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The distribution of allelic effects under mutation and selection

STEVEN A. FRANK*‡ AND MONTGOMERY SLATKIN†
* *Department of Ecology and Evolutionary Biology, University of California, Irvine, CA 92717, USA*
† *Department of Zoology, University of California, Berkeley, CA 94720, USA*

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Summary

The Price (1970, 1972) equation is applied to the problem of describing the changes in the moments of allelic effects caused by selection, mutation and recombination at loci governing a quantitative genetic character. For comparable assumptions the resulting equations are the same as those obtained by different means by Barton & Turelli (1987; Turelli & Barton, 1989). The Price equation provides a natural framework within which to examine certain kinds of non-additive allelic effects, recombination and assortative mating. The use of the Price equation is illustrated by finding the equilibrium genetic variance under multiplicative dominance and epistasis and under assortative mating at an additive locus. The limitations of the use of recursion equations for the moments of allelic effects are also discussed.

1. Introduction

Population genetic models of quantitative characters have proved to be very difficult to analyze because of the potentially large number of independent variables that influence quantitative traits. In principle, the frequency of each allele at a locus will influence the distribution of all characters affected by that locus. The only hope of making progress in this area is to find mathematical simplifications that will lead to predictions of observable features of character distributions. One class of approximation assumes that only a few moments of the distribution of allelic effects at each locus are of importance. For example, the mean and variance alone may determine evolutionary dynamics. A second class of approximation assumes that at each locus the frequencies of only a few alleles are of importance.

In this paper we will use the Price (1970, 1972) equation to derive recursion equations for moments of allelic effects and use these equations to predict phenotypic variances. Our approach to deriving moment equations provides a simpler alternative to the adaptive landscape approach used by Barton & Turelli (1987; Turelli & Barton, 1989). In the process, we will examine several models of genetic effects on quantitative characters, including simple models of dominance and epistasis. Our method can also be applied to cases of assortative mating and inbreeding, which we illustrate in a diploid model in which phenotypes are determined by the additive effects of alleles.

2. Background

The description of quantitative genetic models in terms of moments of allelic effects at individual loci is derived mainly from Lande's (1975) analysis of mutation–selection balance of a single character and his extension to multiple characters (Lande, 1980). Lande assumed that the distribution of allelic effects at all loci affecting a quantitative character is multivariate normal. He based this assumption on Kimura's (1965) derivation of a normal distribution of allelic effects at a single locus. Once the assumption of multivariate normality is made, it is possible to derive recursion equations for the genetic means, variances and covariances under the combined effects of weak selection, mutation, and recombination, thereby allowing the prediction of equilibrium phenotypic means, variances and covariances and the response to stabilizing and directional selection. Turelli (1984) considered a different approximation to the single locus theory than did Kimura (1965) and derived a different distribution of allelic effects, the 'house-of-cards' distribution. Turelli showed that the house-of-cards distribution was more appropriate when selection affecting each locus was much stronger

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‡ Corresponding author.

than mutation, a situation that Turelli argued was more realistic biologically.

Barton & Turelli (1987) introduced a general method for deriving recursion equations for moments of genetic effects at a single locus. They found that the recursion equations for moments of each level depend on higher order moments, so that any subset of the infinite set of equations cannot be solved in general. They then showed that both Lande's (1975) results and Turelli's (1984) results could be obtained from these moment equations by making suitable assumptions about the relationships between the moments. At equilibrium, they obtained Lande's results by assuming that mutation is a relatively stronger force than selection at each locus so that allelic distributions are approximately normal, and then using the well-known moment relations for normal distributions. By contrast, they obtained Turelli's results for the house of cards by assuming that each locus has a common allele and a few rare alleles, and then using a rare-alleles relationship between moments.

3. Moment dynamics with the Price equation

In this section we use the Price (1970, 1972) equation to provide a method for obtaining recursion equations for moments of allelic effects. The simplicity of this method allows us to study important problems such as dominance and epistasis that have been relatively intractable in the past. We will show that we obtain the same recursion equations as Barton & Turelli (1987) for comparable assumptions about selection and the genetic determination of character values.

