THE TWO-LOCUS MODEL WITH SEX DIFFERENCES IN RECOMBINATION

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ABSTRACT

The criteria for stability of the equilibrium with $D=0$ are obtained for the two locus model with multiplicative or symmetric fitnesses when the recombination values in males and females are different. It is shown that if r is defined to be equal to the average of the recombination values in males and females, then the criteria are exactly the same as in the standard two locus model.—The equilibrium values with $D \neq 0$ are obtained for the symmetric fitness model. At this equilibrium, the absolute value of D is always greater (for the same average recombination value) if the recombination values in males and females differ than if they are equal.

THE two-locus model of selection has had an extensive development in recent years (LEWONTIN and KOJIMA 1960; BODMER and FELSENSTEIN 1967; KARLIN and FELDMAN 1970). In all of the models, it is assumed that the recombination value is equal in the two sexes. However, it has been observed that there are sex differences in recombination in many animals (DUNN and BENNETT 1967), as well as the well known example of *Drosophila*.

In this paper both the multiplicative and the symmetric models of fitness values are investigated when there are different recombination values in the two sexes. The criteria for the stability of the equilibrium point, with no linkage disequilibrium, are obtained for both models. Also, the equilibrium with linkage disequilibrium is determined for the symmetric model of fitness values.

GEIRINGER (1948) has shown that if there is no selection, then the average of the recombination values in males and females can be used as the recombination value. Also, CHARLESWORTH and CHARLESWORTH (1973) have shown that the average recombination value is a very good approximation for the purpose of determining the change in gametic frequencies. Thus, the results obtained in this paper are compared to the results from standard two-locus theory with this in mind.

THEORY

In this section the equations for selection are developed for two autosomal loci when there are different recombination values in the two sexes. The usual assumptions of random mating, discrete generations, and infinite population size are made.

Let the two alleles at the first and second loci be denoted by A and a , and B and b , respectively. The gametic frequencies AB , Ab , aB , and ab are designated by X_1 , X_2 , X_3 and X_4 in males and Y_1 , Y_2 , Y_3 and Y_4 in females. The gametic frequencies are subject to the two constraints, $\sum X_i = 1$ and $\sum Y_i = 1$.

It is assumed that the fitness values of the genotypes are the same in both sexes. Let w_{ij} be the fitness value of the genotype produced by the union of the gametes X_i and Y_j . It will be assumed that there are no paternal or maternal components of fitness, that is, $w_{ij} = w_{ji}$. It is also assumed that the fitness values of the coupled and repulsed forms of double heterozygotes are equal, that is, $w_{14} = w_{23}$.

The recombination values are designated by r_m in males and r_f in females.

With these definitions the recurrence equations for selection are given in Table 1. The selection models that are investigated for these equations are (a) the symmetric model of LEWONTIN and KOJIMA (1960) and (b) the multiplicative model.

The Symmetric Model of Lewontin and Kojima

The matrix of fitness values for the symmetric model of LEWONTIN and KOJIMA is

$$W = \begin{pmatrix} 1-\alpha & 1-\beta & 1-\gamma & 1 \\ 1-\beta & 1-\alpha & 1 & 1-\gamma \\ 1-\gamma & 1 & 1-\alpha & 1-\beta \\ 1 & 1-\gamma & 1-\beta & 1-\alpha \end{pmatrix}$$

It can be seen by substitution that $\hat{X}_1 = \hat{X}_2 = \hat{X}_3 = \hat{X}_4 = \hat{Y}_1 = \hat{Y}_2 = \hat{Y}_3 = \hat{Y}_4 = 1/4$ is an equilibrium point for the equations in Table 1 with these fitness values.

