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Finiteness of Equilibria Set for a Nonepistatic Selection under Multilocus Mendel Dominance

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Abstract—It is proven that the equilibria set under multilocus Mendel dominance in a population with any fixed-recombination coefficients is finite generically if the selection is nonepistatic in Karlin's sense. © 2003 Elsevier Science Ltd. All rights reserved.

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In the recent work [1], a general theorem on a finiteness of the equilibria set under phenotypical selection in a multilocus multiallele population with any fixed-recombination coefficients was established. As a consequence, the following result has been proved.

THEOREM 1. *(See [1, Corollary 8.2].) The equilibria set under multilocus Mendel dominance is finite generically.*

In this context, the *genericity means that the finiteness takes place except for a proper algebraic subset E of the fitness space.* The elements of this space are positive vectors of form $\lambda = (\lambda(g,h))$ where g and h run over the set Γ of the gamete genotypes, so that the pairs (g,h) determine the zygote genotypes. The value $\lambda(g,h)$ is called the *fitness coefficient* for the corresponding zygote. This value is symmetric, $\lambda(h,g) = \lambda(g,h)$, moreover, it is invariant with respect to the permutations of homological chromosomes, see [1, Section 6].

Every gamete g can be formally written as the formal product $g_1 \dots g_l$ where g_i is the allele carrying by g at the i^{th} locus, $1 \le i \le l$. We identify the set of loci under consideration with $L = \{1,\dots,l\}$. We will say that the multilocus fitness vector is *decomposable* if there is a function P such that

$$\lambda(g,h) = P\left(\lambda^{(1)}(g_1,h_1),\dots,\lambda^{(l)}(g_l,h_l)\right),$$

with some single-locus fitness vectors $\lambda^{(1)},\dots,\lambda^{(l)}$. This concept includes two important partic-

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ular cases: the *additive selection*,

$$\lambda(g,h) = \sum_{i=1}^{l} \lambda^{(i)}(g_i, h_i),$$

and the *multiplicative selection*

$$\lambda(g,h) = \prod_{i=1}^{l} \lambda^{(i)}(g_i, h_i),$$

both can be considered as the simplest manifestations of the *nonepistasis* (see [2] for a relevant discussion). Karlin [3] suggested a sort of "interpolation" between additive and multiplicative selection he named the *generalized nonepistatic selection*. This model (in a slightly modified notation) is

$$\lambda(g,\, h) = \sum_{U\subset L} c(U) \prod_{i\in U} \lambda^{(i)}(g_i, h_i), \tag{1}$$

where $c(U)$ are some nonnegative coefficients, at least one of them is positive. The additive/multiplicative cases are included in (1) with $c(U) = \delta_{U,L}$ or $c(U) = \delta_{|U|,1}$, respectively. (Here, δ is Kronecker's symbol.)

Now let us clarify what is the Mendel multilocus dominance mentioned in Theorem 1. In a formal sense, this is the direct product of the Mendel single-locus structures, see [1, Section 4]. At the diallele locus with the alleles A and a such that A dominates a, the fitness coefficients are $\lambda(Aa) = \lambda(AA)$ and $\lambda(aa)$. In this situation, we consider $\lambda(AA)$ and $\lambda(aa)$ as independent variables, the coordinates of the two-dimensional fitness vector. A well-known elementary result in this case is that if $\lambda(AA) \neq \lambda(aa)$, then *the number of equilibria is either two or infinity.*

Now we consider two-locus diallele population and suppose that there is the Mendel dominance at each locus. Let the fitness coefficients at the first locus be $\lambda(AA) = \lambda(Aa) = \alpha$, $\lambda(aa) = \varepsilon$, and similarly, let $\lambda(BB) = \lambda(Bb) = \beta$, $\lambda(bb) = \omega$ at the second one. The typical zygotes are $aabb$, $aaBB$, $AAbb$, and $AABB$. Denote their fitness coefficients by λ_1, λ_2, λ_3, λ_4. All other zygotes have the same fitness coefficients, for example, $\lambda(AaBb) = \lambda(AABB)$, etc.

The selection rule (1) yields

$$\lambda_1 = c_0 + c_1\varepsilon + c_2\omega + c_{12}\varepsilon\omega, \tag{2}$$

$$\lambda_2 = c_0 + c_1\varepsilon + c_2\beta + c_{12}\varepsilon\beta, \tag{3}$$

$$\lambda_3 = c_0 + c_1\alpha + c_2\omega + c_{12}\alpha\omega, \tag{4}$$

$$\lambda_4 = c_0 + c_1\alpha + c_2\beta + c_{12}\alpha\beta, \tag{5}$$

where $c_0 = c(\emptyset)$, $c_1 = c(\{1\})$, $c_2 = c(\{2\})$, $c_{12} = c(L)$, $L = \{1,2\}$.

By substitution from (2)–(5) into the equations of the exceptional set E (related to Theorem 1), we obtain a system of algebraic equations for α, ε, β, ω. These equations determine the *exceptional set* $\tilde{E}$ in the space of parameters α, ε, β, ω. The equations of $\tilde{E}$ are of form

$$\sum_{i_1,i_2,i_3,i_4} P^{(j)}_{i_1,i_2,i_3,i_4}(c_0, c_1, c_2, c_{12})\, \alpha^{i_1}\varepsilon^{i_2}\beta^{i_3}\omega^{i_4} = 0, \tag{6}$$

where $P^{(j)}_{i_1,i_2,i_3,i_4}$ are some polynomials, $1 \le j \le N$, N is the total number of them. We show that at least one of polynomials $P^{(j)}_{i_1,i_2,i_3,i_4}$ is not identically zero.

