On an extremum principle in the genetical theory of natural selection

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Abstract. Natural selection causes gene frequency changes in a large population leading to genetic evolution over evolutionary time scales. Such gene frequency changes, however, involve an optimizing principle. According to Kimura, such changes, over a short interval of time, occur in a manner such that the increase in population fitness is maximum for a given distance between parent and daughter generation gene frequencies. But according to Ewens, of all gene frequency changes, including those that lead to the same partial increase in mean fitness as the natural selection gene frequency changes, the natural selection values minimize the generalized distance measure between parent and daughter generation gene frequency values. These two optimality principles happen to be mirror images of each other. However, the optimality principles are restricted to the case where the increase in mean fitness is to the *first order* in natural selection gene frequency changes. I show in this paper that, instead of linear approximation to the increase in mean fitness, the treatment can be fairly general, and the exact increase in mean fitness can be considered so as to include the dominance effects of the genes.

Keywords. Natural selection; evolution; Fisher's fundamental theorem; extremum principle; population fitness.

1. Introduction

In the genetical theory of natural selection, Fisher's fundamental theorem of natural selection plays a pivotal role. However, the interpretation of the theorem, differently by different people, has raised issues basic to population genetics theory. Recently, Ewens (1989, 1992), following Price (1972), interpreted it as relating to what he calls *partial* increase in mean population fitness and advocated an optimality principle based on this concept. According to him, of all gene frequency changes, including those that lead to the same *partial* increase in mean fitness as the natural selection gene frequency changes, the natural selection values minimize a generalized distance measure between parent and daughter generation gene frequency values. Before Ewens's formulation, the only optimality principle available in the literature was that of Kimura (1958), in the form of a theorem applicable to the continuous case. This theorem states that during a short time interval natural selection causes gene frequency changes in such a manner that the increase in mean population fitness is maximum under the restriction that the generalized distance measure (in Ewens's terminology) between parent and daughter generation gene frequencies is a fixed quantity. Edwards (1974) re-examined Kimura's maximum principle and concluded that it reflects a feature of mathematical structure that does not add to or clarify our understanding of the natural selection process. However, towards the end of his paper, he made an important point concerning the minimum principle, where the roles of mean fitness and distance measure are reversed, i.e. of all gene frequency changes, including those that lead to the same increase in mean fitness as the natural selection gene frequency changes, the natural selection values minimize the generalized distance between parent and daughter generation gene frequency values. In other words, the two principles—

the *maximum* and the *minimum*—are mirror images of each other, as they should be in any optimization procedure.

   In the discussion of Kimura and Edwards the optimality principle is restricted to the case where the increase in mean fitness is to the *first order* in natural selection gene frequency changes. On the other hand, Ewens's treatment of the problem is perfectly general in that it relates to any system of mating—random or non-random—, and covers an arbitrary number of loci with an arbitrary number of alleles at each locus, arbitrary fitness values, and arbitrary recombination patterns between loci. But he also considers the increase in mean fitness to the *first order* in natural selection gene frequency changes by using the concept of *partial increase* in mean fitness. In this paper I show that the optimality principle—whether the maximum or the minimum—does not necessarily require us to restrict the treatment to what amounts to a linear approximation to the increase in mean population fitness. Instead, the treatment can be a fairly general one, in which the exact increase in mean fitness can be considered, so as to include the dominance effects of the genes. However, in this paper I restrict the treatment to the random mating case and consider first a single locus with two alleles and then the case of an arbitrary number of alleles at the locus. The case of non-random-mating populations will be dealt with in a subsequent communication. Since the genetic distance measure is crucial to the argument developed in this paper. I shall first deal with it briefly.

2.   Genetic distance

The genetic distance measure is a statistical tool that allows information on allelic frequencies at one or several loci to be combined into a single index for comparison between populations. There are broadly two types of genetic distance measures, those used for population classification and those employed for evolutionary studies. It is the former category we are concerned with. Mahalanobis's (1936) D^2 statistic comes under this category and is the most commonly used distance measure for a set of correlated quantitative characters.