TABLE 1

Equations for selection with two loci and two sexes

$\bar{W} X_1' = w_{11}X_1Y_1 + \frac{1}{2}w_{12}(X_1Y_2 + X_2Y_1) + \frac{1}{2}w_{13}(X_1Y_3 + X_3Y_1) + \frac{1}{2}w_{14}(X_1Y_4 + X_4Y_1) - r_m w_{14}D$
$\bar{W} X_2' = \frac{1}{2}w_{21}(X_1Y_2 + X_2Y_1) + w_{22}X_2Y_2 + \frac{1}{2}w_{23}(X_2Y_3 + X_3Y_2) + \frac{1}{2}w_{24}(X_2Y_4 + X_4Y_2) + r_m w_{14}D$
$\bar{W} X_3' = \frac{1}{2}w_{31}(X_1Y_3 + X_3Y_1) + \frac{1}{2}w_{32}(X_2Y_3 + X_3Y_2) + w_{33}X_3Y_3 + \frac{1}{2}w_{34}(X_3Y_4 + X_4Y_3) + r_m w_{14}D$
$\bar{W} X_4' = \frac{1}{2}w_{41}(X_1Y_4 + X_4Y_1) + \frac{1}{2}w_{42}(X_2Y_4 + X_4Y_2) + \frac{1}{2}w_{43}(X_3Y_4 + X_4Y_3) + w_{44}X_4Y_4 - r_m w_{14}D$
$\bar{W} Y_1' = w_{11}X_1Y_1 + \frac{1}{2}w_{12}(X_1Y_2 + X_2Y_1) + \frac{1}{2}w_{13}(X_1Y_3 + X_3Y_1) + \frac{1}{2}w_{14}(X_1Y_4 + X_4Y_1) - r_f w_{14}D$
$\bar{W} Y_2' = \frac{1}{2}w_{21}(X_1Y_2 + X_2Y_1) + w_{22}X_2Y_2 + \frac{1}{2}w_{23}(X_2Y_3 + X_3Y_2) + \frac{1}{2}w_{24}(X_2Y_4 + X_4Y_2) + r_f w_{14}D$
$\bar{W} Y_3' = \frac{1}{2}w_{31}(X_1Y_3 + X_3Y_1) + \frac{1}{2}w_{32}(X_2Y_3 + X_3Y_2) + w_{33}X_3Y_3 + \frac{1}{2}w_{34}(X_3Y_4 + X_4Y_3) + r_f w_{14}D$
$\bar{W} Y_4' = \frac{1}{2}w_{41}(X_1Y_4 + X_4Y_1) + \frac{1}{2}w_{42}(X_2Y_4 + X_4Y_2) + \frac{1}{2}w_{43}(X_3Y_4 + X_4Y_3) + w_{44}X_4Y_4 - r_f w_{14}D$
$D = \frac{1}{2}(X_1Y_4 + X_4Y_1 - X_2Y_3 - X_3Y_2)$
$W = \sum_i \sum_j w_{ij}X_iY_j$

The criteria for stability of an equilibrium point can be found by determining the eigenvalues of the Jacobian,

$$\mathbf{J} = \begin{pmatrix} \mathbf{A}_{11} & \mathbf{A}_{12} \\ \mathbf{A}_{21} & \mathbf{A}_{22} \end{pmatrix}$$

where

$$\mathbf{A}_{11} = \left(\frac{\partial X_i'}{\partial X_j} \right) \quad \mathbf{A}_{12} = \left(\frac{\partial X_i'}{\partial Y_j} \right)$$

$$\mathbf{A}_{21} = \left(\frac{\partial Y_i'}{\partial X_j} \right) \quad \mathbf{A}_{22} = \left(\frac{\partial Y_i'}{\partial Y_j} \right)$$

evaluated at the equilibrium.