(i) *The Price equation*

The Price equation itself applies to any type of evolutionary modification. We begin with a derivation of the general form and then show which particular assumptions we use to describe selection and mutation. Many applications of the Price equation that we will not consider have been summarized by Grafen (1985), Wade (1985), Uyenoyama (1988) and Taylor (1988).

One particularly powerful aspect of the Price equation is a flexible approach to defining and grouping together the units that will be analysed. For example, a population may be divided into groups according to allelic types, genotypes, individuals, character values, and so on. We will group together individuals according to common genotype and measure some quantitative character associated with genotype.

Our main goal is to study how some character of a population changes. By definition

$$\Delta\bar{z} = \bar{z}' - \bar{z} = \sum_i p_i' z_i' - \sum_i p_i z_i,$$

where $\bar{z}$ is the population average of a character, i indexes genotypes, p_i is the frequency of the population made up by genotype i, and primes denote values at a later time (see below). We are not limited to character means, since z can be the square or any function of a character value.

Next, define w_i by $p_i' = p_i(w_i/\bar{w})$, which describes the frequency of the ith type (here genotype) after selection as current frequency multiplied by relative fitness, and let $z_i' = z_i + \Delta z_i$, which describes the change in character values during transmission of the ith genotype. Substituting into the above equation yields an exact formula for character change

$$\bar{w}\Delta\bar{z} = \mathrm{Cov}(w_i, z_i) + \mathrm{E}(w_i\,\Delta z_i). \qquad (1)$$

This equation partitions total evolutionary change into the part attributable to selection, the covariance term, and the part attributable to transmission, the expectation term. Here and throughout the paper we subscript random variables within expectation and covariance terms to emphasize the groupings over which the covariances and expectations are taken.

Several authors have used the covariance part of the equation as an elegant description for the evolutionary effect of natural selection (Robertson, 1966, 1968; Li, 1967). A standard quantitative genetic interpretation of the entire equation assumes that the covariance refers only to the additive component of the character, and that the expectation term includes non-additive effects such as dominance and epistasis that are intractable in dynamic equations (cf. Lande & Arnold 1983). Here we will use both the selection and transmission parts to develop exact dynamic equations.

(ii) *Comparison with the Barton–Turelli approach*

Before turning to particular models of mutation and stabilizing selection, we illustrate how the Price equation yields a simple derivation for the dynamic recursions of moments of allelic effects. The cases we have chosen are the recursions for the mean and variance of allelic effects under weak selection, random mating, and no mutation, where phenotypes are determined additively according to allelic effects. These assumptions allow us to compare our equations with those obtained by application of the adaptive landscape method of Barton & Turelli (1987).

We can extend eqn (1) to describe the dynamics of the nth non-central moment of the character z

$$\bar{w}\Delta\overline{z^n} = \mathrm{Cov}(w_i, z_i^n) + \mathrm{E}(w_i\,\Delta z_i^n). \qquad (2)$$

In a haploid model with no mutation the second term on the right side will be zero because an allele's contribution to a character does not change between parent and offspring. We will illustrate the calculation of this transmission term when it is nonzero in several cases below.

We now have this simple equation for moment dynamics: $\bar{w}\Delta\overline{z^n} = \mathrm{Cov}(w_i, z_i^n)$. The next step is describe how fitness is related to character value. We follow a standard assumption that selection is weak, stabilizing, and nor-optimal (Lande, 1975; Turelli, 1984)

$$w_i = \exp(-z_i^2/2V_s) \approx 1 - z_i^2/2V_s, \tag{3}$$

where V_s is the strength of selection, and the optimum is centered on zero. Average fitness is $\bar{w} \approx 1 - \overline{z^2}/2V_s$. Substituting into eqn (2) yields the recursions for character moments

$$\begin{aligned}\Delta\overline{z^n} &\approx \mathrm{E}[(w_i - \bar{w})\, z_i^n]/\bar{w} \\ &\approx (\tfrac{1}{2}V_s)(\overline{z^2}\,\overline{z^n} - \overline{z^{(n+2)}}).\end{aligned} \tag{4}$$

