Evolution under Fertility and Viability Selection

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Manuscript received June 11, 1986

Accepted October 27, 1986

ABSTRACT

Evolution at a single multiallelic locus under arbitrary weak selection on both fertility and viability is investigated. Discrete, nonoverlapping generations are posited for autosomal and X-linked loci in dioecious populations, but monoecious populations are studied in both discrete and continuous time. Mating is random. The results hold after several generations have elapsed. With an error of order s [i.e., $O(s)$], where s represents the selection intensity, the population evolves in Hardy-Weinberg proportions. Provided the change per generation of the fertilities and viabilities due to their explicit time dependence (if any) is $O(s^2)$, the rate of change of the deviation from Hardy-Weinberg proportions is $O(s^2)$. If the change per generation of the viabilities and *genotypic* fertilities is smaller than second order [i.e., $o(s^2)$], then to $O(s^2)$ the rate of change of the mean fitness is equal to the genic variance. The mean fitness is the product of the mean fertility and the mean viability; in dioecious populations, the latter is the unweighted geometric mean of the mean viabilities of the two sexes. Hence, as long as there is significant gene frequency change, the mean fitness increases. If it is the fertilities of *matings* that change slowly [at rate $o(s^2)$], the above conclusions apply to a modified mean fitness, defined as the product of the mean viability and the square root of the mean fertility.

IF generations are discrete and nonoverlapping, mating is random, and viabilities are constant, then the mean viability is nondecreasing under viability selection at a single multiallelic locus in a monoecious population (MULHOLLAND and SMITH 1959; SCHEUER and MANDEL 1959; ATKINSON, WATTERSON, and MORAN 1960; KINGMAN 1961). This theorem provides both a conceptual framework for the theory of natural selection and a powerful tool for analyzing the local and global evolution of populations. Therefore, much effort has been devoted to its exact and approximate extension.

The simplest exact extension is to incorporate multiplicative fertilities. If the fertility of each mating can be expressed as a product of factors corresponding to the genotypes involved, then the model reduces to that for pure viability selection, the viability of each genotype being replaced by the product of its viability and fertility (PENROSE 1949; BODMER 1965; KEMPTHORNE and POLLAK 1970; NAGYLAKI 1977a, pp. 51–55). Consequently, if the *genotypic* fertilities are constant, the mean fitness, naturally defined as the mean viability times the mean fertility, is nondecreasing. For multiple loci, EWENS (1969a,b) has shown that if fitnesses are additive between loci, the mean fitness is nondecreasing.

Approximate extensions have focused on FISHER's (1930) fundamental theorem of natural selection—that the rate of increase of the mean fitness is equal to the genic variance. The work of KIMURA (1958, 1965) and HARTL (1972) suggests that this theorem

holds only for weak selection. If several generations have elapsed, the change per generation of the viabilities and *genotypic* fertilities due to their explicit time dependence (if any) is at most second order in the selection intensity s [i.e., $O(s^2)$], and their total change per generation is smaller than second order [i.e., $o(s^2)$], then the theorem holds to $O(s^2)$ for one and two loci in a continuous-time model of a monoecious population (NAGYLAKI, 1976, 1977a, pp. 79–92, 182–188). With discrete, nonoverlapping generations, extensions to two loci in a monoecious population (NAGYLAKI 1976, 1977a, pp. 167–177) and to single autosomal and X-linked loci in a dioecious population (NAGYLAKI 1979) depend on the additional assumption of multiplicative fertilities.

Since the generalizations described in the last paragraph are approximate, exceptions occur for every selection pattern. However, the mean fitness can decrease only if the genic variance is much smaller than s^2 , which is the case if and only if the absolute value of the gene frequency change per generation is much smaller than s . The latter can result from symmetry conditions or proximity to an equilibrium (MORAN 1964; KIMURA 1965; NAGYLAKI 1977b). Stable cycling in two-locus models (AKIN 1979, 1982, 1983; HASTINGS 1981) provides the most striking example of the occasional failure of the fundamental theorem of natural selection.

Much work has been devoted to the analysis of particular models with nonmultiplicative fertilities (LIBERMAN and FELDMAN 1985 and references

therein). Even if there are no viability differences, the fertilities of *matings* are constant, and generations are discrete and nonoverlapping, the mean fertility can decrease at a single locus in a monoecious population (HADELER and LIBERMAN 1975; POLLAK 1978).

Recently, ABUGOV (1985) has studied evolution at single diallelic autosomal and X-linked loci in a dioecious population under weak selection. He posited discrete, nonoverlapping generations and constancy of the viabilities and of the fertilities of *matings*, and found that the product of the mean viability and the square root of the mean fertility is nondecreasing. Although his treatment requires some corrections and further analyses, we shall see below that his conclusion is usually correct and can be generalized, proved rigorously, related to the fundamental theorem of natural selection, and illuminated biologically.

In this paper, we shall investigate evolution at a single multiallelic locus under arbitrary weak selection on both fertility and viability. The fertilities and viabilities may depend on the genotypic frequencies and time. We shall find nondecreasing quantities under the alternative assumptions that the fertilities of genotypes or of matings vary slowly, and we shall determine the rate of increase of these quantities.

Mating is random. We posit discrete, nonoverlapping generations for the exploration of dynamics at autosomal and X-linked loci in dioecious populations, but analyze monoecious populations in both discrete and continuous time.

MONOECIOUS POPULATION

We begin with the case of discrete, nonoverlapping generations and multiplicative fertilities, which is easy to treat exactly and reveals the essential difference between fixing the fertilities of genotypes and fixing those of matings. Next, we analyze arbitrary fertilities. Finally, we show that the same results hold in continuous time.

