hat{x}_2 = \frac{t_1 - t_2 f}{(t_1+t_2)(1-f)}
\tag{2}
$$

where f is a root of

$$
2kf^2 - [2(1-k) - (1-2k)S]f + (1-2k)S = 0
\tag{3}
$$

and

$$
k = \frac{t_1 t_2}{t_1 + t_2} .
$$

The relevant root is

$$f = \{2(1-k) - (1-2k)S - \sqrt{[2(1-k) - (1-2k)S]^2 - 8k(1-2k)S}\}/4. \quad (4)$$

The average fitness at equilibrium is

$$W = 1 - k(1+f) .$$

By solving this equation for f and substituting it into (3), it is seen that W must satisfy

$$2W^2 - \{1 + (1-2k)(1+S)\} W + (1-2k)S = 0. \tag{5}$$

The root of this equation corresponding to (4) is

$$W = \{1 + (1-2k)(1+S) + \sqrt{[1 + (1-2k)(1+S)]^2 - 8(1-2k)S}\}/4.$$

For neutral alleles, $t_1 = t_2 = 0$ and

$$f = \frac{S}{2-S} \tag{6}$$

(CROW and KIMURA 1970).

The stability of the equilibrium (2) is considered by KIMURA and OHTA (1971) by looking at the two endpoints, $x_1 = 0$ and $x_2 = 0$. It is shown that if $t_1, t_2 > 0$ $\hat{x}_1, \hat{x}_2 > 0$, then the two endpoints are unstable, so that the nontrivial equilibrium is stable.

Two-locus theory: In this section the recursion equations for the ten genotypes are given for the two-locus model in a partially selfing population where it is assumed that one locus has a heterozygotic advantage and the second locus is neutral. The equilibria are derived and their stability is investigated.

Let the frequencies of the ten genotypes be denoted by

Genotype	AABB	AABb	AAbb	AaBB	AB/ab	Ab/aB	Aabb	aaBB	aaBb	aabb
Frequency	v_1	v_2	v_3	v_4	v_5	v_6	v_7	v_8	v_9	v_{10}

and the frequencies of the four gametes AB, Ab, aB and ab by x_{11}, x_{10}, x_{01} and x_{00}, rsespectively. As before, it is assumed that the relative fitness values of the genotypes $AA\_\_$, $Aa\_\_$ and $aa\_\_$ are $1-t_1$ 1 and $1-t_2$ and that S is the proportion of selfing. The recombination value between the two loci is denoted by r. The recursion equations for the ten genotypes in the next generation before selection has occurred are given in Table 1.

The equilibria can be obtained by assuming that at equilibrium: first, the frequencies of the genotypes for the A locus are not affected by the neutral locus, *i.e.*, the equilibrium values for the A locus are those given in equation (2) and second, there is no linkage disequilibrium, *i.e.*, $\hat{x}_{11}\hat{x}_{00} - \hat{x}_{10}\hat{x}_{01} = 0$ and $v_5 = v_6$. Third, the frequency of the B allele denoted by p, is equal to the frequency of the B allele in each of the three genotypes at the A locus, *i.e.*,

$$p = v_1 + v_4 + v_8 + (1/2)(v_2 + v_5 + v_6 + v_9) =$$

$$\frac{v_1 + (1/2)v_2}{v_1 + v_2 + v_3} = \frac{v_4 + (1/2)(v_5 + v_6)}{v_4 + v_5 + v_6 + v_7} = \frac{v_8 + (1/2)v_9}{v_8 + v_9 + v_{10}} .$$