For this equilibrium point

$$\mathbf{J} = \begin{pmatrix} \mathbf{A} & \mathbf{A} \\ \mathbf{B} & \mathbf{B} \end{pmatrix}$$

where

$$\mathbf{A} = \begin{pmatrix} \frac{\frac{1}{2}(1-\beta-r_m)}{4-\alpha-\beta-\gamma} + \frac{1}{4} & \frac{\frac{1}{2}(1-\beta-r_m)}{4-\alpha-\beta-\gamma} - \frac{1}{4} & \frac{\frac{1}{2}(1-\beta-r_m)}{4-\alpha-\beta-\gamma} - \frac{1}{4} & \frac{\frac{1}{2}(1-\beta-r_m)}{4-\alpha-\beta-\gamma} - \frac{1}{4} \\ \frac{\frac{1}{2}(1-\beta+r_m)}{4-\alpha-\beta-\gamma} - \frac{1}{4} & \frac{\frac{1}{2}(1-\alpha-r_m)}{4-\alpha-\beta-\gamma} + \frac{1}{4} & \frac{\frac{1}{2}(1-r_m)}{4-\alpha-\beta-\gamma} - \frac{1}{4} & \frac{\frac{1}{2}(1-\gamma+r_m)}{4-\alpha-\beta-\gamma} - \frac{1}{4} \\ \frac{\frac{1}{2}(1-\gamma+r_m)}{4-\alpha-\beta-\gamma} - \frac{1}{4} & \frac{\frac{1}{2}(1-r_m)}{4-\alpha-\beta-\gamma} - \frac{1}{4} & \frac{\frac{1}{2}(1-\alpha-r_m)}{4-\alpha-\beta-\gamma} + \frac{1}{4} & \frac{\frac{1}{2}(1-\beta+r_m)}{4-\alpha-\beta-\gamma} - \frac{1}{4} \\ \frac{\frac{1}{2}(1-r_m)}{4-\alpha-\beta-\gamma} - \frac{1}{4} & \frac{\frac{1}{2}(1-\gamma+r_m)}{4-\alpha-\beta-\gamma} - \frac{1}{4} & \frac{\frac{1}{2}(1-\beta+r_m)}{4-\alpha-\beta-\gamma} - \frac{1}{4} & \frac{\frac{1}{2}(1-\alpha-r_m)}{4-\alpha-\beta-\gamma} + \frac{1}{4} \end{pmatrix}$$

and $\mathbf{B}$ is the same as $\mathbf{A}$ with r_m replaced by r_f .

The three non-zero eigenvalues of $\mathbf{J}$ are

$$\lambda_1 = 1 + \frac{-\alpha + \beta - \gamma}{4 - \beta - \alpha - \gamma}$$

$$\lambda_2 = 1 + \frac{-\alpha - \beta + \gamma}{4 - \beta - \alpha - \gamma}$$

$$\lambda_3 = 1 + \frac{-\alpha + \beta + \gamma - 2(r_m + r_f)}{4 - \beta - \alpha - \gamma}$$

The associated right eigenvectors are

$$\xi_1 = (+1, -1, +1, -1, +1, -1, +1, -1)^T$$

$$\xi_2 = (+1, +1, -1, -1, +1, +1, -1, -1)^T$$

$$\xi_3 = (1+k, -1-k, -1-k, 1+k, 1-k, -1+k, -1+k, 1-k)^T$$

where

$$k = \frac{r_f - r_m}{2 - \alpha - (r_m + r_f)}.$$

The five right eigenvectors of zero can be taken to be

$$\begin{aligned}\xi_4 &= (+1, -1, +1, -1, -1, +1, -1, +1)^T \\ \xi_5 &= (+1, +1, -1, -1, -1, -1, +1, +1)^T \\ \xi_6 &= (+1, -1, -1, +1, -1, +1, +1, -1)^T \\ \xi_7 &= (+1, +1, +1, +1, +1, +1, +1, +1)^T \\ \xi_8 &= (+1, +1, +1, +1, -1, -1, -1, -1)^T.\end{aligned}$$

Since the X_i and Y_i are subject to the constraints $\sum X_i = \sum Y_i = 1$, the deviations from the equilibrium, ε_i^x and ε_i^y are subject to the constraints $\sum \varepsilon_i^x = \sum \varepsilon_i^y = 0$. It can be shown that $\xi_1, \xi_2, \xi_3, \xi_4, \xi_5$, and ξ_6 are a basis for the subspace which satisfies these constraints.