Multiplicative fertilities: The allele A_i has frequency p_i in zygotes. Assume that at least one generation of random mating has occurred and denote the viability of an $A_i A_j$ individual by v_{ij} . Then the frequency of ordered $A_i A_j$ genotypes in adults reads

$$P_{ij}^* = p_i p_j v_{ij} / \bar{v}, \quad \bar{v} = \sum_{ij} v_{ij} p_i p_j. \quad (1)$$

If N , M , $f_{ij,kl}$, and $\tilde{b}_{ij}$ signify the numbers of adults, matings, and offspring of an $A_i A_j \times A_k A_l$ mating and of an $A_i A_j$ adult, respectively, we have

$$N \tilde{b}_{ij} = M \sum_{kl} f_{ij,kl} P_{kl}^*. \quad (2)$$

Instead of $\tilde{b}_{ij}$, it will be more convenient to use the scaled genotypic fertility

$$b_{ij} = N \tilde{b}_{ij} / M = \sum_{kl} f_{ij,kl} P_{kl}^*. \quad (3)$$

If the population is regulated to constancy or is monogamous, and in many other situations, N/M will be constant.

The results in this paragraph are established in NAGYLAKI (1977a, pp. 51–55). Suppose $f_{ij,kl}$ may be expressed as

$$f_{ij,kl} = \beta_{ij} \beta_{kl} \quad (4)$$

for some β_{ij} . Then

$$\beta_{ij} = b_{ij} \bar{f}^{-1/2}, \quad (5)$$

where

$$\bar{f} = \sum_{ijkl} f_{ij,kl} P_{ij}^* P_{kl}^* = \sum_{ij} b_{ij} P_{ij}^* = \bar{b} \quad (6)$$

designates the mean fertility. The fitness of $A_i A_j$ and the mean fitness are given by

$$w_{ij} = v_{ij} b_{ij}, \quad \bar{w} = \bar{v} \bar{f}. \quad (7)$$

Here and below, note carefully that we average viabilities with respect to zygotic frequencies and fertilities with respect to adult frequencies. The frequency of A_i in the next generation is

$$p'_i = p_i w_i / \bar{w}, \quad (8a)$$

where

$$w_i = \sum_j w_{ij} p_j, \quad \bar{w} = \sum_{ij} w_{ij} p_i p_j. \quad (8b)$$

We assume that the viabilities v_{ij} are constant. On the one hand, if the genotypic fertilities b_{ij} are constant, so are the fitnesses w_{ij} , and hence (8) and the classical theorem stated in the first sentence of the introduction imply that the mean fitness $\bar{w} = \bar{v} \bar{f}$ is nondecreasing. On the other, by (4), constancy of the fertilities of matings, $f_{ij,kl}$, implies constancy of β_{ij} . Since (5) enables us to replace w_{ij} in (8) by the scaled fitnesses $W_{ij} = v_{ij} \beta_{ij}$, now we conclude from (5) and (8) that the modified mean fitness $\bar{W} = \bar{v} \bar{\beta} = \bar{v} \bar{f}^{1/2}$ is nondecreasing.

The essential point is that, on account of (3), the fertilities of genotypes and of matings cannot both be constant, and therefore the two different biological assumptions of constancy lead to different results.

General fertilities: We rely on the formulation in NAGYLAKI (1977a, pp. 51–55). Let P_{ij} denote the frequency of ordered $A_i A_j$ genotypes in zygotes. Equation (1) must be generalized to

$$P_{ij}^* = P_{ij} v_{ij} / \bar{v}, \quad \bar{v} = \sum_{ij} v_{ij} P_{ij}, \quad (9)$$

but (2), (3), (6), and (7) still hold. The zygotic frequencies in the next generation read

$$P'_{ij} = \frac{1}{\bar{f}} \sum_{kl} P_{ik}^* P_{lj}^* f_{ik,lj} = \frac{1}{\bar{v}^2 \bar{f}} \sum_{kl} P_{ik} P_{lj} v_{ik} v_{lj} f_{ik,lj}. \quad (10)$$

Equation (8a) remains valid if we replace (8b) by

$$p_i w_i = \sum_j w_{ij} P_{ij}, \quad \bar{w} = \sum_{ij} w_{ij} P_{ij}. \quad (11)$$

Introducing the selective differences

$$\zeta_{ij} = w_{ij} - \bar{w}, \quad \xi_i = w_i - \bar{w}, \quad (12)$$

we can rewrite (8a) in the form

$$\Delta p_i = p_i \zeta_i / \bar{w}. \quad (13)$$

We now posit weak selection. From (10) we see that we can scale the viabilities and fertilities by dividing them by the largest viability and the largest fertility, respectively. After scaling, we define the selection intensity s as the greater one of the largest absolute viability difference between genotypes and the largest absolute fertility difference between matings. Thus, we have

$$v_{ij} = 1 + O(s), \quad f_{ij,kl} = 1 + O(s) \quad (14)$$

for every i, j, k and l . Throughout this paper, order estimates in s are uniform in the genotypic frequencies and time.

Our first task is to prove that the deviations from Hardy-Weinberg proportions,

$$R_{ij} = P_{ij} - p_i p_j, \quad (15)$$

become small after one generation and nearly constant after two. From (10) and (14) we obtain at once

$$P'_{ij} = p_i p_j [1 + O(s)]. \quad (16)$$

Summing (16) over j , we infer

$$\Delta p_i = p_i O(s), \quad (17)$$

whence

$$P'_{ij} = p'_i p'_j [1 + O(s)]. \quad (18)$$

If $t (= 0, 1, \dots)$ designates time in generations, (15) and (18) reveal

$$R_{ij}(t) = p_i p_j O(s), \quad t \geq 1. \quad (19)$$

Furthermore, (17) and (18) inform us

$$\Delta P_{ij} = p_i p_j O(s), \quad t \geq 1. \quad (20)$$

In view of (16) and (17), we may write the recursion relation for R_{ij} as

$$R'_{ij} = s g_{ij}(\mathbf{P}, t), \quad (21)$$

where g_{ij} is bounded as $s \rightarrow 0$. Hence, we have

$$\Delta R'_{ij} = s \Delta g_{ij}(\mathbf{P}, t), \quad (22a)$$

$$\begin{aligned} \Delta g_{ij}(\mathbf{P}, t) = & \{g_{ij}(\mathbf{P}(t+1), t+1) \\ & - g_{ij}(\mathbf{P}(t), t+1)\} \\ & + \{g_{ij}(\mathbf{P}(t), t+1) - g_{ij}(\mathbf{P}(t), t)\}. \end{aligned} \quad (22b)$$

A Taylor series and (20) show that the first brace in (22b) is $O(s)$ for $t \geq 1$. Provided the change per

generation of the viabilities and fertilities due to their explicit time dependence (if any) is $O(s^2)$, the second brace is also $O(s)$. Then we conclude from (22)

$$\Delta R_{ij} = O(s^2), \quad t \geq 2. \quad (23)$$

Before turning to the evolution of the mean fitness, we note that (3), (7), and (14) imply

$$b_{ij} = 1 + O(s), \quad w_{ij} = 1 + O(s), \quad (24)$$

which reduces (13) to

$$\Delta p_i = p_i \zeta_i + O(s^2). \quad (25)$$

This is the more precise version of (17).