TABLE 1

Recursion equations for the genotypic frequencies

$$v_1' = x_{11}^2(1-S) + [(v_1 + (1/4)v_2)(1-t_1) + (1/4)v_4 + (1/4)(1-r)^2v_5 + (1/4)r^2v_6]S/W$$

$$v_2' = 2x_{11}x_{10}(1-S) + [(1/2)v_2(1-t_1) + (1/2)r(1-r)v_5 + (1/2)r(1-r)v_6]S/W$$

$$v_3' = x_{10}^2(1-S) + [(v_3 + (1/4)v_2)(1-t_1) + (1/4)v_7 + (1/4)r^2v_5 + (1/4)(1-r)^2v_6]S/W$$

$$v_4' = 2x_{11}x_{01}(1-S) + [(1/2)v_4 + (1/2)r(1-r)v_5 + (1/2)r(1-r)v_6]S/W$$

$$v_5' = 2x_{11}x_{00}(1-S) + [(1/2)(1-r)^2v_5 + (1/2)r^2v_6]S/W$$

$$v_6' = 2x_{10}x_{01}(1-S) + [(1/2)r^2v_5 + (1/2)(1-r)^2v_6]S/W$$

$$v_7' = 2x_{10}x_{00}(1-S) + [(1/2)v_7 + (1/2)r(1-r)v_5 + (1/2)r(1-r)v_6]S/W$$

$$v_8' = v_{01}^2(1-S) + [(v_8 + (1/4)v_9)(1-t_2) + (1/4)v_4 + (1/4)r^2v_5 + (1/4)(1-r)^2v_6]S/W$$

$$v_8' = x_{01}^2(1-S) + [(v_8 + (1/4)v_9)(1-t_2) + (1/4)v_4 + (1/4)r^2v_5 + (1/4)(1-r)^2v_6]S/W$$

$$v_9' = 2x_{01}x_{00}(1-S) + [(1/2)v_9(1-t_2) + (1/2)r(1-r)v_5 + (1/2)r(1-r)v_6]S/W$$

$$v_{10}' = x_{00}^2(1-S) + [(v_{10} + (1/4)v_9)(1-t_2) + (1/4)v_7 + (1/4)(1-r)^2v_5 + (1/4)r^2v_6]S/W$$

$$Wx_{11} = (v_1 + (1/2)v_2)(1-t_1) + (1/2)v_4 + (1/2)v_5 - (1/2)r(v_5 - v_6)$$

$$Wx_{10} = (v_3 + (1/2)v_2)(1-t_1) + (1/2)v_7 + (1/2)v_6 + (1/2)r(v_5 - v_6)$$

$$Wx_{01} = (v_8 + (1/2)v_9)(1-t_2) + (1/2)v_4 + (1/2)v_6 + (1/2)r(v_5 - v_6)$$

$$Wx_{00} = (v_{10} + (1/2)v_9)(1-t_2) + (1/2)v_7 + (1/2)v_5 - (1/2)r(v_5 - v_6)$$

$$W = 1 - (v_1 + v_2 + v_3)t_1 - (v_8 + v_9 + v_{10})t_2$$

After the equilibria have been obtained, it is then necessary to prove that these three assumptions are true. They are shown to be true if $t_1 = t_2$ during the analysis of the stability of the equilibria. However, since the B locus is neutral, it is intuitively clear that they are also true if $t_1 \neq t_2$.

Using these three assumptions and the equations for v_2', v_5' and v_9' given in Table 1, the equilibria can be determined and are

$$\begin{aligned}
\hat{v}_1 &= \hat{u}_1 p - C_0 C_1/2 & \hat{v}_2 &= C_0 C_1 & \hat{v}_3 &= \hat{u}_1 q - C_0 C_1/2 \\
\hat{v}_4 &= \hat{u}_2 p - C_0 & \hat{v}_5 &= v_6 = C_0 & \hat{v}_7 &= \hat{u}_2 q - C_0 \\
\hat{v}_8 &= \hat{u}_3 p - C_0 C_2/2 & \hat{v}_9 &= C_0 C_2 & \hat{v}_{10} &= \hat{u}_3 q - C_0 C_2/2
\end{aligned} \tag{7}$$