   Let $\bar{x}_i$ and $\bar{y}_i$ be the means of the ith characters in the two populations X and Y respectively. Assume that the variances (V_{ii}) and covariances (V_{ij}) of the characters are the same in the two populations. These can be represented in the form of a variance–covariance matrix V. Then Mahalanobis's D^2 is defined as

$$D^2 = \sum_{i=1}^{k} \sum_{j=1}^{k} V^{ij}(\bar{x}_i - \bar{y}_i)(\bar{x}_j - \bar{y}_j),$$

where V^{ij} is the element in the ith row and jth column of the inverse matrix V^{-1}.

   Steinberg *et al.* (1967) modified it for gene frequency data. Considering $m - 1$ alleles at a locus, the elements of covariance matrix V of order $(m - 1) \times (m - 1)$ are

$$V_{ii} = z_i(1 - z_i)$$
$$V_{ij} = -z_i z_j, \quad (i \neq j),$$

where $z_i = (x_i + y_i)/2$, and x_i and y_i are frequencies of the ith allele in populations X and Y respectively. It can be shown then that D^2 is related to the χ^2 used for testing

allele frequency differences between two populations. We can therefore write D^2 as

$$\chi^2 = \sum_{i=1}^{m} (x_i - y_i)^2 / z_i.$$

This is identical with Sanghvi's (1953) distance. For equal sample sizes in the two populations, the χ^2 is $2nX^2$, in which, if we write $(x_i - y_i) = (\Delta y_i)$ and consider terms up to $(\Delta y_i)^2$, we can approximate X^2 as

$$X^2 = \sum_{i=1}^{m} (\Delta y_i / y_i)^2 [1 + (\Delta y_i)/2 + (\Delta y_i)^2 / 3! + \ldots]$$

$$= \sum_{i=1}^{m} (\Delta y_i)^2 / y_i.$$

In vector notation, this is expressed as $(\Delta y)^{\mathrm{T}} Y^{-1}(\Delta y)$, where $(\Delta y)^{\mathrm{T}} = (\Delta y_1, \ldots, \Delta y_m)$ and $Y = \mathrm{diag}(y_1, y_2, \ldots, y_m)$. This is a quadratic form in (Δy), the changes in the gene frequencies over one generation for the set of alleles with the constraint $(\Delta y)^{\mathrm{T}} e = 0$, where e is an $m \times 1$ vector of units. Such a quadratic form is quite general as well as amenable to the type of optimization problem considered in this paper.

3. One locus with two alleles

To fix our approach conceptually it is better to start with the simplest case of two alleles A_1 and A_2 at the locus, with frequencies p_1 and p_2 $(p_1 + p_2 = 1)$, in a random mating population. Let the relative fitnesses of the three genotypes $A_1 A_1$, $A_1 A_2$ and $A_2 A_2$ be, respectively, W_{11}, W_{12} and W_{22}, with $W_{21} = W_{12}$. The average fitness of such a population, denoted by $\bar{W}$, is then

$$\bar{W} = p_1^2 W_{11} + 2 p_1 p_2 W_{12} + p_2^2 W_{22}$$

$$= p_1 W_{11} + p_2 W_{22} + 2 p_1 p_2 d_{12}, \tag{1}$$

where

$$d_{12} = [W_{12} - (W_{11} + W_{22})/2] \tag{2}$$

expresses the degree of dominance on the arithmetic scale. We may also note that the marginal fitnesses of alleles A_1 and A_2 are given by

$$w_1 = p_1 W_{11} + p_2 W_{12},$$
$$w_2 = p_1 W_{21} + p_2 W_{22}, \tag{3}$$

so that $\bar{W}$ can also be expressed as

$$\bar{W} = p_1 w_1 + p_2 w_2. \tag{4}$$

As we see later, these forms are easily generalized to k alleles. The total genetic variance in fitness, σ_W^2, is given by

$$\sigma_W^2 = p_1^2 (W_{11} - \bar{W})^2 + 2 p_1 p_2 (W_{12} - \bar{W})^2 + p_2^2 (W_{22} - \bar{W})^2$$

$$= (p_1^2 W_{11}^2 + 2 p_1 p_2 W_{12}^2 + p_2^2 W_{22}^2) - (\bar{W})^2. \tag{5}$$

The variation in the marginal fitnesses of the alleles, σ_w^2, is

$$\sigma_w^2 = p_1(w_1 - \bar{W})^2 + p_2(w_2 - \bar{W})^2$$
$$= (p_1 w_1^2 + p_2 w_2^2) - (\bar{W})^2. \tag{6}$$