In order to relate this equation to the distribution of allele frequencies we must specify how alleles affect character value. For this haploid model let $z_i = ci$, where c is constant that defines the scale of allelic effects, and alleles range over $i = 0, \pm 1, \pm 2, \ldots$. Substituting into the above equation yields the recursion for the moments of allelic effects

$$\Delta\alpha_n \approx s(\alpha_2\alpha_n - \alpha_{n+2}), \tag{5}$$

where $s = c^2/2V_s$ and $\alpha_n = \mathrm{E}(i^n)$. Defining m_n to be the nth central moment of i, we can use eqn (5) directly to obtain recursions for the mean and variance

$$\Delta m_1 \approx -s(2m_1 m_2 + m_3)$$

$$\Delta m_2 \approx -s[2m_1 m_3 + (m_4 - m_2^2)],$$

which agrees with the recursions obtained from Barton & Turelli (1987). In Appendix 1 we illustrate how our general approach can be used to obtain moment equations for more complicated situations by presenting an equation for the dynamics of linkage disequilibrium in a two-locus problem.

Our approach differs from that of Barton & Turelli (1987; Turelli & Barton, 1989) even though the dynamic equations we derive for the moments are the same in this particular example. Barton and Turelli begin by obtaining a general relationship for the gradient of population mean fitness with respect to the moments of the distribution of the character. They then make specific genetic assumptions that relate genotypes and phenotypes, which lead to recursion equations for the moments of allelic effects, the m_i in both our and Barton and Turelli's notation. These allelic moments depend on the function that relates phenotypic value to fitness. Specifying the fitness function completes the specification of the recursions.

Our approach begins with a basic recursion equation for each phenotypic moment that is the Price equation itself. Specification of the genetic details and the fitness function lead directly to the recursion equations for moments of allelic effects. One advantage of our approach is that we begin with general phenotypic recursions without making any assumptions, whereas Barton and Turelli begin by assuming that selection maximizes population mean fitness in order to derive their basic relation between fitness and phenotypic moments. In order to apply their approach to frequency dependent selection or other cases in which $\bar{w}$ is not maximized, they must first replace the gradient of $\bar{w}$ with the gradient of a frequency dependent fitness surface.

4. One locus and one character

In this section we show how to apply the Price equation to the study of mutation–selection balance. In the first example we rederive known results for a haploid model in order to illustrate our method. In the second example we derive general results for a diploid model with additive allelic effects under inbreeding or assortative mating, including a new result for character variance in a single locus model. In the third we derive a new result for a non-additive diploid model.

We use the Price equation in each case to derive an equation that relates the moments of the distribution of allelic effects at equilibrium. This moment equation is then used to derive the expected phenotypic and genetic variance at equilibrium by using approximations for the relation among moments. These approximations depend on either assuming that selection is relatively strong or weak compared with mutation. We also discuss past work on gene frequency analyses when the relative strengths of mutation and selection fall between these two extremes.

In all models selection will be as described in eqn (3) and phenotypes z will depend on some function of allelic states, where alleles are indexed as $i, j, k, l = 0, \pm 1, \pm 2, \ldots$. Mutation is assumed to be stepwise, with the state of an allele equally likely to increase or decrease by one after a mutation. The mutation rate per allele is μ. This model of mutation is the same as that used by Slatkin (1987).

(i) *Haploid model*

Let i be the allelic state of a haploid genotype, and let the character value for this genotype be $z_i = ci$. When the population is at equilibrium the mean and higher moments of the character do not change over time. Using eqn (2) at equilibrium we can write

$$\mathrm{Cov}(w_i, z_i^n) = -\mathrm{E}(w_i\,\Delta z_i^n) \tag{6}$$

for any moment $\overline{z^n}$. For $n = 2$ this is

$$\mathrm{E}[(w_i - \bar{w})\, z_i^2] = -\mathrm{E}(w_i\,\Delta z_i^2). \tag{7}$$