where

$$C_0 = \frac{2\hat{x}_1 \hat{x}_2 pq(1-S)W}{W - (1/2)[(1-r)^2 + r^2]S}$$

$$C_1 = \frac{(\hat{x}_1/\hat{x}_2)\{W - (1/2)[(1-r)^2 + r^2]S\} + r(1-r)S}{W - (1/2)(1-t_1)S}$$

$$C_2 = \frac{(\hat{x}_2/\hat{x}_1)\{W - (1/2)[(1-r)^2 + r^2]S\} + r(1-r)S}{W - (1/2)(1-t_2)S}$$

and $q = 1 - p$.

For the purpose of analyzing the stability of these equilibria, it is convenient to transform to the variables

$$\begin{aligned}
u_1 &= v_1 + v_2 + v_3 & u_2 &= v_4 + v_5 + v_6 + v_7 & u_3 &= v_8 + v_9 + v_{10} \\
u_4 &= v_1 - v_3 & u_5 &= v_4 - v_7 & u_6 &= v_8 - v_{10} & u_7 &= v_5 - v_6 \\
u_8 &= v_1 - 2v_2 + v_3 & u_9 &= v_4 - v_5 - v_6 + v_7 & u_{10} &= v_8 - 2v_9 + v_{10} \\
x_1 &= x_{11} + x_{10} & x_2 &= x_{01} + x_{00} & x_3 &= x_{11} - x_{10} & x_4 &= x_{01} - x_{00} \ .
\end{aligned}$$

The recursion equations for these variables are given in Table 2.

From Table 2, it is seen that the equations for u_1', u_2', and u_3' involve only u_1, u_2, and u_3 and are the same equations as (1). Therefore the equilibrium values for these variables are given in (2), and the stability of this equilibrium is the same as in the one-locus model. This proves the first assumption used in determining the equilibria for the two locus-model.

It is also seen from Table 2 that if u_1, u_2, and u_3 are at their equilibrium values, then the equations for u_4', u_5', u_6', and u_7' are linear and involve only these variables. With the simplifying assumption of symmetric fitness values, $i.e.$, $t=t_1=t_2$, so that $\hat{x}_1=\hat{x}_2=1/2$, the recursion equations for the deviations from equilibrium, $\varepsilon_i=u_i-\hat{u}_i$ $(i=4,5,6,7)$, are

$$\varepsilon' = \begin{bmatrix} \varepsilon_4' \\ \varepsilon_5' \\ \varepsilon_6' \\ \varepsilon_7' \end{bmatrix} = W/2 \begin{bmatrix} (1+S)(1-t) & 1/2 & 0 & (1-2r)/2 \\ (1-S)(1-t) & 1 & (1-S)(1-t) & 0 \\ 0 & 1/2 & (1+S)(1-t) & -(1-2r)/2 \\ (1-S)(1-t) & 0 & -(1-S)(1-t) & 1-2r \end{bmatrix} \begin{bmatrix} \varepsilon_4 \\ \varepsilon_5 \\ \varepsilon_6 \\ \varepsilon_7 \end{bmatrix} = A\varepsilon$$

when u_1, u_2, and u_3 are at their equilibrium values. In order for the equilibrium to be asymptotically stable, all of the eigenvalues must be less than one in absolute value. If the largest eigenvalue is one, then the equilibrium can be asymptotically stable, stable or unstable depending on the second-order terms. In this case, since the equations are linear, if the largest eigenvalue is one, the equilibrium is (neutrally) stable (SAATY 1967).