From (11) we find for the change in mean fitness

$$\begin{aligned} \Delta \bar{w} = & \sum_{ij} [(w_{ij} + \Delta w_{ij}) P'_{ij} - w_{ij} P_{ij}] \\ = & \bar{\Delta w} + \sum_{ij} w_{ij} \Delta P_{ij}, \end{aligned} \quad (26)$$

in which

$$\bar{\Delta w} = \sum_{ij} P'_{ij} \Delta w_{ij} \quad (27)$$

represents the change in genotypic fitnesses averaged over the next generation. Since

$$\sum_{ij} \Delta P_{ij} = 0, \quad (28)$$

we can replace w_{ij} in (26) by ζ_{ij} ; invoking (15), we get

$$\begin{aligned} \Delta \bar{w} = & \bar{\Delta w} + \sum_{ij} \zeta_{ij} [p_i \Delta p_j + p_j \Delta p_i \\ & + (\Delta p_i)(\Delta p_j) + \Delta R_{ij}]. \end{aligned} \quad (29)$$

Employing (17), (23), and (25) in (29) yields

$$\Delta \bar{w} = \bar{\Delta w} + 2 \sum_{ij} \zeta_{ij} \zeta_i p_i p_j + O(s^3), \quad t \geq 2. \quad (30)$$

From (11), (12), (15), and (19) we deduce

$$\zeta_i = p_i^{-1} \sum_j \zeta_{ij} (p_i p_j + R_{ij}) = \sum_j \zeta_{ij} p_j + O(s^2) \quad (31)$$

for $t \geq 1$; inserting (31) into (30) gives

$$\Delta \bar{w} = V_w + \bar{\Delta w} + O(s^3), \quad t \geq 2, \quad (32)$$

where

$$V_w = 2 \sum_i \zeta_i^2 p_i. \quad (33)$$

It remains only to show that for weak selection the variance V_w is very close to the genic variance V_g . If α_i denotes the average effect of A_i on fitness, we have (FISHER 1930; KIMURA 1958; NAGYLAKI 1977a, pp. 89-90)

$$p_i \zeta_i = p_i \alpha_i + \sum_j P_{ij} \alpha_j, \quad (34)$$

$$V_g = 2 \sum_i \zeta_i \alpha_i p_i. \quad (35)$$

Substituting (15) into (34) and noting that

$$\sum_j \alpha_j p_j = 0$$

lead to

$$\zeta_i = \alpha_i + \frac{1}{p_i} \sum_j R_{ij} \alpha_j. \quad (36)$$

Since $\zeta_i = O(s)$, from (19) and (36) we obtain

$$\zeta_i = \alpha_i + O(s^2), \quad t \geq 1. \quad (37)$$

With the aid of (37), we infer from (33)

$$V_w = V_g + O(s^3), \quad t \geq 1, \quad (38)$$

and therefore (32) becomes

$$\Delta \bar{w} = V_g + \bar{\Delta w} + O(s^3), \quad t \geq 2. \quad (39)$$

Consequently, excluding the exceptional cases discussed in the introduction, $\Delta \bar{w} \approx V_g$ if $\bar{\Delta w} = o(s^2)$. By (7) and (27), the average change in the genotypic fitnesses will be $o(s^2)$ if

$$\Delta v_{ij} = o(s^2), \quad \Delta b_{ij} = o(s^2), \quad (40)$$

i.e., if the viabilities and genotypic fertilities are nearly constant. Thus, (40) generically suffices for the validity of Fisher's fundamental theorem of natural selection.

Suppose now that the fertilities of matings, rather than those of genotypes, vary slowly: instead of (40), we posit

$$\Delta v_{ij} = o(s^2), \quad \Delta f_{ij,kl} = o(s^2). \quad (41)$$

We proceed to show that the contribution of $\bar{\Delta w}$ to (39) is no longer negligible, and its evaluation leads to a different nondecreasing function.

For v_{ij} , the analogue of (30) reads

$$\Delta \bar{v} = \bar{\Delta v} + 2 \sum_{ij} (v_{ij} - \bar{v}) \zeta_i p_i p_j + O(s^3) = O(s^2), \quad t \geq 2; \quad (42)$$

the last step comes from (14) and (41). Appealing to (3), (41), the fact that (28) also holds for P_{ij}^* , (14), and (20), we find

$$\Delta b_{ij} = \sum_{kl} f_{ij,kl} \Delta P_{kl}^* + o(s^2) \quad (43)$$

$$= O(s^2), \quad t \geq 1. \quad (44)$$

With the definition

$$\bar{\Delta b} = \sum_{ij} P_{ij}^* \Delta b_{ij}, \quad (45)$$

(43) and (44) imply

$$\bar{\Delta b} = \sum_{ijkl} f_{ij,kl} P_{ij}^* \Delta P_{kl}^* + o(s^2) \quad (46)$$

$$= O(s^2), \quad t \geq 1. \quad (47)$$

From (6), (41), (45), (46), and (47) we derive

$$\Delta \bar{f} = \sum_{ijkl} f_{ij,kl} [2P_{ij}^* \Delta P_{kl}^* + (\Delta P_{ij}^*)(\Delta P_{kl}^*)] + o(s^2)$$

$$= 2\bar{\Delta b} + o(s^2), \quad t \geq 1 \quad (48)$$

$$= O(s^2), \quad t \geq 1. \quad (49)$$

The following simple result will be useful here and in the subsequent sections. Let $h = \phi^\gamma \psi^\delta$, where γ and δ denote constants and the functions ϕ and ψ satisfy

$$\phi = 1 + O(s), \quad \psi = 1 + O(s), \quad (50a)$$

$$\Delta \phi = O(s^2), \quad \Delta \psi = O(s^2). \quad (50b)$$

Then Taylor's theorem gives

$$\begin{aligned} \Delta h &= \frac{\partial h}{\partial \phi} \Delta \phi + \frac{\partial h}{\partial \psi} \Delta \psi + O[(\Delta \phi)^2 + (\Delta \psi)^2] \\ &= \gamma \Delta \phi + \delta \Delta \psi + O(s^3). \end{aligned} \quad (51)$$