The term Δz_i^2 in a haploid model is the change in the square of the character between offspring and parent. Thus the left side of eqn (7) is the rate at which selection removes phenotypic variance from the population, whereas the right side is the rate at which mutation adds variance by introducing a lack of fidelity in transmission of the character from parent to offspring. The value of Δz_i^2 can be calculated from the above assumptions about the mutation process

$$\begin{aligned}\Delta z_i^2 &= z_i'^2 - z_i^2 \\ &= c^2\mu\{(\tfrac{1}{2})[(i-1)^2+(i+1)^2]\}+c^2(1-\mu)\,i^2-c^2i^2 \\ &= c^2\mu. \qquad (8)\end{aligned}$$

From eqns (3), (5), (7), (8) and $z_i = ci$ an equilibrium equation relating the moments of allelic effects is

$$s(\alpha_2^2-\alpha_4)+\mu \approx 0, \qquad (9)$$

where α_n is the nth noncentral moment of allelic effects.

Suppose that selection is much stronger than mutation, $s \gg \mu$. Then the zero allele will be common, the ±1 alleles will be rare, and we can ignore all other alleles, yielding the three-allele house-of-cards approximation (Turelli, 1984). With these assumptions $\bar{w} \approx 1$ and $\alpha_4 \approx \alpha_2$, and since the character mean is zero, the character and allelic-effect variances are simply the second moment. From eqn (9) the second moment of allelic effects is $\alpha_2 \approx \mu/s$ and character variance is $\overline{z^2} = c^2\alpha_2 = 2\mu V_s$, as found by Turelli (1984).

When mutation is much stronger than selection, $\mu \gg s$, the distribution of alleles is approximately normal (Kimura, 1965). The moments are then related by $\alpha_4 \approx 3\alpha_2^2$. Mean fitness $\bar{w}$ is approximately $1-s\alpha_2$. Substituting into eqn (9) and solving as above yields an equilibrium character variance of approximately $c^2\surd(\mu/2s)$, in agreement with Kimura (1965) and Lande (1975).

When selection and mutation are of approximately the same order of magnitude, neither of the previous two approximations for the fourth moment in eqn (9) works well. The reason is that the relationship between the lower order and higher order moments cannot be easily predicted. To illustrate this point, consider Slatkin's (1987) five-allele model. Slatkin showed that, at equilibrium, an adequate approximation to the variance maintained in an additive model under intermediate levels of selection can be obtained by keeping track of two classes of alleles, those one step removed from the optimal class and those two steps removed. If selection and mutation are symmetric, only two allele frequencies, p_1 and p_2, are needed. Those frequencies can be found as solutions to a pair of simple algebraic equations. In the symmetric five-allele model, $m_2 = c^2(p_1+4p_2)$ and $m_4 = c^4(p_1+16p_2)$. It is easy to see that the relationship between m_2 and m_4 depends on p_2, and hence that relationship cannot be predicted without knowledge of p_2.

In general, recursion equations for the moments of allelic effects do not form a closed system unless it is possible to express higher order moments as simple function of lower order moments. The normal and house-of-cards approximations provide two ways to close the system of equations. It is not at all clear that recusion equations for the moments will be useful in other cases because, as we have illustrated, it may not be possible to close the system of equations in general. If that is so, then it will be necessary either to model changes in allele frequencies directly or to devise some other set of variables that will lead to tractable equations. This conclusion is a bit discouraging because it is the difficulty in analysing allele frequencies in general that motivated the use of recusion equations for the moments.

(ii) *Diploid model with additive phenotype and assortative mating*

For diploidy we can write the Price equation, eqn (1), for the nth moment as

$$\bar{w}\,\Delta\overline{z^n} = \mathrm{Cov}\,(w_{ij}, z_{ij}^n)+\mathrm{E}(w_{ij}\,\Delta z_{ij}^n), \qquad (10)$$

where groups are now defined by genotype ij. Following the argument for the haploid case, we can use diploid analogues of eqns (6), (7), indexing terms by ij instead of just i. Here we assume that alleles have additive effects on phenotype:

$$z_{ij} = c(i+j) \quad \text{and} \quad w_{ij} \approx 1-z_{ij}^2/2V_s = 1-s(i+j)^2.$$

For changes in the second moment of allelic effects, $n = 2$, at equilibrium the effects of selection among parents described by the covariance term can be obtained directly from eqn (4), yielding

$$\begin{aligned}\mathrm{Cov}\,(w_{ij}, z_{ij}^2) = 2sc^2[2\alpha_2^2+4\alpha_{11}\,\alpha_2+2\alpha_{11}^2-\alpha_4 \\ -4\alpha_{31}-3\alpha_{22}],\end{aligned}$$

where $\alpha_{nm} = \mathrm{E}(i^n j^m)$. Note that α_{11} is the covariance of allelic effects within an individual and describes departures from random mating. Under random mating $\alpha_{nm} = \alpha_n\,\alpha_m$.