TABLE 2

Recursion equations for the transformed genotypic frequencies

$u_1' = x_1{}^2(1-S) + [u_1(1-t_1) + (1/4)u_2]S/W$

$u_2' = 2x_1x_2(1-S) + (1/2)u_2 S/W$

$u_3' = x_2{}^2(1-S) + [u_3(1-t_2) + (1/4)u_2]S/W$

$u_4' = x_1x_3(1-S) + [u_4(1-t_1) + (1/4)u_5 + (1/4)(1-2r)u_7]S/W$

$u_5' = (x_1x_4 + x_2x_3)(1-S) + (1/2)u_5 S/W$

$u_6' = x_2x_4(1-S) + [u_6(1-t_2) + (1/4)u_5 - (1/4)(1-2r)u_7]S/W$

$u_7' = (x_2x_3 - x_1x_4)(1-S) + (1/2)(1-2r)u_7 S/W$

$u_8' = ((3/2)x_3{}^2 - (1/2)x_1{}^2)(1-S) + (1/2)\{(u_1 + u_8)(1-t_1) + (1/4)u_2 + (1/4)u_9 + (1/4)[1-6r(1-r)](u_2 - u_9)\}S/W$

$u_9' = 2x_3x_4(1-S) + (1/4)\{u_2 + u_9 - [1-4r(1-r)](u_2 - u_9)\}S/W$

$u_{10}' = ((3/2)x_4{}^2 - (1/2)x_2{}^2)(1-S) + (1/2)\{(u_3 + u_{10})(1-t_1) + (1/4)u_2 + (1/4)u_9 + (1/4)[1-6r(1-r)](u_2 - u_9)\}S/W$

$Wx_1 = u_1(1-t_1) + (1/2)u_2$

$Wx_2 = u_3(1-t_2) + (1/2)u_2$

$Wx_3 = u_4(1-t_1) + (1/2)u_5 + (1/2)(1-2r)u_7$

$Wx_4 = u_6(1-t_2) + (1/2)u_5 - (1/2)(1-2r)u_7$

$W = 1 - u_1t_1 - u_3t_2$

The four eigenvalues of A are the roots of

$$\lambda^2 - (1/2W)[1 + (1+S)(1-t)]\lambda + (1/2W^2)(1-t)S = 0 \qquad (8a)$$

and

$$\lambda^2 - (1/2W)[1 - 2r + (1+S)(1-t)]\lambda + (1/2W^2)(1-t)S(1-2r) = 0. \qquad (8b)$$

The roots of (8a) are

$$\lambda_1 = \frac{1 + (1+S)(1-t) + \sqrt{[1 + (1+S)(1-t)]^2 - 8(1-t)S}}{4W} = 1$$

and

$$\lambda_2 = \frac{1 + (1+S)(1-t) - \sqrt{[1 + (1+S)(1-t)]^2 - 8(1-t)S}}{4W}$$

For $S > 0$, $0 \le \lambda_2 < 1$ since $1 + (1+S)(1-t) > 0$ and $\lambda_1 = 1$. The necessary and sufficient conditions for the roots of (8b) to be less than one in absolute value (GOLDBERG 1958) are

$$1 - (1/2W)[1 - 2r + (1+S)(1-t)] + (1/2W^2)(1-t)S(1-2r) > 0 \qquad (9a)$$

$$1 + (1/2W)[1 - 2r + (1+S)(1-t)] + (1/2W^2)(1-t)S(1-2r) > 0 \qquad (9b)$$

$$1 - (1/2W^2)(1-t)S(1-2r) > 0 . \qquad (9c)$$

It is seen that (9b) is always satisfied since all the terms are positive. To see that (9a) and (9c) are always satisfied, notice that (8b) reduces to (8a) when $r=0$. Thus, if $r=0$, the left hand side of (9a) is equal to zero (since $\lambda_1=1$) and the left hand side of (9c) is greater than zero (since $\lambda_1\lambda_2 < 1$). Since the partial derivatives with respect to r of the left hand side of both equations are positive, both (9a) and (9c) are always satisfied if $r>0$. Therefore, both roots of (8b) are less than one in absolute value.