Formulas (2)–(5) yield a linear transformation $(c_0, c_1, c_2, c_{12}) \mapsto (\lambda_1, \lambda_2, \lambda_3, \lambda_4)$. Its determinant is

$$\begin{vmatrix} 1 & \varepsilon & \omega & \varepsilon\omega \\ 1 & \varepsilon & \beta & \varepsilon\beta \\ 1 & \alpha & \omega & \alpha\omega \\ 1 & \alpha & \beta & \alpha\beta \end{vmatrix} = -(\alpha - \varepsilon)^2(\beta - \omega)^2.$$

This is different from zero if $\alpha \neq \varepsilon$ and $\beta \neq \omega$. Without loss of generality, one can assume that this condition is fulfilled. Take $(\lambda_1,\ \lambda_2,\ \lambda_3,\ \lambda_4) \notin E$ and solve the linear system (2)–(5) with respect to c_0, c_1, c_2, c_{12}. (The solution cannot be positive, no matter.) By definition of equations (6), at least one of them turns out to be broken. Thus, there exists a nonvanishing polynomial among $P^{(j)}_{i_1,i_2,i_3,i_4}$.

Now the system of all equations

$$P^{(j)}_{i_1,i_2,i_3,i_4}(c_0,c_1,c_2,c_{12}) = 0,$$

coming from (6) defines a proper algebraic subset $C \subset \mathbf{R}^4$.

THEOREM 2. *If $(c_0,c_1,c_2,c_{12}) \notin C$, then the set of equilibria under selection rule (2)–(5) is finite generically with respect to α, ε, β, ω.*

PROOF. Take any above-mentioned four-tuple (c_0,c_1,c_2,c_{12}). Then the exceptional set $\tilde{E} \subset \mathbf{R}^4$ defined by (6) is a proper algebraic subset. For any four-tuple $(\alpha,\varepsilon,\beta,\omega) \notin \tilde{E}$, the corresponding four-tuple $(\lambda_1,\lambda_2,\lambda_3,\lambda_4) \notin E$. The latter means, by definition of E, that the equilibria set is finite. ∎

The same method works for the generalized nonepistatic selection (1) under the Mendel dominance at each of l diallele loci takes place. The only assertion we need to prove is the following.

LEMMA. *Let for any $i = 1,\dots,l$ some distinct numbers $\lambda_0^{(i)}$ and $\lambda_1^{(i)}$ be given. Then the system of 2^l linear equations*

$$\lambda_{\nu_1,\dots,\nu_l} = \sum_{U\subset L} c(U) \prod_{i\in U} \lambda^{(i)}_{\nu_i} \qquad (\nu_i \in \{0,1\},\ 1 \le i \le l) \tag{7}$$

is solvable with respect to the unknowns $\{c(U) : U \subset L\}$, whichever are 2^l numbers $\lambda_{\nu_1,\dots,\nu_l}$.

PROOF. Since we have as many equations as there are unknowns in (7), it is sufficient to show that the system with all $\lambda_{\nu_1,\dots,\nu_l} = 0$ has the only trivial solution. This is obvious for $l = 1$ and we actually know this for $l = 2$. Let us pass from $(l-1)$ to l by induction.

Assume that

$$\sum_{U\subset L} c(U) \prod_{i\in U} \lambda^{(i)}_{\nu_i} = 0 \qquad (\nu_i \in \{0,1\},\ 1 \le i \le l). \tag{8}$$

It is sufficient to prove that all $c(U) = 0$ for $U \neq \emptyset$. For definiteness, we will prove that $c(U) = 0$ if $1 \in U$. Consider two subsystems of (8) which correspond to $\nu_1 = 0$ and $\nu_1 = 1$, respectively:

$$\sum_{1\in U\subset L} c(U)\lambda_0^{(1)} \prod_{i\in U\setminus\{1\}} \lambda^{(i)}_{\nu_i} + \sum_{1\notin U\subset L} c(U) \prod_{i\in U} \lambda^{(i)}_{\nu_i} = 0 \tag{9}$$

and

$$\prod_{1\in U\subset L} c(U)\lambda_1^{(1)} \prod i \in U\setminus\{1\}\lambda^{(i)}_{\nu_i} + \sum_{1\notin U\subset L} c(U) \prod_{i\in U} \lambda^{(i)}_{\nu_i} = 0. \tag{10}$$

Subtracting (10) from (9) and cancelling $\lambda_0^{(1)} - \lambda_1^{(1)} \neq 0$, we get

$$\sum_{1\in U\subset L} c(U) \prod_{i\in U\setminus\{1\}} \lambda^{(i)}_{\nu_i} = 0.$$

Thus, the system is of form (7) with $L\setminus\{1\}$ instead of L. By the induction, assumption $c(U) = 0$ for $1 \in U$. ∎

As a result, we obtain the following theorem.

THEOREM 3. *In the l-locus diallele population with the Mendel dominance at each locus, there exists a proper algebraic subset* $C\mathbf{R}^{2^l}$ *such that if* $(c(U) : U \subset L) \notin C$, *then under generalized nonepistatic selection rule (1), the set of equilibria is finite generically with respect to the single-locus fitness coefficients.*

In addition, *the number of equilibria does not exceed* $3^{|\Gamma|-1}$, see [1, Corollary 8.1].

Note that Theorem 3 says nothing for *a priori* given selective weights $c(U)$ in (1), in particular, for the additive or the multiplicative selection. However, in the additive case, the finiteness result follows from [4, Theorem 9.6.13 and Corollary 9.13]. The generic finiteness of the equilibria set under the multiplicative selection has been recently proved in [5].

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