The change in gene frequency of A_1 after selection and random mating is given by

$$\Delta p_1 = p_1(w_1 - \bar{W})/\bar{W}. \tag{7}$$

The change in mean fitness after one round of random mating can be determined by expressing the mean fitness around its previous value by Taylor's expansion as

$$\bar{W} = \bar{W}_0 + (d\bar{W}/dp_1)(\Delta p_1) + (d^2\,\bar{W}/dp_1^2)(\Delta p_1/2)^2$$

as higher-order terms would be zero. We have

$$(d\bar{W}/dp_1) = (W_{11} - W_{22}) + 2(1 - 2p_1)d_{12},$$
$$(d^2\,\bar{W}/dp_1^2) = -4d_{12}.$$

This gives

$$\Delta\bar{W} = a(\Delta p_1) + b(\Delta p_1)^2, \tag{8}$$

where

$$a = (W_{11} - W_{22}) + 2(p_2 - p_1)d_{12}, \tag{9}$$
$$b = d_{12}. \tag{10}$$

We see that $\Delta\bar{W}$ has a linear approximation

$$\Delta\bar{W}^* = a(\Delta p_1)$$
$$= 2\sigma_w^2/\bar{W}. \tag{11}$$

However, if we do not make this approximation, we can express $\Delta\bar{W}$ exactly as

$$\Delta\bar{W} = (2\sigma_w^2/\bar{W}) - 2p_1^2 p_2^2(w_1 - w_2)^2 d_{12}/(\bar{W})^2$$
$$= (2\sigma_w^2/\bar{W})[1 - p_1 p_2 d_{12}/\bar{W}]. \tag{12}$$

If we put $\sigma_A^2 = 2\sigma_w^2$, we get the same expression as the one given by Li (1967). However, it may be noted that when there is no dominance in fitness on the arithmetic scale, i.e. $d_{12} = 0$, we get, from equation (10), $b = 0$, which converts the linear approximation to the increase in mean fitness into an exact one.

The divergence in gene frequency of the two alleles between parent and offspring generations can be expressed in terms of a genetic distance squared as discussed in section 2 as

$$D^2 = (\Delta p_1)^2/p_1 + (\Delta p_2)^2/p_2$$
$$= (\Delta p_1)^2/C, \tag{13}$$

where

$$C = p_1 p_2. \tag{14}$$

We first maximize equation (8) for variations in Δp_1 subject to the constraint that D^2 given by equation (13) is some fixed quantity λ. This is the optimization given by Kimura (1958). Lagrange's multiplier technique gives

$$Q = a(\Delta p_1) + b(\Delta p_1)^2 - \mu[(\Delta p_1)^2/C - \lambda].$$

Differentiating with respect to Δp_1 and equating to zero gives

$$\Delta p_1 = a/[2(\mu/C - b)]. \tag{15}$$

Substituting from equation (15) in equation (13) for Δp_1 gives

$$\lambda = a^2/[4(\mu/C - b)^2], \tag{16}$$

which gives

$$\mu = [bC + (a/2)(C/\lambda)^{1/2}]. \tag{17}$$

This leads finally to

$$\Delta p_1 = (\lambda C)^{1/2}. \tag{18}$$

It may be noted that this result is independent of whether $b = 0$ or not. Hence, in this optimality principle, maximization of either the linear approximation to the increase in mean fitness ($\Delta \bar{W}^*$) or the exact increase in mean fitness ($\Delta \bar{W}$), subject to equation (13), will yield identical results. If equation (18) is to give the same Δp_1 as that given by equation (7), we must have

$$\lambda = \sigma_w^2/(\bar{W})^2. \tag{19}$$

If we replace $2\sigma_w^2$, by σ_A^2, the additive genetic variance, we get the same result as the one given by Kimura (1958).