A right eigenvector of $\lambda_1 = 1$ is $\xi_1 = (\hat{u}_1, \hat{u}_2, \hat{u}_3, 0)^T$. Thus after a pertubation from an equilibrium, the system goes to a new equilibrium given by

$$\begin{bmatrix} \hat{u}_4{}^* \\ \hat{u}_5{}^* \\ \hat{u}_6{}^* \\ \hat{u}_7{}^* \end{bmatrix} = \begin{bmatrix} \hat{u}_4 \\ \hat{u}_5 \\ \hat{u}_6 \\ \hat{u}_7 \end{bmatrix} + \begin{bmatrix} \hat{u}_1 \\ \hat{u}_2 \\ \hat{u}_3 \\ 0 \end{bmatrix} C$$

where C is a constant determined by the pertubation, and therefore

$$\hat{u}_4{}^* = \hat{u}_1(p-q) + \hat{u}_1 C = \hat{u}_1(p^* - q^*)$$
$$\hat{u}_5{}^* = \hat{u}_2(p-q) + \hat{u}_2 C = \hat{u}_2(p^* - q^*)$$
$$\hat{u}_6{}^* = \hat{u}_3(p-q) + \hat{u}_3 C = \hat{u}_3(p^* - q^*)$$
$$\hat{u}_7{}^* = \hat{u}_7 = 0$$

where p^* and q^* are the new equilibrium frequencies of B and b. This proves assumptions two and three used in determining the equilibria for the two-locus model when there are symmetric fitness values.

Lastly, it can be seen from Table 2 that if all the other variables are in equilibrium, then the equations for u_8', u_9', and u_{10}' are linear and involve only themselves. The recursion equations for the deviations about the equilibrium, ε_i $(i=8,9,10)$ are

$$
\varepsilon' = \begin{bmatrix} \varepsilon_8' \\ \varepsilon_9' \\ \varepsilon_{10}' \end{bmatrix} = 1/2W \begin{bmatrix} (1-t_1)S & (3/2)r(1-r)S & 0 \\ 0 & 2r(1-r)S & 0 \\ 0 & (3/2)r(1-r)S & (1-t_2)S \end{bmatrix} \begin{bmatrix} \varepsilon_8' \\ \varepsilon_9' \\ \varepsilon_{10}' \end{bmatrix} = B\varepsilon
$$

The eigenvalues of B are

$$
\mu_1 = (1/2W)(1-t_1)S \qquad \mu_2 = (1/W)r(1-r)S \qquad \mu_3 = (1/2W)(1-t_2)S \ ,
$$

which are all less than one since from the equation for u_2' in (1) it can be seen that $S/2 < W$ at equilibrium.

In summary, the stability analysis shows that if $t_1 = t_2 = t$, then the equilibria are the set of all points given by (7) with $0<p<1$. For a particular value of p, the equilibrium is stable but not asymptotically stable (there exists one eigenvalue of one). However, the set of equilibria is the limit set of the difference equations in Table 1, i.e., after a perturbation the solution will converge to one of the equilibria in the set as time goes to infinity.

APPLICATIONS

From the equilibria frequencies (7), the frequency of the heterozygotes at a neutral locus linked to a locus at which there is a heterozygotic advantage can be determined. If this is compared to the expected frequency of heterozygotes at a neutral locus using one-locus theory, it is found that there is an excess of heterozygotes. Thus there is an apparent heterozygotic advantage at the neutral locus, and the "fitness values" of the genotypes of the neutral locus is calculated using one-locus theory. The extent and magnitude of this phenomenon is studied in this section. For convenience, the fitness values at the A locus are assumed to be symmetric, $t=t_1=t_2>0$, throughout this section, which implies that $\hat{x}_1 = \hat{x}_2 = 1/2$.

