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A Two Loci Viability Matrix with Implications in Current Population Genetics Models

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Summary. Some equilibrium properties of a two loci deterministic system subject to a postulated viability matrix are given. Two conclusions are reached: i) linkage can not stabilize additive equally contributing two-loci systems under optimizing selection. ii) Hybrid protein superiority can not be invoked for the maintenance of polymorphisms shared by duplicated structural loci.

Key words: Linkage – Optimizing selection – Duplicate structural genes – Hybrid protein

1 Introduction

The standard approach to a deterministic two loci two alleles system, which is described in various population genetics textbooks (eg. Ewens 1969; Kimura and Ohta 1971), can be summarized as follows.

Consider a two loci, two alleles per locus, system. Let the frequencies of the gametes AB, Ab, aB and ab be given by x_1, x_2, x_3 and x_4, respectively; $p_1 = x_1 + x_2$ and $p_2 = x_1 + x_3$ will be the frequencies of the genes A and B, respectively. The viability of the zygote formed by the gametic types i and j will be given by w_{ij}. It is usually assumed that $w_{ij} = w_{ji}$ and that $w_{14} = w_{23}$, so that the 4×4 $|w_{ij}|$ matrix is reduced to

	BB	Bb	bb
AA	w_{11}	w_{12}	w_{22}
Aa	w_{13}	w_{14}	w_{24}
aa	w_{33}	w_{34}	w_{44}

The recursions giving the frequencies x_i' as functions of those of the previous generation x_i are

$$x_i' = (w_i x_i - r w_{14} D_i)/\bar{w} = \phi_i(x_k), \quad (k = 1,2,3,4), \tag{1}$$

where

$$D_i = D = x_1 x_4 - x_2 x_3, \quad i = 1,4$$
$$D_i = -D, \quad i = 2,3.$$

r is the recombination fraction between loci.

$$w_i = \sum_j x_j w_{ij} = w_i^* + D E_i, \quad \text{and}$$
$$\bar{w} = \sum_i x_i w_i = \bar{w}^* + 2 D \bar{E}^* + D^2 (E_1 - E_2 - E_3 + E_4), \tag{2}$$

are the chromosomal and the average viabilities, respectively, where $E_i = w_{i1} - w_{i2} - w_{i3} + w_{i4}$, is a measure of additive viability interaction, and the asterisk (*) stands for the value of the parameter at D = 0 (e.g. $\bar{E}^* = E_1 p_1 p_2 + E_2 p_1 (1-p_2) + E_3 (1-p_1) p_2 + E_4 (1-p_1)(1-p_2)$).

From (1) the equilibrium equations are

$$e_i: \quad x_i(\bar{w} - w_i) = -w_{14} r D_i \tag{3}$$

The necessary and sufficient conditions for the stability of the equilibria are that all eigenvalues of the matrix

$$[a_{ij}] = \left[\frac{\partial \phi_i}{x_j}\right]^{\wedge} \tag{4}$$

(where $\wedge$ means evaluated at equilibrium point) be less than unity in absolute value.

In this paper I will apply this theory to a little studied two loci model and use the results to discuss two specific population genetics models.

2 Results

2.1 The viability Matrix

Hereafter I will deal with the two loci viability matrix

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$$\begin{vmatrix} 1-\delta_1 & 1-\beta & 1-\alpha \\ 1-\beta & 1 & 1-\gamma \\ 1-\alpha & 1-\gamma & 1-\delta_2 \end{vmatrix}$$

This matrix is of the type investigated by Franklin and Feldman (1977). Given its symmetry, one is tempted to call it symmetrical, but as this name is already applied to another type of matrix (Bodmer and Felsenstein 1967), I will refer to it as 'diagonal'. In the following, I will impose the further restriction $E_i = E$, (i = 1,2,3,4), except when indicated.