We next minimize equation (13) for variation in Δp_1 subject to the constraint that $\Delta \bar{W}$ given by equation (8) is some fixed quantity λ^*. We get, using Lagrange's multiplier technique,

$$Q = (\Delta p_1)^2/C - \mu^*[a(\Delta p_1) + b(\Delta p_1)^2 - \lambda^*].$$

Differentiating with respect to Δp_1 and equating to zero, we get

$$(\Delta p_1)^* = \mu^* aC/[2(1 - bC\mu^*)]. \tag{20}$$

Substituting from equation (20) in equation (8) for Δp_1 gives a quadratic equation in μ^*:

$$bC^2(a^2 + 4\lambda^* b)\mu^{*2} - 2C(a^2 + 4\lambda^* b)\mu^* + 4\lambda^* = 0,$$

which gives

$$\mu^* = [1 - a/(a^2 + 4\lambda^* b)^{1/2}]bC. \tag{21}$$

This leads finally to

$$(\Delta p_1)^* = (a/2b)[(1 + 4\lambda^* b/a^2)^{1/2} - 1]. \tag{22}$$

Unlike the previous case, here the result depends on whether b is zero or not. If we take b not equal to zero, and if equation (22) is to give the same Δp_1 as that given by equation (7), we must have

$$\lambda^* = (2\sigma_w^2/\overline{W})[1 - p_1 p_2 d_{12}/\overline{W}]. \tag{23}$$

But if $b = 0$, then minimization of equation (13) subject to equation (8) gives λ^* as $(2\sigma_w^2/\overline{W})$. In case dominance is zero, i.e. $d_{12} = 0$, we have $b = 0$, and we again get this result.

In fact, the most general relation between λ and λ^* is obtained by equating the two (Δp_1)s given by equations (18) and (22). This is

$$\lambda^* = (bC)\lambda + [a(C)^{1/2}](\lambda)^{1/2}. \tag{24}$$

Apparently, the choice of λ given by equation (19) coupled with whether b is zero or not determines λ^* as $(2\sigma_w^2/\overline{W})$ or that given by equation (23) respectively.

4.   One locus with k alleles

I now consider k alleles $A_1, A_2, \ldots, A_k$ at the locus, with frequencies $p_1, p_2, \ldots, p_k$ $(\Sigma p_i = 1)$, in a random-mating population. Let the relative fitnesses of the $k(k+1)/2$ genotypes be expressed in the form of a symmetric matrix W of order $k \times k$, with i, jth element W_{ij}, the relative fitness of genotype $A_i A_j$ $(i,j = 1, 2, \ldots, k$ and $W_{ij} = W_{ji})$. Also let the gene frequencies of the k alleles be expressed in the form of a $k \times 1$ column vector p. Further, let the marginal fitnesses of the alleles A_i be denoted by w_i, where $w_i = \Sigma_{j=1}^{k} p_j W_{ij}$, $i = 1, 2, \ldots, k$, and let the set of k marginal fitnesses be expressed in the form of a $k \times 1$ column vector w. In matrix notation,

$$w = Wp$$
$$= WPe, \tag{25}$$

where

$$P = \mathrm{diag}(p_1, p_2, \ldots, p_k) \tag{26}$$

and e is a $k \times 1$ column vector of units. The average fitness of the population can be expressed in several ways. As a generalization of equation (1), this is

$$\overline{W} = \Sigma_i p_i W_{ii} + 2\Sigma_{i<j} p_i p_j d_{ij}, \tag{27}$$

where

$$d_{ij} = [W_{ij} - (W_{ii} + W_{jj})/2], \quad i < j = 1, 2, \ldots, k \tag{28}$$

is the degree of dominance in fitness for the pair of alleles A_i and A_j. In matrix notation the average fitness can be written in several ways:

$$\overline{W} = p^T W p$$
$$= p^T w$$
$$= e^T P W P e. \tag{29}$$

The total genetic variance in fitness now takes the form

$$\sigma_W^2 = \Sigma_i \Sigma_j p_i p_j (W_{ij} - \bar{W})^2$$
$$= \Sigma_i \Sigma_j p_i p_j W_{ij}^2 - (\bar{W})^2, \tag{30}$$

whereas the variance in the marginal fitnesses of the alleles is

$$\sigma_w^2 = \Sigma_i p_i (w_i - \bar{W})^2$$
$$= \Sigma_i p_i w_i^2 - (\bar{W})^2. \tag{31}$$