Recalling (7), (14), (42), and (49), from (51) we get

$$\Delta \bar{w} = \Delta \bar{v} + \Delta \bar{f} + O(s^3), \quad t \geq 2. \quad (52)$$

Next, we invoke (7) and (41):

$$\Delta w_{ij} = v_{ij} \Delta b_{ij} + o(s^2). \quad (53)$$

We can calculate $\bar{\Delta w}$ by successive use of (27), (53), (20), (44), (9), (45), (14), (44) again, and (48):

$$\begin{aligned} \bar{\Delta w} &= \sum_{ij} P_{ij}' v_{ij} \Delta b_{ij} + o(s^2) \\ &= \sum_{ij} P_{ij} v_{ij} \Delta b_{ij} + o(s^2), \quad t \geq 1 \\ &= \sum_{ij} P_{ij}^* \bar{v} \Delta b_{ij} + o(s^2), \quad t \geq 1 \\ &= \bar{\Delta b} + o(s^2), \quad t \geq 1 \\ &= \frac{1}{2} \Delta \bar{f} + o(s^2), \quad t \geq 1. \end{aligned} \quad (54)$$

Substituting (52) and (54) into (39), we obtain

$$\Delta(\bar{v} + \frac{1}{2} \bar{f}) = V_g + o(s^2), \quad t \geq 2. \quad (55)$$

With the aid of (51), we can transform (55) to

$$\Delta \bar{W} = V_g + o(s^2), \quad t \geq 2, \quad (56)$$

in which $\bar{W} = \bar{v} \bar{f}^{1/2}$ signifies the modified mean fitness. Consequently, as in the special case of multiplicative fertilities, here $\bar{W}$ is nondecreasing.

Continuous time: Here we prove that, *mutatis mutandis*, the results for discrete, nonoverlapping generations remain valid for a continuous-time model with no age dependence or a stationary age distribution. Let d_{ij} , $f_{ij,kl}$, and b_{ij} designate the mortality rate of an $A_i A_j$ individual and the fertilities per unit time of an $A_i A_j \times A_k A_l$ mating and an $A_i A_j$ individual, respectively. The mean fertility and the mean mortality read

$$\bar{f} = \sum_{ijkl} f_{ij,kl} P_{ij} P_{kl}, \quad \bar{d} = \sum_{ij} d_{ij} P_{ij}, \quad (57)$$

where P_{ij} represents the frequency of ordered A_iA_j genotypes at time t ; we define the fitness of A_iA_j and the mean fitness as

$$m_{ij} = b_{ij} - d_{ij}, \quad \bar{m} = \bar{f} - \bar{d}. \quad (58)$$

Suppose now

$$d_{ij} = d + O(s), \quad f_{ij,kl} = b + O(s), \quad (59)$$

in which d and b denote positive constants, and

$$\frac{\partial}{\partial t} d_{ij} = O(s^2), \quad \frac{\partial}{\partial t} f_{ij,kl} = O(s^2). \quad (60)$$

If the gene frequencies are bounded away from zero, for which it is sufficient but not necessary to assume that $t \leq c/s$ for some constant c , then (NAGYLAKI 1976, 1977a, pp. 79–92)

$$\dot{\bar{m}} = V_g + \bar{m} + O(s^3), \quad t \geq t_2, \quad (61)$$

where $t_2 \approx -2b^{-1} \ln s$, the superior dot signifies the time derivative, and

$$\bar{m} = \sum_{ij} \dot{m}_{ij} P_{ij}. \quad (62)$$

If the mortalities and genotypic fertilities vary slowly, i.e.,

$$\dot{d}_{ij} = o(s^2), \quad \dot{b}_{ij} = o(s^2), \quad (63)$$

then (61) implies that $\dot{\bar{m}} \approx V_g$, so $\bar{m}$ is generally non-decreasing.

If the fertilities of matings are nearly constant, instead of (63) we assume

$$\dot{d}_{ij} = o(s^2), \quad \dot{f}_{ij,kl} = o(s^2). \quad (64)$$

From (57) and (64) we deduce

$$\dot{\bar{f}} = 2 \sum_{ijkl} f_{ij,kl} P_{ij} \dot{P}_{kl} + o(s^2), \quad (65)$$

$$\dot{\bar{b}} = \sum_{ijkl} f_{ij,kl} P_{ij} \dot{P}_{kl} + o(s^2) = \frac{1}{2} \dot{\bar{f}} + o(s^2). \quad (66)$$

Substituting (58) and (66) into (64) leads to

$$\dot{\bar{M}} = V_g + o(s^2), \quad t \geq t_2, \quad (67)$$

where the modified mean fitness is $\bar{M} = \frac{1}{2} \bar{f} - \bar{d}$.

Clearly, (61) and (67) are the precise continuous analogues of (39) and (56), respectively.