2.2 *Equilibrium Properties*

From (1), it is easily seen that no $x_i = 0$ equilibrium with both loci polymorphic can exist except for r = 0. If the expression $-e_1/x_1 + e_2/x_2 + e_3/x_3 - e_4/x_4$ is calculated (Bodmer and Felsenstein 1967), the equality

$$\overline{E} = E = r\,D \sum_i 1/x_i \tag{5}$$

is obtained. Therefore, at equilibrium, linkage disequilibrium should have the same sign as E, and no nontrivial equilibrium with D = 0 exists except for E = 0.

The viabilities of the repulsion chromosomes,

$$\begin{aligned} w_2 &= 1-\beta x_1 - \gamma x_4 - \alpha x_2 \\ w_3 &= 1-\beta x_1 - \gamma x_4 - \alpha x_3 \end{aligned} \tag{6}$$

indicates that if $x_2 = x_3$, then $w_2 = w_3$, therefore from (3) $x_2 = x_3$, $p_1 = p_2 = p$ is a type of solution. In the present paper I will deal only with this type of solution.

2.3 *Stability of the Equilibria*

It is easily shown that, for the equilibrium points of the $x_2 = x_3$ type, a 'diagonal' system gives an $|\,a_{ij}\,|$ matrix (4) in which $a_{i2} = a_{i3}$, $a_{2i} = a_{3i}$ (i = 1,4), $a_{22} = a_{33}$ and $a_{23} = a_{32}$. This result does not require the $E_i = E$, (i = 1,2,3,4), restriction. Therefore, by taking $b_{ij} = a_{ij} - a_{i3}$ (Ewens 1969), the eigenvalues of the system are the solutions of the quadratic equation

$$\begin{vmatrix} b_{11}-\lambda & b_{14} \\ b_{41} & b_{44}-\lambda \end{vmatrix} = 0,$$

and

$$\lambda_1 = b_{22} = \left(\frac{\partial \phi_2}{\partial x_2}\right)\hat{} - \left(\frac{\partial \phi_2}{\partial x_3}\right)\hat{} = \frac{\hat{w}_2 - \alpha \hat{x}_2}{\hat{\bar{w}}}, \tag{7}$$

as shown in the appendix

2.4 *The Case α = 0*

If $\alpha = 0$, from (6) $w_2 \equiv w_3$. Therefore the only possible solutions to the system are of the type $x_2 = x_3$.

Suppose that $E < 0$, from (5), $D < 0$ at equilibrium. From e_2 (3), $\hat{w}_2 > \hat{\bar{w}}$, and from (7), $\lambda_1 > 1$. The system does not have any stable (nontrivial) equilibria.

Therefore a necessary condition for an $\alpha = 0$, $E_i = E$, (i = 1,2,3,4) diagonal system to have stable equilibrium points, with both loci polymorphic, is that $E > 0$.

3 Discussion: Models Upon Which These Results Impinge

3.1 *Additive Loci With Equal Contributions to a Metric Trait Subject to Optimizing Selection*

Selection acting upon a metric trait for a optimum value θ, is supposed to be a common phenomenon in nature (Maynard-Smith 1979). In its simplest formulation (Kojima 1959) the fitness of a genotype i j is given by

$$w_{ij} = 1-(s_{ij}-\theta)^2$$

where s_{ij} stand for the metric trait value of the genotype.

In our case, the metric trait matrix is

	a	0	−a
a	2a	a	0
0	a	0	−a
−a	0	−a	−2a

and the viability matrix is

$$\begin{vmatrix} 1-(2a-\theta)^2 & 1-(a-\theta)^2 & 1-\theta^2 \\ 1-(a-\theta)^2 & 1-\theta^2 & 1-(a+\theta)^2 \\ 1-\theta^2 & 1-(a+\theta)^2 & 1-(2a+\theta)^2 \end{vmatrix},$$

which is equivalent to a diagonal matrix with $\alpha = 0$, and its E's are

$$E_i = -\frac{2a^2}{1-\theta^2}, \quad (i = 1,2,3,4).$$

The denominator, being a viability, is always positive, and E will be negative. Therefore linkage can not stabilize this type of model.