Next we must establish the effects of transmission on the relationship between offspring and parent phenotype described by the expectation term. Following the haploid case, eqn (8), we need an expression for $\Delta z_{ij}^2 = z_{ij}'^2-z_{ij}^2$, where z_{ij}' is the phenotype of offspring produced by a parent with genotype ij. We can derive the change in offspring phenotype relative to a parent as

$$\begin{aligned}z_{ij}'^2-z_{ij}^2 = c^2\{(1-\mu)\,(\tfrac{1}{2})\,&[(i+\gamma)^2+(j+\gamma)^2] \\ +\mu(\tfrac{1}{4})\,&[(i-1+\gamma)^2+(i+1+\gamma)^2 \\ +&(j-1+\gamma)^2+(j+1+\gamma)^2]\}-c^2(i+j)^2 \\ = c^2[\mu+\gamma^2-(\tfrac{1}{2})&\,(i^2+j^2)+(i\gamma+\gamma j)-2ij], \qquad (11)\end{aligned}$$

where γ is the gamete obtained from the parent's mate. The expectation term describing the effects of transmission can now be written as

$$\begin{aligned}\mathrm{E}(w_{ij}\,\Delta z_{ij}^2) = c^2\{\mu-s[2\alpha_2^2-\alpha_4-5\alpha_{22} \\ +2\alpha_2\,\alpha_{11}-4\alpha_{31}+6\alpha_{211}]\},\end{aligned}$$

where $\alpha_{211} = \mathrm{E}(i^2 j\gamma)$. Combining the covariance and expectation terms the moment equation at equilibrium is

$$0 \approx \mu+s[2\alpha_2^2-\alpha_4-\alpha_{22}-4\alpha_{31}+4\alpha_{11}^2+6\alpha_2\,\alpha_{11}-6\alpha_{211}]. \qquad (12)$$

Under random mating this reduces to $s\,(\alpha_2^2-\alpha_4)+\mu$

≈ 0, which is identical with the haploid case. The distribution of allelic effects is therefore the same for haploid and diploid models with additive gene action and random mating, with character variance being twice as great in the diploid model.

When there is inbreeding or assortative mating, the moments of cross-product terms cannot be simplified to the cross product of the moments as above. For either $\mu \gg s$ and $s \gg \mu$ certain moment simplifications can be applied to eqn (12), but no expression is available for α_{211}. We can obtain an independent equation that relates this three-dimensional cross product to the other moments by treating $y = ij$ as a character with fitness w_{ij} and applying the Price equation at equilibrium. The covariance and expectation terms describing the effects of selection and transmission in the Price equation are

$$\mathrm{Cov}\,(w_{ij}, y) = 2s[\alpha_{11}(\alpha_2+\alpha_{11})-(\alpha_{31}+\alpha_{22})]$$

$$\mathrm{E}(w_{ij}\,\Delta y) = s(\alpha_{31}+2\alpha_{22}-3\alpha_{211}).$$

Combining these terms yields $\alpha_{211} \approx (2\alpha_2\alpha_{11} + 2\alpha_{11}^2 - \alpha_{31})/3$.