Arranging the genotypes in the form of a two-way analysis-of-variance (ANOVA) table, with rows and columns contributing identical variances σ_w^2, gives the remainder variance

$$\sigma_R^2 = \sigma_W^2 - 2\sigma_w^2$$
$$= \Sigma_i \Sigma_j p_i p_j [W_{ij} - w_i - w_j + \bar{W}]^2$$
$$= \Sigma_i \Sigma_j p_i p_j \left[\left\{ d_{ij} - \sum_k p_k d_{ik} - \sum_k p_k d_{jk} \right\} + 2 \sum_{k<l} p_k p_l d_{kl} \right]. \tag{32}$$

The remainder variance is thus entirely in terms of the pair-wise degrees of dominance in fitness, i.e. the d_{ij}s. The partitioning of σ_W^2 into the two components $2\sigma_w^2$ and σ_R^2 is thus analogous to the case of two alleles.

The change in the gene frequency of A_i after selection and random mating is given by

$$\Delta p_i = p_i (w_i - \bar{W})/\bar{W}, \quad i = 1, 2, \ldots, k \tag{33}$$

with $\Sigma_i \Delta p_i = 0$. This can be expressed in vector notation as

$$(\Delta p) = (\bar{W})^{-1} P(w - \bar{W}e), \tag{34}$$

with

$$(\Delta p)^T e = 0, \tag{35}$$

where (Δp) is a $k \times 1$ column vector of Δp_is.

The change in mean fitness after one round of random mating can be determined, following Li (1978), by expressing the mean fitness around its previous value by Taylor's expansion of a function of several variables. That is

$$\bar{W} = \bar{W}_0 + \sum_i (\Delta p_i)(\partial \bar{W}/\partial p_i)' + (1/2) \sum_i \sum_j (\Delta p_i)(\Delta p_j)(\partial^2 \bar{W}/\partial p_i \partial p_j)$$

as higher-order terms would be zero. We then have

$$\left. \begin{array}{rll} \partial \bar{W}/\partial p_i & = & 2w_i, \\ \partial^2 \bar{W}/\partial p_i^2 & = & 2W_{ii}, \\ \partial^2 \bar{W}/\partial p_i \partial p_j & = & 2W_{ij}. \end{array} \right\} \begin{array}{l} i = 1, 2, \ldots, k \\ j = 1, 2, \ldots, k \end{array}$$

This gives

$$\Delta\bar{W} = 2\sum_i (\Delta p_i)w_i + \sum_i (\Delta p_i)^2 \ W_{ii} + \sum_{i \neq j}\sum (\Delta p_i)(\Delta p_j) \ W_{ij}$$

$$= 2(\Delta p)^{\mathrm{T}} w + (\Delta p)^{\mathrm{T}} W(\Delta p). \tag{36}$$

In view of equations (28), (31) and (33), $\Delta\bar{W}$ can also be expressed as

$$\Delta\bar{W} = 2\sum_i p_i(w_i - \bar{W})w_i/\bar{W} + \sum_i \sum_j p_i p_j \ W_{ij}(w_i - \bar{W})(w_j - \bar{W})/(\bar{W})^2$$

$$= (2\sigma_w^2/\bar{W}) + \sum_i \sum_j p_i p_j d_{ij}(w_i - \bar{W})(w_j - \bar{W})/(\bar{W})^2. \tag{37}$$

If D is a matrix defined as below, noting that $d_{ii} = 0$ for $i = 1, 2, \ldots, k$,

$$D = \begin{bmatrix} 0 & d_{12} & \cdots & d_{1k} \\ d_{21} & 0 & \cdots & d_{2k} \\ d_{k1} & d_{k2} & \cdots & 0 \end{bmatrix}, \tag{38}$$

the matrix form of equation (37) is

$$\Delta\bar{W} = 2(\Delta p)^{\mathrm{T}} w + (\Delta p)^{\mathrm{T}} D(\Delta p). \tag{39}$$

Thus we see that $\Delta\bar{W}$ has the same linear approximation as in the two-allele case given by equation (11). This approximation also becomes an exact expression for $\Delta\bar{W}$ if there is no dominance in fitness on the arithmetic scale for all the pairs of alleles, i.e. $d_{ij} = 0$ for all $i \neq j$. But when there is dominance, the exact expression for $\Delta\bar{W}$ depends on σ_w^2 as well as the d_{ij}s and we do not have the simple form of equation (12) of the two-allele case.