AN AUTOSOMAL LOCUS IN A DIOECIOUS POPULATION

For simplicity, we assume that the locus under consideration does not influence the sex ratio at birth. Then the genotypic frequencies are the same in male and female zygotes. Let P_{ij} and p_i denote the frequencies of ordered A_iA_j genotypes and A_i alleles in zygotes, respectively. Single and double asterisks signify the respective frequencies in adult males and females. If u_{ij} and v_{ij} designate the viabilities of A_iA_j males and

females, respectively, we have

$$P_{ij}^* = P_{ij} u_{ij} / \bar{u}, \quad \bar{u} = \sum_{ij} u_{ij} P_{ij}, \quad (68a)$$

$$P_{ij}^{**} = P_{ij} v_{ij} / \bar{v}, \quad \bar{v} = \sum_{ij} v_{ij} P_{ij}. \quad (68b)$$

Let $f_{ij,kl}$ represent the number of progeny from the mating of an A_iA_j male with an A_kA_l female. We do not assume that reciprocal crosses are equally fertile, i.e., we allow $f_{ij,kl} \neq f_{kl,ij}$. The zygotic frequencies in the next generation are

$$P'_{ij} = \frac{1}{2\bar{f}} \sum_{kl} (P_{ik}^* P_{lj}^{**} f_{ik,lj} + P_{lj}^* P_{ik}^{**} f_{lj,ik}), \quad (69)$$

where the mean fertility reads

$$\bar{f} = \sum_{ijkl} f_{ij,kl} P_{ij}^* P_{kl}^{**}. \quad (70)$$

Let M , N^* and N^{**} denote the numbers of matings and adult males and females, respectively. If $\tilde{a}_{ij}$ and $\tilde{b}_{ij}$ designate the respective fertilities of A_iA_j males and females, we get the scaled fertilities

$$a_{ij} = N^* \tilde{a}_{ij} / M = \sum_{kl} f_{ij,kl} P_{kl}^{**}, \quad (71a)$$

$$b_{ij} = N^{**} \tilde{b}_{ij} / M = \sum_{kl} f_{kl,ij} P_{kl}^*, \quad (71b)$$

whence we obtain the mean fertilities

$$\bar{a} = \sum_{ij} a_{ij} P_{ij}^* = \bar{f}, \quad \bar{b} = \sum_{ij} b_{ij} P_{ij}^{**} = \bar{f}. \quad (72)$$

Define the fitnesses of A_iA_j males and females as

$$x_{ij} = u_{ij} a_{ij}, \quad y_{ij} = v_{ij} b_{ij}. \quad (73)$$

Then (73), (68), and (72) give the mean fitnesses of males and females:

$$\bar{x} = \sum_{ij} x_{ij} P_{ij} = \bar{u} \bar{f}, \quad \bar{y} = \sum_{ij} y_{ij} P_{ij} = \bar{v} \bar{f}. \quad (74)$$

The fitnesses x_i and y_i of A_i in males and females, respectively, are given by

$$p_i x_i = \sum_j x_{ij} P_{ij}, \quad p_i y_i = \sum_j y_{ij} P_{ij}. \quad (75)$$

We sum (69) over j and use (71), (68), (73), (74), and (75):

$$p'_i = \frac{1}{2} p_i \left(\frac{x_i}{\bar{x}} + \frac{y_i}{\bar{y}} \right). \quad (76)$$

We scale so that

$$u_{ij} = 1 + O(s), \quad v_{ij} = 1 + O(s), \quad (77)$$

$$f_{ij,kl} = 1 + O(s),$$

and again utilize (15) as an index of departure from Hardy-Weinberg proportions. Then (17), (19), (20), and (23) still hold. We define

$$w_{ij} = \frac{1}{2}(x_{ij} + y_{ij}) \quad (78)$$

as the average fitness of A_iA_j and retain (11) and (12). Inserting (78) into (11) produces

$$\bar{w} = \frac{1}{2}(\bar{x} + \bar{y}), \quad (79)$$

and using (77), (78), (79), and (12) in (76) establishes (25). As in the monoecious case, (39) holds.

If the viabilities and genotypic fertilities are almost constant, *i.e.*,

$$\Delta u_{ij} = o(s^2), \quad \Delta v_{ij} = o(s^2), \quad (80a)$$

$$\Delta a_{ij} = o(s^2), \quad \Delta b_{ij} = o(s^2), \quad (80b)$$

then (39) informs us that $\Delta \bar{w} \approx V_g$, so the mean fitness generally increases at a rate equal to the genic variance. We can prove the same result for the geometric mean fitness. By direct analogy with (42), we have

$$\Delta \bar{x} = O(s^2), \quad \Delta \bar{y} = O(s^2) \quad (81)$$

for $t \geq 2$. Therefore, we may apply (51), so that (39) and (79) demonstrate

$$\Delta \hat{w} = V_g + o(s^2), \quad t \geq 2, \quad (82)$$

where $\hat{w} = (\bar{x}\bar{y})^{1/2}$. On account of (74), we can express $\hat{w}$ as $\hat{w} = \bar{U}\bar{f}$, in which $\bar{U} = (\bar{u}\bar{v})^{1/2}$ represents the geometric mean viability.

Now let us retain (80a), but posit that the fertilities of matings are almost constant; thus, we replace (80b) by

$$\Delta f_{ij,kl} = o(s^2). \quad (83)$$

As in (42),

$$\Delta \bar{u} = O(s^2), \quad \Delta \bar{v} = O(s^2), \quad t \geq 2; \quad (84)$$

as in (43) and (44),

$$\Delta a_{ij} = \sum_{kl} f_{ij,kl} P_{kl}^{**} + o(s^2) = O(s^2), \quad t \geq 1, \quad (85a)$$

$$\Delta b_{ij} = \sum_{kl} f_{kl,ij} P_{kl}^{**} + o(s^2) = O(s^2), \quad t \geq 1. \quad (85b)$$

Instead of (48), now we have

$$\Delta \bar{f} = \bar{\Delta a} + \bar{\Delta b} + o(s^2), \quad t \geq 1, \quad (86)$$

where

$$\bar{\Delta a} = \sum_{ij} P_{ij}^* \Delta a_{ij}, \quad \bar{\Delta b} = \sum_{ij} P_{ij}^{**} \Delta b_{ij}; \quad (87)$$

(49) still holds. From (79), (74), and (51) we obtain

$$\Delta \bar{w} = \frac{1}{2}(\Delta \bar{u} + \Delta \bar{v}) + \Delta \bar{f} + O(s^3), \quad t \geq 2. \quad (88)$$