The frequency of heterozygotes at the neutral locus is

$$
\begin{aligned}
v_2 + v_5 + v_6 + v_9 &= \frac{pq(1-S)W}{W - (S/2)[(1-r)^2+r^2]} \left[1 + \frac{W - (S/2)(1-2r)^2}{W - (S/2)(1-t)}\right] \\
&= 2pq \frac{2(1-S)}{2-S} \frac{(2-S)W}{4[W - (S/2)(1-t)]} \left[2 + \frac{(St/2)}{W - (S/2)[(1-r)^2+r^2]}\right] .
\end{aligned}
\tag{10}
$$

In order for there to be an excess of heterozygotes, the inequality

$$
\frac{(2-S)W}{4[W - (S/2)(1-t)]} \left[2 + \frac{(St/2)}{W - (S/2)[(1-r)^2+r^2]}\right] \geq 1
\tag{11}
$$

must hold since $2pq\dfrac{2(1-S)}{2-S}$ is the expected frequency of heterozygotes for a neutral locus from one-locus theory. Since $(1-r)^2 + r^2 \geq 0.5$ with equality holding if and only if $r = 0.5$, the inequality (11) can be replaced by

$$\frac{(2-S)W}{4[W-(S/2)(1-t)]}\left(2+\frac{(St/2)}{W-(S/4)}\right) \geq 1$$

which upon rearranging becomes

$$S\{2W^2 - [1 + [1+(S/2)](1-t)]W + (S/2)(1-t)\} \leq 0 .$$

Both $W - (S/2)(1-t)$ and $W - (S/4)$ are greater than zero since $W > (S/2)$. But from (5)

$$2W^2 - [1 + (1+S)(1-t)]W + S(1-t) = 0 ,$$

thus, the inequality further reduces to

$$(S^2/2)(1-t)(W-1) \leq 0$$

with equality if and only if $t=1$. Therefore, there is always an excess of heterozygotes at the neutral locus over what is expected from one-locus theory unless $t=1$ and $r=0.5$.

Let the apparent fitness values of the genotypes BB, Bb, and bb be $1-s_1$, 1, and $1-s_2$, respectively The apparent selection coefficients s_1 and s_2 can be obtained from the generalized inbreeding coefficient at the B locus, $\hat{f}$, and the frequencies of the B and b alleles, p and q, at equilibrium. From (10)

$$\hat{f} = 1 - \frac{(1/2)(1-S)W}{W-(S/2)[(1-r)^2+r^2]}\left\{1 + \frac{W-(S/2)(1-2r)^2}{W-(S/2)(1-t)}\right\} \qquad (12)$$

and from (3)

$$\hat{k} = \frac{2\hat{f}-S\hat{f}-S}{2(\hat{f}-S)(1+\hat{f})} . \qquad (13)$$

Using the definition of $\hat{k}$

$$\hat{k} = \frac{s_1 s_2}{s_1+s_2}$$

and

$$p = \frac{s_2-s_1\hat{f}}{(s_1+s_2)(1-\hat{f})} \quad \text{and} \quad q = \frac{s_1-s_2\hat{f}}{(s_1+s_2)(1-\hat{f})}$$

from (2),

$$s_1 = \frac{(1+\hat{f})\hat{k}}{1-q(1-\hat{f})} \quad \text{and} \quad s_2 = \frac{(1+\hat{f})\hat{k}}{1-p(1-\hat{f})} \qquad (14)$$

are obtained. Notice that $\hat{k}$ does not depend on the frequency of the alleles at the B locus, but both s_1 and s_2 do.