The divergence in gene frequencies of the k alleles between parent and offspring generations can be expressed, as before, in terms of the genetic distance squared as

$$D^2 = \sum_{i=1}^{k} (\Delta p_i)^2/p_i$$

$$= (\Delta p)^{\mathrm{T}} P^{-1}(\Delta p), \tag{40}$$

which is a quadratic form with matrix P^{-1}.

Now we first maximize equation (36) for variation in (Δp) subject to the condition in equation (35) and the constraint that D^2 given by equation (40) is some fixed quantity λ. Lagrange's multiplier technique gives

$$Q = 2(\Delta p)^{\mathrm{T}} w + (\Delta p)^{\mathrm{T}} \ W(\Delta p) - \mu_1 [(\Delta p)^{\mathrm{T}} P^{-1}(\Delta p) - \lambda] - \mu_2 [(\Delta p)^{\mathrm{T}} e].$$

Vector differentiation with respect to (Δp) and equating to zero gives

$$(\Delta p) = (\mu_1 P^{-1} - W)^{-1}(w - (\mu_2/2)e)$$

$$= (\mu_1 I - PW)^{-1}[PWP - (\mu_2/2)P]e. \tag{41}$$

Substituting from equation (41) in equation (35) for (Δp), we get

$$e^{\mathrm{T}}[PWP - (\mu_2/2)P](\mu_1 I - WP)^{-1}e = 0.$$

This shows that we must have

$$e^{\mathrm{T}}[PWP - (\mu_2/2)P] = O^{\mathrm{T}}.$$

Post-multiplying by e and using equation (29) gives

$$\mu_2 = 2\bar{W}. \tag{42}$$

Substituting this value of μ_2 in equation (41), we get

$$(\Delta p) = (\mu_1 I - PW)^{-1}P(w - \bar{W}e). \tag{43}$$

Substituting from equation (43) into equation (40) for (Δp) leads to

$$(w^{\mathrm{T}} - \bar{W}e^{\mathrm{T}})P(\mu_1 I - WP)^{-1}P^{-1}(\mu_1 I - PW)^{-1}P(w - \bar{W}e) = \lambda$$

or

$$(w^{\mathrm{T}} - \bar{W}e^{\mathrm{T}})(\mu_1 I - WP)^{-2}P(w - \bar{W}e) = \lambda.$$

This is satisfied if

$$(\mu_1 I - PW)^{-2} = \lambda I/[(w - \bar{W}e)^{\mathrm{T}}P(w - \bar{W}e)] = \lambda I/\sigma_w^2,$$

giving

$$\mu_1 I = (\lambda^{-1/2}\sigma_w)I + PW. \tag{44}$$

Using equation (44) in equation (43), we get the optimum Δp_is that maximize the increase in mean fitness, subject to the two conditions, as

$$(\Delta p) = (\lambda^{1/2}\sigma_w^{-1})(w - We). \tag{45}$$

This optimum solution has been obtained by taking the exact form of the mean fitness given by equation (36). If we maximize the linear approximation to the increase in mean fitness [the first term, $2(\Delta p)^{\mathrm{T}}w$, in equation (36)], subject to the same two conditions given by equations (35) and (40), as Kimura (1958) did, we still get the same result for optimum (Δp) as in equation (45). So this result is independent of the presence or absence of dominance effects, i.e. the d_{ij}s.

If equation (45) is to give the same changes in allelic frequencies in one generation as natural selection gene frequency changes given by equation (34), we must have

$$\lambda = \sigma_w^2/(\bar{W})^2, \tag{46}$$

which is the same result as that obtained by Kimura (1958), if we replace $2\sigma_w^2$ by σ_A^2. The *maximum* principle in the genetical theory of natural selection can therefore be stated as follows:

Of all the per-generation gene frequency changes, including those that lead to the same genetic distance $[\sigma_w^2/(\bar{W})^2]$ between parent and daughter generation gene frequency values as the natural selection gene frequency changes, the natural selection values

maximize the increase in mean fitness of the population ($\Delta \bar{W}$), irrespective of the presence or absence of dominance in fitness values.