The equilibrium is stable if all of the eigenvalues (whose eigenvectors satisfy the constraints) are less than one in absolute value and unstable if any one of them is greater than one in absolute value. The conditions for stability are therefore

$$\begin{aligned}-\alpha + \beta - \gamma &< 0 \\ -\alpha - \beta + \gamma &< 0 \\ \frac{r_m + r_f}{2} &> \frac{-\alpha + \beta + \gamma}{4}\end{aligned}\tag{1}$$

It is seen that if r is defined to be equal to $\frac{r_m + r_f}{2}$ then the conditions given in

(1) are exactly the same as the conditions given in KARLIN and FELDMAN (1970). Thus, for the purpose of determining the stability of the equilibrium with no linkage disequilibrium for the symmetric model of LEWONTIN and KOJIMA, the recombination value can be thought of as the average of the recombination values in the males and females.

If the inequality

$$\frac{r_m + r_f}{2} > \frac{-\alpha + \beta + \gamma}{4}$$

is not satisfied the equilibrium will be unstable and the deviations from equilibrium will eventually increase exponentially along the eigenvector ξ_3 . This suggests that the new equilibrium reached might have the form

$$\begin{aligned}\hat{X}_1 &= \hat{X}_4 = 1/4 + (1+k)D \\ \hat{X}_2 &= \hat{X}_3 = 1/4 - (1+k)D \\ \hat{Y}_1 &= \hat{Y}_4 = 1/4 + (1-k)D \\ \hat{Y}_2 &= \hat{Y}_3 = 1/4 - (1-k)D\end{aligned}\tag{2}$$

where k has been defined to be equal to

$$k = \frac{r_f - r_m}{2 - \alpha - (r_m + r_f)}.$$

If the values of X_i and Y_i given in (2) are substituted into any of the equations given in Table 1, then, after considerable manipulation, the quadratic equation

$$16(1 - k^2)D^2 = 1 - \frac{4 \left(\frac{r_m + r_f}{2} \right)}{-\alpha + \beta + \gamma}$$

is obtained. Thus

$$D = \pm \frac{1}{4} \sqrt{\frac{1 - \frac{4 \left(\frac{r_m + r_f}{2} \right)}{-\alpha + \beta + \gamma}}{1 - \frac{(r_f - r_m)^2}{(2 - \alpha - r_m - r_f)^2}}}. \quad (3)$$

If r is defined to be equal to $\frac{r_m + r_f}{2}$, then the numerator under the radical is

identical to what is underneath the radical in the expression for D in the standard two-locus model (KARLIN and FELDMAN 1970). Since the denominator is always less than or equal to one (with equality holding only if $r_m = r_f$), D as defined by (3) is always greater than or equal to its value in the standard case. Thus, for the purpose of determining the equilibrium points with linkage disequilibrium, the recombination value does not equal the average of the recombination values in males and females.

The Multiplicative Model

The matrix of fitness values for the multiplicative model is

$$\mathbf{W} = \begin{pmatrix} w_1 w_2 & w_1 & w_2 & 1 \\ w_1 & w_1 v_2 & 1 & v_2 \\ w_2 & 1 & v_1 w_2 & v_1 \\ 1 & v_2 & v_1 & v_1 v_2 \end{pmatrix}$$

where w_1 , 1, and v_1 are the fitness values of the genotypes AA , Aa , and aa ; and w_2 , 1, and v_2 of BB , Bb , and bb .