As in the derivation of (54), we find

$$\bar{\Delta x} = \sum_{ij} P'_{ij} \Delta x_{ij} = \bar{\Delta a} + o(s^2), \quad t \geq 1, \quad (89a)$$

$$\bar{\Delta y} = \sum_{ij} P'_{ij} \Delta y_{ij} = \bar{\Delta b} + o(s^2), \quad t \geq 1. \quad (89b)$$

Substituting (88), (89), and (86) into (39) yields

$$\frac{1}{2}\Delta(\bar{u} + \bar{v} + \bar{f}) = V_g + o(s^2), \quad t \geq 2. \quad (90)$$

By (51), we can transform (90) to (56); now the modified mean fitness $\bar{W}$ is the geometric mean of the modified mean fitnesses of males and females:

$$\bar{W} = (\bar{W}^* \bar{W}^{**})^{1/2}, \quad \bar{W}^* = \bar{u} \bar{f}^{1/2}, \quad (91)$$

$$\bar{W}^{**} = \bar{v} \bar{f}^{1/2}.$$

In precise analogy with the monoecious result, we have $\bar{W} = \bar{U} \bar{f}^{1/2}$.

AN X-LINKED LOCUS

We assume that the locus under consideration does not influence the sex ratio at birth. Let p_i , Q_{ij} , and q_i denote the frequencies of A_i male zygotes, ordered A_iA_j female zygotes, and A_i in female zygotes, respectively. If u_i and v_{ij} designate the respective viabilities of A_i males and A_iA_j females, we have the adult frequencies

$$p_i^* = p_i u_i / \bar{u}, \quad \bar{u} = \sum_i u_i p_i, \quad (92a)$$

$$Q_{ij}^* = Q_{ij} v_{ij} / \bar{v}, \quad \bar{v} = \sum_{ij} v_{ij} Q_{ij}. \quad (92b)$$

Let f_{ijk} represent the number of progeny from the mating of an A_i male with an A_jA_k female. The zygotic frequencies in the next generation are

$$p'_i = \frac{1}{\bar{f}} \sum_{kl} p_k^* Q_{kl}^* f_{k,il}, \quad (93a)$$

$$Q'_{ij} = \frac{1}{2\bar{f}} \sum_k (p_i^* Q_{kj}^* f_{i,kj} + p_j^* Q_{ik}^* f_{j,ik}), \quad (93b)$$

where the mean fertility reads

$$\bar{f} = \sum_{ijk} f_{ijk} p_i^* Q_{jk}^*. \quad (94)$$

We define M , N^* and N^{**} as in the previous section and let $\tilde{a}_i$ and $\tilde{b}_{ij}$ designate the respective fertilities of A_i males and A_iA_j females. Then we get the scaled fertilities

$$a_i = N^* \tilde{a}_i / M = \sum_{kl} f_{i,kl} Q_{kl}^*, \quad (95a)$$

$$b_{ij} = N^{**} \tilde{b}_{ij} / M = \sum_k f_{k,ij} p_k^*, \quad (95b)$$

whence

$$\bar{a} = \sum_i a_i p_i^* = \bar{f}, \quad \bar{b} = \sum_{ij} b_{ij} Q_{ij}^* = \bar{f}. \quad (96)$$

With fitnesses

$$x_i = u_i a_i, \quad y_{ij} = v_{ij} b_{ij} \quad (97)$$

for A_i males and A_iA_j females, respectively, from (97), (92), and (96) we deduce the mean fitnesses of males and females:

$$\bar{x} = \sum_i x_i p_i = \bar{u} \bar{f}, \quad \bar{y} = \sum_{ij} y_{ij} Q_{ij} = \bar{v} \bar{f}. \quad (98)$$

We complete our formulation by using (93), (95), (92), (97), and (98):

$$p'_i = q_i y_i / \bar{y}, \quad q'_i = \frac{1}{2} \left(\frac{p_i x_i}{\bar{x}} + \frac{q_i y_i}{\bar{y}} \right), \quad (99)$$

where

$$q_i y_i = \sum_j y_{ij} Q_{ij}. \quad (100)$$

The analysis of the dynamics is a little more involved than in the autosomal case, and the approach to the neighborhood of the Hardy-Weinberg surface is not quite as rapid. We scale so that

$$u_i = 1 + O(s), \quad v_{ij} = 1 + O(s), \quad (101)$$

$$f_{ijk} = 1 + O(s),$$

and set

$$P_i = \frac{1}{3}(p_i + 2q_i), \quad R_{ij} = Q_{ij} - P_i P_j, \quad (102)$$

$$r_i = \sum_j R_{ij} = q_i - P_i = \frac{1}{3}(q_i - p_i); \quad (103)$$

P_i signifies the mean frequency of A_i in zygotes, and R_{ij} is a measure of deviation from Hardy-Weinberg proportions. From (102) and (103) we have

$$p_i = P_i - 2r_i, \quad q_i = P_i + r_i, \quad Q_{ij} = P_i P_j + R_{ij}. \quad (104)$$

Let

$$\xi_i = x_i - \bar{x}, \quad \eta_{ij} = y_{ij} - \bar{y}, \quad \eta_i = y_i - \bar{y}. \quad (105)$$

Appealing to (102), (99), (101), and (105), we find

$$\Delta P_i = \frac{1}{3}(p_i \xi_i + 2q_i \eta_i) + O(s^2) \quad (106)$$

$$= O(s). \quad (107)$$

Equations (92), (93), and (101) yield

$$p'_i = q_i + O(s), \quad Q'_{ij} = \frac{1}{2}(p_i q_j + p_j q_i) + O(s), \quad (108)$$

whence

$$q'_i = \frac{1}{2}(p_i + q_i) + O(s). \quad (109)$$

From (103), (108), and (109) we infer

$$r'_i = -\frac{1}{2}r_i + O(s). \quad (110)$$

If t_1 is the shortest time such that

$$|r_i(0)|^{(1/2)^{t_1}} \leq s \quad (111)$$

for every i , iterating (110) establishes

$$r_i(t) = O(s), \quad t \geq t_1. \quad (112)$$

Invoking (102), (108), (107), (104), and (112) leads to $R'_{ij} = O(s)$ for $t \geq t_1$, which means

$$R_{ij}(t) = O(s), \quad t > t_1. \quad (113)$$

From (104), (107), and (112) we derive

$$\Delta p_i = O(s), \quad t \geq t_1, \quad (114a)$$

and (104), (107), and (113) demonstrate

$$\Delta Q_{ij} = O(s), \quad t > t_1. \quad (114b)$$

The proof of (23) now gives

$$\Delta R_{ij} = O(s^2), \quad t \geq t_2 = t_1 + 2, \quad (115)$$

provided the rate of change of the viabilities and fertilities due to their explicit time dependence (if any) is $O(s^2)$.

