Developments of the Price equation and natural selection under uncertainty

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Many approaches to the study of adaptation, following Darwin, centre on the number of offspring of individuals. Population genetics theory makes clear that predicting gene frequency changes requires more detailed knowledge, for example of linkage and linkage disequilibrium and mating systems. Because gene frequency changes underly adaptation, this can lead to a suspicion that approaches ignoring these sophistications are approximate or tentative or wrong. Stochastic environments and sexual selection are two topics in which there are widespread views that focusing on number of offspring of individuals is not enough, and that proper treatments require the introduction of further details, namely variability in offspring number and linkage disequilibrium, respectively. However, the bulk of empirical research on adaptation and a great deal of theoretical work continue to employ these approaches. Here, a new theoretical development arising from the Price equation provides a formal justification in very general circumstances for focusing on the arithmetic average of the relative number of offspring of individuals.

Keywords: Price equation; bet-hedging; stochastic environments; natural selection; maximization; reproductive value

1. INTRODUCTION

Grafen (1999) proposed a project to unify a wide class of optimization approaches used in biology that centre on individual reproductive success, following Darwin (1859). Here, this project is pursued by developing the Price equation, first in a minor way by expressing it in terms of relative reproductive success in § 2, then extending it to cover uncertainty in § 3, and finally exhibiting multi-generational forms in § 4. These forms are identities linking the arithmetic average of relative offspring number to gene frequency changes over arbitrary numbers of generations, and their significance is discussed in § 5. A simple model with stochastic environments is shown in § 6, to show how arithmetic averages apply in that case.

2. PRICE AND RELATIVE REPRODUCTIVE SUCCESS

The selection mathematics of Price (1970, 1972) provides identities, that is, equations that are true by definition, about the operation of selective processes. It begins by indexing each individual in a parental population by $i \in I$. We denote the 'p-score' (Grafen 1985) of an individual by p_i. A p-score is a weighted sum of arbitrary allelic values, and interpretations will be discussed shortly. The number of successful gametes of an individual, per haploid set, is indicated by w_i, and the difference between the average p-score of the successful gametes and the parent's p-score is Δp_i. A successful gamete is one that contributes to an organism in the next generation and whose genes will therefore be counted in the gene frequencies of the next generation. Averages over the individuals in a population are notated by dropping the subscript, thus p is the average p-score in the population and w is the average number of successful gametes. In both of these averages, as in all future averages, individuals are weighted by their ploidy (see Grafen (1985) for

details). The fundamental equation of Price (1970, 1972) (which was foreshadowed by the 'secondary theorem of natural selection' of Robertson (1966, 1968)) is

$$w\Delta p = C_i[p_i,w_i] + E_i[w_i\Delta p_i], \tag{1}$$

where E_i and C_i are the expectation and covariance across individuals in the population. E_i can be regarded as a population average. It can equivalently be regarded as an expectation with regard to the random drawing of an individual from the population (with relative chances weighted by ploidies). Formal results on expectation operators are more directly applied using the second interpretation.

Because w does not depend on i, and expectations and covariances are linear, we can let $v_i = w_i/w$ and rewrite the Price equation as

$$\Delta p = C_i[p_i,v_i] + E_i[v_i\Delta p_i]. \tag{2}$$

Hence, the change in the mean p-score is equal to the sum of two terms. The first is the covariance over individuals between p-score and number of successful gametes relative to the population average. The second is a measure of the extent to which segregation deviates from the Mendelian expectation of fairness. When the deviation is systematic, this term can represent meiotic drive; when it results only from sampling error, this term represents the effects of drift. The equation is an identity and so holds exactly.

The term v_i is a property of an individual, and can fairly be called the 'target of selection'. Note that by definition v, the average of v_i, is $E_i[w_i/w] = 1$. The Price identity holds for all p-scores. The frequency of an allele is a p-score in which that allele has a weight of unity, and all others have a weight of zero. Thus any allele whose presence in individuals is positively correlated with v_i will increase in frequency. The additive genetic value of a trait is also a p-score (Falconer 1981) whatever the genetic architecture of the trait. The additive genetic component

of a character will therefore increase or decrease according to whether it is positively or negatively correlated with v_i. This makes v_i a good candidate for an initial measure of 'biological fitness' or 'reproductive value'.

The role of individual fitness can be brought out in a different way in the following reformulation:

$$\Delta p = C_i[p_i, v_i] + E_i[v_i \Delta p_i] = E_i[p_i(v_i - v)] + E_i[v_i \Delta p_i].$$
(3)

Thus the systematic part of the change in p-score equals the expected product of the p-score with the 'reproductive success discrepancy', that is, the difference between the reproductive success of an individual and the average reproductive success in the population.

3. PRICE AND UNCERTAINTY

We now elaborate the covariance identity (2) to cover stochastic effects and succeeding generations. This will provide a generalization of the Price covariance identity. It will also be revealing to substitute using equation (3) at that stage.

Therefore, let there be different states of nature $\omega \in \Omega$, with a probability distribution defined over them. We denote the expectation with regard to the states of nature as E_ω. Denote the number of successful gametes per haploid set of individual i in state of nature ω as $w_{i(\omega)}$. Then the Price equation holds in each state of nature, but now the average p-score in the offspring generation may depend on ω, so we write $\Delta p_{(\omega)}$ as the change in mean p-score. We also write the average of $w_{i(\omega)}$ as $w_{(\omega)}$, and the relative values of $w_{i(\omega)}$ as $v_{i(\omega)} = w_{i(\omega)}/w_{(\omega)}$. Hence in state of nature ω,

$$\Delta p_\omega = C_i[p_i, v_{i(\omega)}] + E_i[v_{i(\omega)} \Delta p_{i(\omega)}].$$

The expected change over states of nature is $E_\omega[\Delta p_\omega]$.