Suppose that the trait follows a normal distribution $\{N(s_{ij},\sigma)\}$ due to the environmental and/or the genetic background, and that the selective process follows a normal distribution $\{N(\theta,\sigma_s)\}$ as well. The E's can be approximated, following Robertson (1956), as

$$E_i \simeq E_j \simeq -\frac{a^2}{\sigma^2+\sigma_s^2}$$

and the same conclusions are reached.

3.2 Duplicated Structural Loci Sharing a Polymorphism

Duplicated structural loci that share a polymorphism have been described (Clegg 1970), and the suggestion made by Slighton et al. (1980), recently proved by Klein and Petes (1981), that duplicated loci can exchange DNA makes this case an attractive one to model.

Suppose that the gene exists in two forms A_1 and A_2 determining the polypeptides α_1 and α_2, respectively, and that the mature protein is a dimer. The proportion of the different dimers ($\alpha_1\alpha_1$, $\alpha_2\alpha_2$, and the hybrid $\alpha_1\alpha_2$) usually follow the rule $(xa_1 + ya_2)^2$, where x and y are, respectively, the number of A_1 and A_2 genes in the zygote.

If the viability of the zygote is determined as

$$w_{ij} = a\ \mathrm{prop}(\alpha_1\alpha_1) + b\ \mathrm{prop}(\alpha_1\alpha_2) + c\ \mathrm{prop}(\alpha_2\alpha_2)$$

where $\mathrm{prop}(\alpha_i\alpha_j)$ stand for the proportion of the dimer $\alpha_i\alpha_j$, the viability matrix is

16a	9a+6b+c	4a+8b+4c
9a+6b+c	4a+8b+4c	a+6b+9c
4a+8b+4c	a+6b+9c	16c

this matrix is equivalent to a diagonal matrix with $\alpha = 0$ and $E_i = E$, (i = 1,2,3,4), and the sign of E is given by

$$\frac{a+c}{2} - b.$$

For the system to be stable, the contribution to viability of the hybrid protein ought to be less than the average of the contributions of the homologous non hybrid dimers. It seems, therefore, that the hypothesis of hybrid protein superiority (Fincham 1972) cannot be invoked for the maintenance of this type of polymorphism.

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Appendix

Following Ewens (1969),

$$\lambda_1 = b_{22} = a_{22} - a_{23} = \left(\frac{\partial\phi_2}{\partial x_2}\right)\hat{} - \left(\frac{\partial\phi_2}{\partial x_3}\right)\hat{}.$$

If we call $w_2 x_2 - r w_{14} D$ in (1), h

$$\left(\frac{\partial\phi_2}{\partial x_i}\right)\hat{} = \left[\left(\frac{\partial h}{\partial x_i}\right)\hat{} - \hat{x}_2\left(\frac{\partial\bar{w}}{\partial x_i}\right)\hat{}\right] \Big/ \hat{\bar{w}},$$

but, it is easily shown that, for equilibria in which $x_2 = x_3$,

$\left(\frac{\partial\bar{w}}{\partial x_2}\right)\hat{} = \left(\frac{\partial\bar{w}}{\partial x_3}\right)\hat{}$. Therefore

$$\lambda_1 = \left[\left(\frac{\partial h}{\partial x_2}\right)\hat{} - \left(\frac{\partial h}{\partial x_3}\right)\hat{}\right] \Big/ \hat{\bar{w}}.$$

From (6),

$$\left(\frac{\partial h}{\partial x_2}\right)\hat{} = \hat{w}_2 - \alpha\hat{x}_2 - r\hat{x}_3, \text{ and}$$

$$\left(\frac{\partial h}{\partial x_3}\right)\hat{} = -r\hat{x}_2.$$

Therefore

$$\lambda_1 = \frac{\hat{w}_2 - \alpha\hat{x}_2}{\hat{\bar{w}}}$$

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