We next minimize equation (40) for variation in (Δp) subject to the condition in equation (35) and the constraint that $\Delta \bar{W}$ given by equation (36) is some fixed quantity λ^*. We get, using Lagrange's multiplier technique,

$$Q^* = (\Delta p)^T P^{-1} (\Delta p) - \eta_1 [2(\Delta p)^T w + (\Delta p)^T W (\Delta p) - \lambda^*] - \eta_2 [(\Delta p)^T e].$$

Vector differentiation with respect to (Δp) and equating to zero gives

$$(\Delta p) = (I - \eta_1 PW)^{-1} P[\eta_1 w + (\eta_2/2)e]. \tag{47}$$

Substituting from equation (47) in equation (35) for (Δp), we get

$$[\eta_1 w^T + (\eta_2/2)e^T] P (I - \eta_1 WP)^{-1} e = 0.$$

This gives

$$\eta_2 = \eta_1 \bar{W}. \tag{48}$$

Substituting this value of η_2 in equation (47), we get

$$(\Delta p) = \eta_1 (I - \eta_1 P W)^{-1} P(w - \bar{W} e). \tag{49}$$

Substituting from equation (49) into equation (36) for (Δp), we get the quadratic in G given by

$$BG^2 + AG - \lambda^* = 0, \tag{50}$$

where G, A and B are scalars with

$$GI = \eta_1 (I - \eta_1 WP)^{-1}, \tag{51}$$

$$A = 2(w - \bar{W} e)^T P w = 2\sigma_w^2, \tag{52}$$

$$B = (w - \bar{W} e)^T P W P (w - \bar{W} e). \tag{53}$$

The solution is

$$G = (A/2B) [(1 + 4B\lambda^*/A^2)^{1/2} - 1]. \tag{54}$$

This gives the optimum value of (Δp) as

$$(\Delta p) = (A/2B) [(1 + 4B\lambda^*/A^2)^{1/2} - 1] P(w - \bar{W} e). \tag{55}$$

If equation (55) is to give the same changes in allelic frequencies in one generation as the natural selection gene frequency changes given by equation (34), we must have

$$\lambda^* = (\bar{W})^{-1} A [1 + B/(A\bar{W})]. \tag{56}$$

It is easy to verify that this is the same as equation (37).

When there is no dominance or when we take the linear approximation to $\Delta \bar{W}$, the above procedure leads to the optimum value of (Δp) as

$$(\Delta p)^* = (\lambda^*/2\sigma_w^2) P(w - \bar{W} e). \tag{57}$$

Comparing with equation (34), we find that λ^* has to be

$$\lambda^* = (2\sigma_w^2/\bar{W}), \tag{58}$$

which is what we got in the two-allele case, as well as the same as that given by Ewens (1992) when we replace $2\sigma_w^2$ by σ_A^2. The *minimum* principle in the genetical theory of natural selection can therefore be stated as follows:

Of all the per-generation gene frequency changes, including those that lead to the same increase in the mean fitness of the population $(\Delta\bar{W})$ as the natural selection gene frequency changes, the natural selection values minimize the genetic distance between parent and daughter generation gene frequency values.

When there is no dominance or when the linear approximation to the increase in mean fitness is considered, the natural selection values minimizing the genetic distance are such that the rate of increase in mean fitness of the population is $(2\sigma_w^2/\bar{W})$.

The most general relation between λ and λ^* is obtained by equating the two (Δp)s given by equations (45) and (55). This gives

$$\lambda^* = (B/\sigma_w^2)\lambda + (A/\sigma_w)(\lambda)^{1/2}. \tag{59}$$

This is useful for determining the constraint in the minimum principle and clearly depends on whether B is zero or not, or, in other words, whether dominance is absent or present respectively. In the latter case, the linear approximation to $\Delta\bar{W}$ is taken, which Ewens (1992) interprets as *partial increase* in mean fitness. In this paper, however, the minimum principle is more general as it takes into account the dominance effects.

To express λ in terms of λ^*, we substitute the value of λ^* from equation (56) in the quadratic solution of λ obtained from equation (59). This gives

$$\lambda = \sigma_w^2/(\bar{W})^2 \tag{60}$$

irrespective of whether B is zero or not. So, in the maximum principle, the constraint is always the relation in equation (60) whether dominance effects are present or not. This is similar to the constraint adopted by Kimura (1958), who used it, without giving any reasons for doing it, for maximization of the linear approximation to the increase in mean fitness. It is apparent from the foregoing that the same constraint can be used for maximization of the *exact* increase in mean fitness as well.