Before proceeding to the evolution of the mean fitness, we employ (104) and (112) to rewrite (106) in the form

$$\Delta P_i = P_i \zeta_i + O(s^2), \quad t \geq t_1, \quad (116)$$

where

$$\zeta_i = \frac{1}{3}(\xi_i + 2\eta_i). \quad (117)$$

By manipulations similar to those that produce (29), from (98) and (105) we find

$$\Delta \bar{x} = \bar{\Delta x} + \sum_i \xi_i \Delta p_i, \quad \Delta \bar{y} = \bar{\Delta y} + \sum_{ij} \eta_{ij} \Delta Q_{ij}, \quad (118)$$

where

$$\bar{\Delta x} = \sum_i p'_i \Delta x_i, \quad \bar{\Delta y} = \sum_{ij} Q'_{ij} \Delta y_{ij}. \quad (119)$$

Despite the unequal weighting in (117), we must weight the male and female mean fitnesses equally (HARTL 1972; NAGYLAKI 1979). Therefore, we retain (79), but now define $\bar{x}$ and $\bar{y}$ by (98). From (79) and (118) we obtain

$$\Delta \bar{w} = \bar{\Delta w} + \frac{1}{2} \sum_i \xi_i \Delta p_i + \frac{1}{2} \sum_{ij} \eta_{ij} \Delta Q_{ij}, \quad (120)$$

in which

$$\bar{\Delta w} = \frac{1}{2}(\bar{\Delta x} + \bar{\Delta y}). \quad (121)$$

Applying (107) and (115) to (104), we see that

$$\Delta p_i = \Delta P_i + O(s^2), \quad t \geq t_2, \quad (122a)$$

$$\Delta Q_{ij} = P_i \Delta P_j + P_j \Delta P_i + O(s^2), \quad t \geq t_2. \quad (122b)$$

Suppose now that the gene frequencies P_i are bounded away from zero. For this it is sufficient but not necessary to assume that $t \leq c/s$ for some constant c . Then, by (105), (104), (112), and (113),

$$\eta_i = \sum_j \eta_{ij} P_j + O(s^2), \quad t > t_1. \quad (123)$$

Substituting (122), (123), (116), and (117) into (120) produces the analogue of (32):

$$\Delta \bar{w} = V_\zeta + \bar{\Delta w} + O(s^3), \quad t \geq t_2, \quad (124)$$

where

$$V_\zeta = \frac{3}{2} \sum_i \zeta_i^2 P_i. \quad (125)$$

Equations (33) and (125) both display the mean number of genes (2 and $\frac{3}{2}$, respectively) at the locus under consideration.

To establish the analogue of (39), we must prove that $V_{\bar{f}}$ is close to the genic variance V_g . We analyze the total variance

$$V = \frac{1}{3} \sum_i \xi_i^2 p_i + \frac{2}{3} \sum_{ij} \eta_{ij}^2 Q_{ij} \quad (126)$$

with respect to deviations from complete dosage compensation and no dominance (*cf.* special cases in HARTL 1972; NAGYLAKI 1979):

$$\xi_i = 2\alpha_i + d_i, \quad \eta_{ij} = \alpha_i + \alpha_j + D_{ij}. \quad (127)$$

The weighting in (126) is by the number of sex chromosomes per individual, as in (102) and (117); α_i , d_i , and D_{ij} represent the average effect of A_i on fitness and the dominance deviations from complete dosage compensation in males and females, respectively. The genic and dominance variances read

$$V_g = \frac{1}{3} \sum_i p_i (2\alpha_i)^2 + \frac{2}{3} \sum_{ij} Q_{ij} (\alpha_i + \alpha_j)^2, \quad (128a)$$

$$V_d = \frac{1}{3} \sum_i p_i d_i^2 + \frac{2}{3} \sum_{ij} Q_{ij} D_{ij}^2. \quad (128b)$$

Fixing ξ_i and η_{ij} and minimizing V_d with respect to α_i leads to

$$p_i (\xi_i - 2\alpha_i) + 2 \sum_j Q_{ij} (\eta_{ij} - \alpha_i - \alpha_j) = 0; \quad (129)$$

in view of (127), this is identical to

$$p_i d_i + 2 \sum_j Q_{ij} D_{ij} = 0. \quad (130)$$

With the aid of (129), we can reduce (128a) to

$$V_g = \frac{2}{3} \sum_i \alpha_i (p_i \xi_i + 2q_i \eta_i). \quad (131)$$

Summing (129) over i and recalling (105) and (102) proves that the mean additive effect is zero:

$$\sum_i \alpha_i P_i = 0. \quad (132)$$

We insert (127), (128), and (130) into (126) to demonstrate the additivity of the variance components:

$$V = V_g + V_d. \quad (133)$$

Successive use of (104), (132), (117), (112), and (113) in (129) yields

$$\alpha_i = \frac{3}{4} \xi_i + O(s^2), \quad t > t_1. \quad (134)$$

Employing (104), (112), (117), (134), and (125) simplifies (131) to

$$V_g = V_{\bar{f}} + O(s^3), \quad t > t_1, \quad (135)$$

where (124) becomes

$$\Delta \bar{w} = V_g + \overline{\Delta w} + O(s^3), \quad t \geq t_2. \quad (136)$$