Instead of using the variables X_i and Y_i , which are subject to the constraints $\Sigma X_i = \Sigma Y_i = 1$, it is more convenient for the multiplicative model to use the six unconstrained variables

$$p_0 = X_1 + X_2$$

$$p_1 = Y_1 + Y_2$$

$$p_2 = \frac{X_1}{X_1 + X_2}$$

$$\begin{aligned}
 p_3 &= \frac{X_3}{X_3 + X_4} \\
 p_4 &= \frac{Y_1}{Y_1 + Y_2} \\
 p_5 &= \frac{Y_3}{Y_3 + Y_4}
 \end{aligned}
 \tag{4}$$

The variables p_0 and p_1 are the frequencies of the A allele in males and females, respectively. After one generation $p_0 = p_1$, so only one of these variables will be used (this eliminates one of the eigenvalues of zero). The gametic frequencies in terms of these five variables are

$$\begin{aligned}
 X_1 &= p_1 p_2 & Y_1 &= p_1 p_4 \\
 X_2 &= p_1 (1 - p_2) & Y_2 &= p_1 (1 - p_4) \\
 X_3 &= (1 - p_1) p_3 & Y_3 &= (1 - p_1) p_5 \\
 X_4 &= (1 - p_1) (1 - p_3) & Y_4 &= (1 - p_1) (1 - p_5)
 \end{aligned}
 \tag{5}$$

The recurrence equations for selection in these five variables can be obtained by substituting the gametic frequencies given in (5) into the equations in Table 1 and using the relationships given in (4) to define the recurrence equations.

It can be seen by substitution that an equilibrium point for these equations is

$$\begin{aligned}
 \hat{p}_1 &= \frac{b_1}{a_1 + b_1} \\
 \hat{p}_2 &= \hat{p}_3 = \hat{p}_4 = \hat{p}_5 = \frac{b_2}{a_2 + b_2}
 \end{aligned}$$

with $a_i = w_i - 1$ and $b_i = v_i - 1$.

The Jacobian evaluated at this equilibrium is the matrix

$$\mathbf{J} = \begin{pmatrix} \mathbf{A} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{B} & \mathbf{B} \\ \mathbf{0} & \mathbf{C} & \mathbf{C} \end{pmatrix}$$

with $\mathbf{A} = \left(1 + \frac{K_1}{1 + K_1} \right)$

$$\mathbf{B} = \frac{1}{2} \begin{pmatrix} 1 + \frac{(K_1 + \hat{p}_1)K_2 - r_m \hat{q}_1}{(1 + K_1)(1 + K_2)} & \frac{\hat{q}_1 K_2 + r_m \hat{q}_1}{(1 + K_1)(1 + K_2)} \\ \frac{\hat{p}_1 K_2 + r_m \hat{p}_1}{(1 + K_1)(1 + K_2)} & 1 + \frac{(K_1 + \hat{q}_1)K_2 - r_m \hat{p}_1}{(1 + K_1)(1 + K_2)} \end{pmatrix}$$

and **C** is the same as **B** with r_m replaced by r_f . In these matrices, $\hat{q}_i = 1 - \hat{p}_i$ and

$$K_i = \frac{a_i b_i}{a_i + b_i}.$$

(The average fitness at equilibrium of the i^{th} locus is $1 + K_i$. If there is heterozygotic superiority at the i^{th} locus, then $-\frac{1}{2} \leq K_i < 0$ and if there is heterozygotic inferiority, $0 < K_i < \infty$.)

The eigenvalues of **J** are

$$\lambda_1 = 1 + \frac{K_1}{1 + K_1}$$

$$\lambda_2 = 1 + \frac{K_2}{1 + K_2}$$

$$\lambda_3 = 1 + \frac{K_1 K_2 - \frac{r_m + r_f}{2}}{(1 + K_1)(1 + K_2)}$$

$$\lambda_4 = \lambda_5 = 0.$$

The conditions required for the equilibrium to be stable are therefore

$$K_1 < 0$$

$$K_2 < 0$$

$$\frac{r_m + r_f}{2} > K_1 K_2.$$

The first two inequalities (and the requirement that the gametic frequencies must be between zero and one) imply that there must be a heterozygotic advantage at each of the two loci. If r is defined to be equal to $\frac{r_m + r_f}{2}$, the third inequality is the same as the inequality on r in the standard two-locus model (BODMER and FELSENSTEIN 1967). Thus, again, the recombination value can be thought of as the average of the recombination values in males and females.

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