5. Discussion

It seems that without concerning ourselves too much with what Fisher (1930, 1941) meant in his discussion of the fundamental theorem of natural selection, the fact is that natural selection causes per-generation gene frequency changes in a prescribed manner that can be stated in two ways. Firstly, of all the per-generation gene frequency changes, including those that lead to the same genetic distance $[\sigma_w^2/(\bar{W})^2]$ between parent and daughter generation gene frequency values as the natural selection gene frequency changes, the natural selection values maximize the increase in mean fitness irrespective of the presence or absence of dominance in fitness values. Apparently, this is because genetic distance is independent of dominance effects. Secondly, of all the per-generation gene frequency changes, including those that lead to the same

increase in mean fitness of the population ($\Delta \bar{W}$) as the natural selection gene frequency changes, the natural selection values minimize the genetic distance between parent and daughter generation gene frequency values. However, the rate of increase in mean fitness of the population fixed for this optimization would depend on the presence or absence of dominance. The former case, termed *maximum principle*, is therefore more appealing. The optimality principle of Ewens (1992), which is in fact a *minimum principle* requiring the concept of *partial* increase in mean fitness to avoid dominance effects, is thus not necessary. It can very well hold with total increase in mean fitness.

In the description adopted in this paper, I have not invoked the notion of the average effect of gene substitution, which requires use of the least-squares principle. This principle is also some sort of an optimizing principle in that it *minimizes* the dominance deviations in the fitness values of the concerned genotypes. When there are no such deviations because of absence of dominance effects, the least-squares fit is perfect, and Ewens (1989, 1992) interprets it as the case of *partial* increase in mean fitness. For instance, in the one-locus case, if we regress the fitnesses of genotypes on the number of A_1 alleles in the genotypes, the regression sum of squares is found to be $2\sigma_w^2$, which is defined as the additive genetic variance in fitness (σ_A^2)—one of the two components of total variance σ_W^2—in the literature. However, such a partitioning of variation implies choice of the best-fitting regression line by the method of least squares and hence indirectly implies an optimality principle. We may note that the regression coefficient (β) of the genotypic fitnesses on the number of A_1 genes present, interpreted as the average effect of gene substitution, is

$$\beta = p_1(W_{11} - W_{12}) + p_2(W_{21} - W_{22})$$
$$= (W_{12} - W_{22}) - 2p_1 d_{12}$$
$$= (w_1 - w_2),$$

and σ_A^2 is then $2p_1 p_2 \beta^2$.

It can be seen, however, without fitting any regression, that σ_W^2, the total variance in fitness, is the sum of variation in the marginal fitnesses—row-wise and column-wise—plus a remainder term in the two-way ANOVA table. Because of symmetry, row and column contributions are each equal to σ_w^2, so that the remainder sum of squares is

$$\sigma_R^2 = \sigma_W^2 - 2\sigma_w^2$$
$$= 4p_1^2 p_2^2 d_{12}^2.$$

This is exactly the same as the dominance variance in fitness if we adopt the regression approach but in the sense that choice of the best-fitting regression line implies minimizing the variance due to dominance deviations. In this paper, I have not invoked this optimality principle, and have treated simply, on the basis of the arithmetic of ANOVA, the partitioning of σ_W^2 into $2\sigma_w^2$ and σ_R^2, which would hold for any given set of Ws and p_1.

The interpretation on the basis of least squares is, however, necessary for Fisher's theorem in that it requires interpreting additive genetic variance in fitness. This can be done in terms of changes in the genotypic frequencies between parent and daughter generations when the fitnesses of genotypes are expressed in terms of their least-

squares estimates. This is what Ewens (1989) does, and later uses to develop the optimizing principle of natural selection in evolutionary population genetics. Since dominance effects are made zero by the concept of *partial increase* in mean fitness, the treatment can easily be extended to the case of several loci as well as to any arbitrary mating system. As soon as dominance effects are included, the generalization to several loci and the treatment for a non-random mating system can become complex.

Acknowledgements

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