In order to obtain some feeling for the magnitude of the apparent fitness values at the B locus, $\hat{s} = s_1 = s_2 = 2\hat{k}$ (assuming $p = q = 1/2$) is plotted against $t = 2k$ at the A locus for S equal to 0.5, 00.9 and 0.99 for $r = 0.01$ (Figure 1), $r = 0.1$ (Figure 2) and $r = 0.5$ (Figure 3). It should be emphasized that there is signifi-
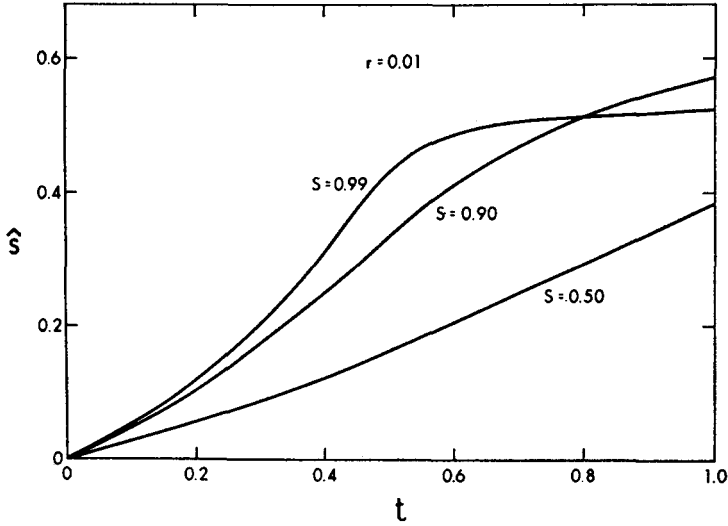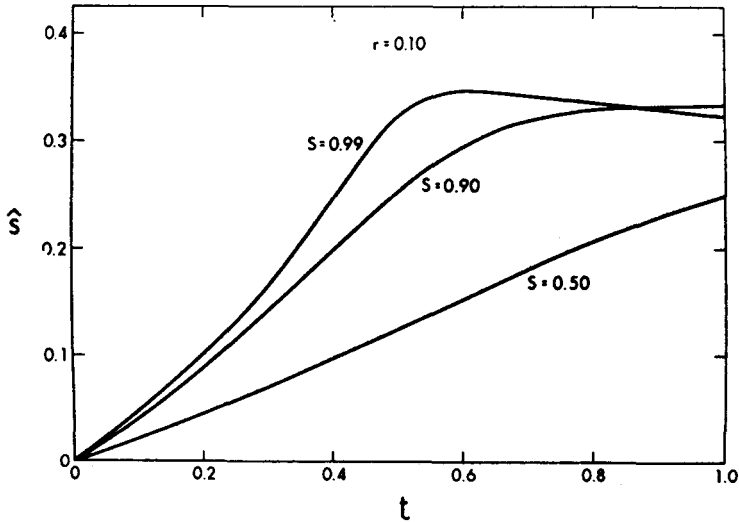

FIGURE 1.—The apparent fitness value $\hat{s} = 2\hat{k}$ at the neutral B locus plotted against the fitness value $t = 2k$ at the A locus for $r = 0.01$ for the three proportions of selfing $S = 0.5$, 0.9, and 0.99.

FIGURE 2.—The apparent fitness value $\hat{s} = 2\hat{k}$ at the neutral B locus plotted against the fitness value $t = 2k$ at the A locus for $r = 0.1$ for the three proportions of selfing $S = 0.5$, 0.9, and 0.99.
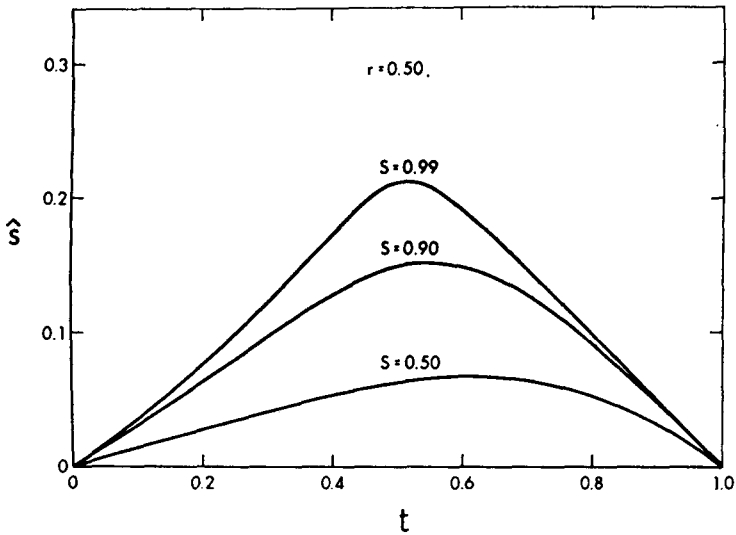
FIGURE 3.—The apparent fitness value $\hat{s} = 2\hat{k}$ at the neutral B locus plotted against the fitness value $t = 2k$ at the A locus for $r = 0.5$ for the three proportions of selfing $S = 0.5$, 0.9, and 0.99.