When selection is a relatively stronger force than mutation, we can use the house-of-cards moment relations $\alpha_{31} \approx \alpha_{11}$ and $\alpha_{22} \approx |\alpha_{11}|$ in eqn (12) to obtain the variance in allelic effects, α_2, and the character variance, $\overline{z^2}$,

$$\alpha_2 \approx \left(\frac{1}{1+2f+|f|}\right)\frac{\mu}{s}$$

$$\overline{z^2} \approx 2c^2(1+f)\alpha_2 = \left(\frac{1+f}{1+2f+|f|}\right)V_0,$$

where V_0 is the character variance expected with no inbreeding, and $f = \alpha_{11}/\alpha_2$ is the correlation of allelic effects in uniting gametes and measures inbreeding. Assortative mating can be described by $2f/(1+f)$, which is the phenotypic correlation between mates. For $f > 0$, this house-of-cards model agrees with the result obtained by a different method (Turelli, 1986). As pointed out by Turelli, strong inbreeding can decrease the character variance by one-half. With negative assortative mating, $f < 0$, the variance in allelic effects increases, whereas the phenotypic variance is unchanged. The house-of-cards assumptions are invalid when there is strong negative assortative mating.

When mutation is a relatively stronger force than selection, the distribution of allelic effects is approximately gaussian and the moment relations in Kendall & Stuart (1977, p. 85) can be used in eqn (12), yielding

$$\alpha_2 \approx \frac{1}{1+f}\sqrt{\frac{\mu}{2s}}$$

$$\overline{z^2} \approx 2c^2(1+f)\,\alpha_2 = V_0,$$

where V_0 is the character variance when there is no inbreeding. This analysis shows that the variance in allelic effects may be reduced by half under inbreeding or increased towards infinity by negative assortative mating. Remarkably, character variance is independent of positive or negative assortative mating of any intensity. This occurs because the character value associated with a particular allelic value increases linearly with $1+f$. By contrast, selection intensity increases with the square of the character value and thus with $(1+f)^2$. Since character variance is inversely related to the square root of selection intensity, the effects of assortative mating and selection on character variance cancel.

The only previous work under similar assumptions is Lande's (1977, 1984). He studied a polygenic model of mutation-selection-recombination balance under inbreeding. He showed that when a trait is controlled by many freely recombining loci, the correlation in breeding values between parents typically remains close to the single-locus inbreeding coefficient f. This occurs because linkage disequilibrium rarely becomes strong among loci under his assumptions about the magnitudes of mutation and selection. Therefore, for sufficiently large numbers of loci, the variance in allelic effects at each locus depends on $1/(1+f)$ as in the single-locus theory above, and the character variance is unaffected by inbreeding (Lande 1977). For assortative mating and a large number of freely recombining loci controlling a character, f will be approximately equal to the correlation in parental breeding values because, once again, linkage disequilibrium will tend to be weak under his assumptions about mutation and selection (Lande, 1977).

(iii) *Diploid model with multiplicative phenotype*

Dynamic equations under nonadditive allelic effects are difficult to handle with standard quantitative genetic approaches. To illustrate how the Price equation applies to nonadditive cases let the phenotypic deviation from zero be the product of the deviations of the allelic effects from the optimum, $z_{ij} = c|ij|$. Recall that alleles range over $0, \pm 1, \pm 2, \ldots$. With this specification of z_{ij}, the zero allele is dominant and favoured by selection, and the other alleles are deleterious recessives, those with higher values having lower penetrance and increasingly deleterious effects.

To analyse this model, we note that the distribution of allelic effects depends only on the fitnesses associated with phenotypes and not on the phenotypic values. Then using the symmetry of the nor-optimal selection scheme, we can derive phenotypic fitnesses and the distribution of allelic effects by assuming an alternative phenotype $y_{ij} = cij$, and then translating from the distribution of allelic effects back into correct moments for the distribution of z. Note that selection is stabilizing on the y scale but directional on the z scale. Mutation-selection balance is therefore expected to cause a deviation from the optimum on the z scale but not the y scale.

The value for Δy_{ij}^2 can be obtained by the process outlined in eqn (11), with allelic effects multiplying rather than adding to determine phenotype.

Applying this recipe to obtain $\mathrm{E}(w_{ij}\Delta y_{ij}^2)$ yields $c^2(\mu\alpha_2 - s(\alpha_{422} - \alpha_{44}))$. The covariance term is obtained as in the additive case yielding $c^2 s(\alpha_{22}^2 - \alpha_{44})$. Substituting into a diploid analogue of eqn (7) yields

$$\mu\alpha_2 + s(\alpha_{22}^2 - \alpha_{422}) \approx 0. \tag{13}$$

Under random mating this reduces to $\mu + s(\alpha_2^3 - \alpha_4\alpha_2) \approx 0$.