If the viabilities and genotypic fertilities are nearly constant, *i.e.*,

$$\Delta u_i = o(s^2), \quad \Delta v_{ij} = o(s^2), \quad (137a)$$

$$\Delta a_i = o(s^2), \quad \Delta b_{ij} = o(s^2), \quad (137b)$$

then (136) becomes

$$\Delta \bar{w} = V_g + o(s^2), \quad t \geq t_2, \quad (138)$$

so after a short time t_2 , $\bar{w}$ generally increases. To see that (138) also holds for $\hat{w} = (\hat{x} \hat{y})^{1/2}$, we observe that (118), (137), (101), and (114) imply the validity of (81) for $t > t_1$. Hence, (51) applies, and the desired result follows from (79) and (138). By (98), we have $\hat{w} = \bar{U} \bar{f}$, where $\bar{U} = (\bar{u} \bar{v})^{1/2}$, as in the autosomal case.

Now we retain the hypothesis (137a) for the viabilities, but instead of (137b) posit approximate constancy of the fertilities of matings:

$$\Delta f_{ijk} = o(s^2). \quad (139)$$

Writing (118) for $\bar{u}$ and $\bar{v}$ and appealing to (137a), (101), and (114) demonstrates

$$\Delta \bar{u} = O(s^2), \quad \Delta \bar{v} = O(s^2), \quad t > t_1. \quad (140)$$

From (95), (139), (92), (137a), (101), and (114) we obtain

$$\Delta a_i = \sum_{kl} f_{i,kl} \Delta Q_{kl}^* + o(s^2) = O(s^2), \quad t > t_1, \quad (141a)$$

$$\Delta b_{ij} = \sum_k f_{k,ij} \Delta p_k^* + o(s^2) = O(s^2), \quad t \geq t_1. \quad (141b)$$

We invoke (94), (139), (141), (92), (101), and (114) to prove

$$\bar{f} = \overline{\Delta a} + \overline{\Delta b} + o(s^2), \quad t > t_1, \quad (142)$$

where

$$\overline{\Delta a} = \sum_i p_i^* \Delta a_i, \quad \overline{\Delta b} = \sum_{ij} Q_{ij}^* \Delta b_{ij}. \quad (143)$$

On account of (141) and (142), we have

$$\Delta \bar{f} = O(s^2), \quad t > t_1. \quad (144)$$

From (79), (98), and (51) we get

$$\Delta \bar{w} = \frac{1}{2} (\Delta \bar{u} + \Delta \bar{v}) + \Delta \bar{f} + O(s^3), \quad t > t_1. \quad (145)$$

Furthermore, (97), (137a), (119), (114), (92), (141), and (143) imply

$$\overline{\Delta x} = \overline{\Delta a} + o(s^2), \quad t \geq t_1, \quad (146a)$$

$$\overline{\Delta y} = \overline{\Delta b} + o(s^2), \quad t > t_1. \quad (146b)$$

Inserting (145), (121), (146), and (142) into (136) yields (90) for $t \geq t_2$. With the definition (91), we deduce

$$\Delta \bar{W} = V_g + o(s^2), \quad t \geq t_2 \quad (147)$$

for the modified mean fitness $\bar{W} = \bar{U} \bar{f}^{1/2}$, as for an autosomal locus.

DISCUSSION

We have investigated the dynamics at a single multiallelic locus under arbitrary weak selection on both fertility and viability. We posited discrete, nonoverlapping generations for autosomal and X-linked loci in dioecious populations, but studied monoecious populations in both discrete and continuous time. Mating is random in all cases. The results hold after several generations have elapsed. The divergence of the population from Hardy-Weinberg proportions is $O(s)$, where s represents the selection intensity. Provided the change per generation of the fertilities and viabilities due to their explicit time dependence (if any) is $O(s^2)$, the rate of change of the deviation from Hardy-Weinberg proportions is $O(s^2)$.

The mean fitness is the product of the mean fertility and the mean viability; in dioecious populations, the latter is the unweighted geometric mean of the mean viabilities of the two sexes. As shown in (39), (61), and (136), the rate of change of the mean fitness ($\Delta\bar{w}$) is close to the sum of the additive component of the genetic variance (V_g) and the average rate of change of the genotypic fitnesses (Δw), the error being $O(s^3)$. Suppose the change per generation of the viabilities is $o(s^2)$. Then different biological assumptions concerning the approximate constancy of the fertilities crucially affect the value of $\Delta\bar{w}$, and thereby influence the form of the Fundamental Theorem of Natural Selection.

On the one hand, if the change per generation of the fertilities of *genotypes* is $o(s^2)$, then $\Delta\bar{w}$ is negligible, and hence $\Delta\bar{w} \approx V_g$, as stated below (39) and (63) and in (82) and (138). This implies that as long as there is substantial gene frequency change, the mean fitness increases.

On the other hand, if it is the fertilities of *matings* that change at a rate $o(s^2)$, then $\Delta\bar{w}$ contributes significantly and now $\Delta\bar{w} \approx V_g$, where the modified mean fitness $\bar{W}$ is the product of the mean viability and the square root of the mean fertility; see (56), (67), below (90), and (147).

The choice between the alternative assumptions discussed in the last two paragraphs can only be made on biological grounds; both assumptions lead to sensible mathematical models. Perhaps the assumption of nearly constant genotypic fertilities is reasonable for polygamous species, whereas the fertilities of matings may be almost constant in monogamous ones. It is easy to see that if, instead of mating, each genotype sheds gametes and these gametes fuse at random, then the standard selection models with zygotes in generalized Hardy-Weinberg proportions apply, and each genotypic fitness is the product of the viability and half the number of gametes produced (*cf.* CROW and KIMURA 1970, pp. 188–189; NAGYLAKI 1977a, pp. 54, 155–156, 163–164; ROUGHGARDEN 1979, pp. 26–

29). Clearly, in this case the first assumption makes biological sense, whereas the second has no meaning.

I thank ETHAN AKIN for helpful comments. This work was supported by National Science Foundation grant BSR-8512844.

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Communicating editor: W. J. EWENS