cant apparent selection at the neutral locus even if the selected locus is on a different chromosome, i.e., $r = 0.5$. The greatest effect for $r = 0.5$ shown in Figure 3 is with $S = 0.99$ and $t \simeq 0.5$. The apparent fitness values at the neutral locus in this are $\hat{s} = s_1 = s_2 = 0.211$.

DISCUSSION

It is shown in this paper that if there is only a single locus at which there is a heterozygotic advantage, there is an apparent selection not only at closely linked loci, but at any locus in the whole genome. Presumably, if two loci were selected, the effect on the neutral locus would be still greater. Therefore, any estimates of fitness values based on one-locus theory, such as the maximum likelihood estimates for four esterase loci by ALLARD, KALHAR and WEIR (1972), are not estimating the fitness values at a single locus, but the effect of all selected loci in the genome. Thus, what is needed is neither a one-locus, nor even an n-locus model of selection in a partially selfing population, but a model that considers the whole genome.

The results also suggest that since there is a greater frequency of heterozygotes at a neutral locus than that expected from one-locus theory, the criteria for polymorphism to be maintained at two or more selected loci are less stringent than the conditions obtained from one-locus theory (ESHEL 1978).

LITERATURE CITED

ALLARD, R. W., A. L. KAHLER and B. S. WEIR, 1972   The effect of selection on esterase allozymes in a barley population. Genetics **72**: 489–503.

BARTLETT, M. S. and J. B. S. HALDANE, 1935   The theory of inbreeding with forced heterozygosis. J. Genet **31**: 327–340.

BENNETT, J. H. and F. E. BINET, 1956   Association between Mendelian factors with mixed selfing and random mating. Heredity **10**: 51–56.

COCKERHAM, C. C. and J. O. RAWLINGS, 1967   Apparent heterosis of a neutral gene with inbreeding. Ciencia E Cultura **19**: 89–94.

CROW, J. F. and M. KIMURA, 1970   *An Introduction to Population Genetics.* Harper and Row, New York.

ESHEL, I., 1978   On a mutual maintenance of a polymorphism in two non-epistamic loci with partial selfing. Theoret. Pop. Biol. **13**: 99–111.

GOLDBERG, S., 1958   *Introduction to Difference Equations.* John Wiley and Sons, New York.

KIMURA, M. and T. OHTA, 1971   *Theoretical Aspects of Population Genetics.* Princeton University Press, Princeton, New Jersey.

OHTA, T. and C. C. COCKERHAM, 1974   Detrimental genes with partial selfing effects on a neutral locus. Genet. Res. **23**: 191–200.

OHTA, T. and M. KIMURA, 1970   Development of associative overdominance through linkage disequilibrium in finite populations. Genet. Res. **21**: 247–262.

SAATY, T. L., 1967   *Modern Nonlinear Equations.* McGraw-Hill, Inc., New York.

WEIR, B. S. and C. C. COCKERHAM, 1973   Mixed self and random mating at two loci. Genet. Res. **21**: 247–262.

WORKMAN, P. L. and S. K. JAIN, 1966   Zygotic selection under mixed random mating and self-fertilization: Theory and problems of estimation. Genetics **54**: 159–171.

Corresponding editor: R. C. LEWONTIN and B. V. WEIR