When $s \gg \mu$ then only alleles 0 and ± 1 are at appreciable frequency, so $\alpha_4 \approx \alpha_2$. Solving eqn (13) under random mating yields $\alpha_2 \approx \surd(\mu/s)$. The average of the phenotypic distribution is

$$\bar{z} = \mathrm{E}(c|ij|) \approx c\alpha_2^2 = c\mu/s.$$

The second moment is

$$\overline{z^2} = \mathrm{E}(c^2|ij|^2) = c^2\alpha_2^2 \approx c^2\mu/s.$$

Thus character variance is

$$\mathrm{Var}(z) \approx c^2\mu/s(1-\mu/s) \approx c^2\mu/s.$$

Compared with the additive case, the allelic variance under this scheme of dominance is much larger but the character variance is approximately the same. Correspondingly, most of the genetic variance is dominance variance in the form of recessive alleles of low penetrance. This is an interesting example of how non-additive variance can be maintained.

When $s \ll \mu$ then $\alpha_4 \approx 3\alpha_2^2$, and solving under random mating yields $\alpha_2 \approx (\mu/2s)^{\frac{1}{3}}$. The average character value is $\mathrm{E}(c|ij|) = 2c\alpha_2/\pi$, since the mean absolute value of a $N(0, \sigma^2)$ variable is $\surd(2\sigma^2/\pi)$. The deviation from the optimum phenotype is considerable in this case. The second moment is $\overline{z^2} = \mathrm{E}(c^2|ij|^2) = c^2\alpha_2^2$. The character variance is thus $\mathrm{Var}(z) = c^2\alpha_2^2(1-4/\pi^2)$.

5. Two loci with epistatic effects on one character

In this section we present an example of epistatic interactions between two diploid loci. Let allelic effects be multiplicative within and between loci, $z_{ijkl} = cijkl$. In effect, the four alleles jointly determine phenotype, with the zero allele favored by selection and dominant to all other allelic states. The other alleles can be viewed as deleterious recessives, those with higher values having lower penetrance and increasingly deleterious effects. Following our usual procedure under random mating and the assumption of approximate linkage equilibrium we obtain

$$s(\alpha_2^5 - \alpha_2\alpha_4^2) + \mu \approx 0. \tag{14}$$

When $\mu \ll s$, the gametic variance $\mathrm{E}(i^2) = \alpha_2 \approx \alpha_4$, as above. Substitution yields $\alpha_2 \approx (\mu/s)^{(\frac{1}{3})}$. Character variance is $\overline{z^2} \approx c^2\alpha_2^4 = c^2(\mu/s)^{(\frac{4}{3})}$. When $\mu \gg s$, the fourth and second gametic moments are related by $\alpha_4 \approx 3\alpha_2^2$. Substitution yields the character variance $\overline{z^2} \approx c^2(\mu/2s)^{(\frac{4}{5})}$.

6. Discussion and conclusions

We have shown how to derive recursion equations for the moments of allelic effects in a quantitative character subject to mutation, stabilizing selection and recombination using the Price (1970, 1972) equation. The Price equation partitions the change in a character into the change caused by selection among parents and the change in transmission from parent to offspring. The selection term has been used previously in quantitative genetics (Robertson, 1966; Lande & Arnold, 1983) but the transmission term has not. We show that the transmission term can be used to describe mutation, recombination, and non-additive interactions such as dominance and epistasis. The Price equation also provides a simple way to incorporate the effects of assortative mating.

For comparable assumptions the recursion equations we derive for the moments of allelic effects at individual loci are the same as those derived by Barton & Turelli (1987; Turelli & Barton, 1989) using a different method. Our method has the advantage of being relatively simple and of being easily related to other models of selection, especially models of kin and group selection to which the Price equation has been extensively applied. In addition, the Price equation applies naturally to traits under frequency dependent selection (Frank, 1987) or other situations in which population mean fitness is not maximized. Barton and Turelli's approach requires that, in their calculations, the surface of population mean fitness must be replaced by a fitness surface that depends on genotypic frequencies.

Although one can derive recursion equations for the moments of allelic effects, using either our or Barton and Turelli's method, the resulting equations are limited in their utility to those cases in which there is a simple relationship between lower and higher order moments. At present, only the house-of-cards and normal approximations lead to a closed system of equations that can be further analyzed. It appears that different methods will have to be applied to cases in which one of these two approximations cannot be used. We agree with Turelli (1988) that recursion equations for the moments of allelic effects therefore should not be regarded as having provided a complete understanding of the dynamics of quantitative characters. New approaches and methods will be needed.

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Appendix

Here we briefly introduce some of the necessary recursions for addressing linkage disequilibrium. Consider a two-locus haploid model with allele i at the first locus and j at the second. To add the process of recombination at rate r in this haploid model, let an individual of genotype ij have offspring ij with probability $1-r$, and offspring of genotype $i\beta$ and ξj each with probability $r/2$, where ξ and β are alleles obtained from a randomly chosen mate. Let the expected product of the m and n powers of allelic effects within an individual be $d_{nm} = \mathrm{E}(i^n j^m)$. Linkage disequilibrium can be described by the covariance between alleles at the two loci, which is $d_{11}-d_{10}d_{01}$. We have derived a general recursion expression for the change in these two dimensional moments without any assumptions about initial distributions or symmetry between the loci, defining these moment changes as $\Delta d_{nm} = d'_{nm}-d_{nm}$, where primes denote values in the next time step, and characters are determined by $z = c(i+j)$. We outline the derivation for $n = m = 1$.

The derivation of the covariance term for any values of n and m under the nor-optimal selection scheme in eqn (3) is

$$\begin{aligned}\mathrm{Cov}(w_{ij}, i^n j^m) &= \mathrm{E}[(w_{ij}-\bar{w})\, i^n j^m] \\ &= sd_{nm}\,\mathrm{E}[(i+j)^2]-s\mathrm{E}[i^n j^m(i+j)^2] \\ &= sd_{nm}(d_{20}+2d_{11}+d_{02}) \\ &\quad -s(d_{n+2,\,m}+2d_{n+1,\,m+1}+d_{n,\,m+2}).\end{aligned}$$

The derivation of the expectation term for any values of n and m begins with

$$\begin{aligned}\Delta i^n j^m = {} & (1-\mu)[(1-r)(i^n j^m)+(r/2)[i^n \beta^m+\xi^n j^m]] \\ & +\mu[(1-r)[i^n j^m+M(i^n j^m)] \\ & +(r/2)[i^n \beta^m+\beta^m M(i^n)+\xi^n j^m+\xi^n M(j^m)]] \\ & -i^n j^m,\end{aligned}$$

where $M(x)$ is the change in x between parent and offspring caused by mutation. The expectation term for $n = m = 1$ is relatively easy since mutation does not affect transmission for these moments:

$$\begin{aligned}\mathrm{E}(w_{ij}\,\Delta ij) &= \mathrm{E}[(1-s(i+j)^2)\Delta ij \\ &= -rd_{11}+(r/2)(d_{10}d'_{01}+d'_{10}d_{01}) \\ &\quad +rs(d_{31}+2d_{22}+d_{13})-(r/2) \\ &\quad \times[d'_{01}(d_{30}+2d_{21}+d_{12}) \\ &\quad +d'_{10}(d_{03}+2d_{12}+d_{21})].\end{aligned}$$

The overall change $\bar{w}\,\Delta d_{11}$ is obtained by adding the covariance term and the expectation term.

Equations can be similarly derived for d'_{01} and d'_{10}, which together allow for explicit recursions for the components of linkage disequilibrium and the change of allelic distributions at each locus. To solve these equations some further assumptions are needed about the relationship of lower and higher order moments, such as selection being much stronger than mutation so that $d_{13} \approx d_{11}$. For example, under the house-of-cards assumption, the equilibrium linkage disequilibrium can be obtained from the three equations for Δd_{11}, Δd_{22}, and Δd_{20}.

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