We now make assumptions to ensure that the second term in this equation becomes zero once expectations are taken with respect to states of nature. It is worthwhile to elaborate the argument formally in view of the abstract and general nature of the results. We suppose the state of nature ω can be rewritten as $\omega = (\sigma, \tau)$, where σ represents all the uncertain events except those associated with the segregation of alleles at meiosis, in a form that denotes successful alleles as ik for the kth successful allele of individual i. τ contains information only about segregation at meiosis, and states, conditional on σ, for each successful allele ik what alleles it obtained at meiosis. The assumptions must both hold conditional on σ, and are that meiosis is fair and there is no selection on gametic genotypes. Fairness ensures that, averaging over τ, the population of all gametes of an individual is representative of that individual's genome. Absence of gametic selection ensures that the population of successful gametes is similarly representative. Representativeness means that the p-score of the successful gametes, averaged over τ, equals the p-score of the adult. With these assumptions, we can write $v_{i(\sigma)}$ instead of $v_{i(\omega)}$, and, bearing in mind that the term is conditional on σ, $\Delta p_{i(\tau)}$ instead of $\Delta p_{i(\omega)}$. Then the assumptions can be formally represented as $E_\tau[\Delta p_{i(\tau)}] = 0$ for each i, for all σ.

We now apply for the first time, and will use again directly, a standard result (see, for example, Weir 1973) that allows the order of expectation operators to be exchanged when the random variable takes non-negative values, and by extension when the random variable is bounded. With the notations just established, and exchanging E_τ and E_i at the crucial point, we obtain

$$E_\omega[E_i[v_{i(\omega)} \Delta p_{i(\omega)}]]$$
$$= E_\sigma E_\tau[E_i[v_{i(\sigma)} \Delta p_{i(\tau)}]]$$
$$= E_\sigma[E_i[v_{i(\sigma)} E_\tau[\Delta p_{i(\tau)}]]] = 0.$$

The simple forms obtained justify proceeding on the basis of these assumptions which, though not universally made, are widely useful.

We now return to the main development and apply these assumptions to the expectation over ω of equation (3). Exchanging expectation operators as above, we derive

$$E_\omega[\Delta p_\omega] = E_\omega C_i[p_i, v_{i(\omega)}] = C_i[p_i, E_\omega[v_{i(\omega)}]]$$
$$E_\omega[\Delta p_\omega] = E_\omega E_i[p_i(v_{i(\omega)} - v_{(\omega)})] = E_i[p_i E_\omega[v_{i(\omega)} - v_{(\omega)}]].$$
(4)

The form (4) shows that the target of selection is generalized from v_i to $E_\omega[v_{i(\omega)}]$, which becomes the natural measure of reproductive success in the presence of uncertainty. This shows that gene frequencies and additive genetic components of characters alter on average according to whether they correlate positively or negatively with the arithmetic mean over uncertainty of an individual's relative number of successful gametes.

The types of uncertainty that can be represented by the states of nature are very general, and in particular include (i) the randomness of segregation at meiosis; (ii) the randomness of which action is produced in a mixed strategy played by the individual itself; (iii) the randomness of which type of opponent is encountered in a contest or series of contests; and (iv) environmental stochasticity affecting all members of the population. The second and third properties are routinely assumed in biological game theory models, and it is reassuring to have them confirmed so securely and directly in a population genetic setting. The fourth property has been shown, employing more elaborate mathematics, in more detailed models of life histories (McNamara 1995; Sasaki & Ellner 1995; Haccou & Iwasa 1995), but stands in contrast to work on bet-hedging that emphasizes the role of variability in fitness (Seger & Brockmann 1987; Seger & Stubblefield 1996).

4. MULTI-GENERATIONAL FORMS

To extend the identity to succeeding generations it is necessary to distinguish the different generations $t = 0, 1 \ldots$, and let I_t be the set of individuals in generation t, and Ω_t be the set of states of nature in generation t. Clearly, I_t and Ω_t must depend on the state of nature in the previous generation, ω_{t-1}. This dependence will not usually need to be made explicit. It is convenient for this next section to adapt notation, and use $p_{t,i}$ for the p-score of individual $i \in I_t$ in generation t, and p_t for the mean p-score in generation t; and similarly for $w_{t,i}$ and $v_{t,i}$. Formally, $p_{t,i}$ is a random variable depending

on $\omega_0 \in \Omega_0$, $\omega_1 \in \Omega_1 \ldots \omega_{t-1} \in \Omega_{t-1}$. Expectation operators will be denoted $E_{i \in I_t}$ over individuals in generation t and $E_{\omega:t}$ over states of nature in generation t. Again the form of these operators is conditional on ω_{t-1}, and the arguments of the operators should be regarded as conditional on ω_{t-1}. It will also be convenient to define a shorthand notation for compound expectations over a succession of generations as follows:

$$E_{\omega:(t_0 \ldots t_1)} = E_{\omega:t_0} E_{\omega:t_0+1} \cdots E_{\omega:t_1}.$$

The generation-specific Price equation for given states of nature can be given in two forms. Both are conditional on the states of nature up to and including generation $t-1$. The first form holds separately for each $\omega \in \Omega_t$, while in the second expectations have been taken over $\omega \in \Omega_t$.

$$p_{t+1} - p_t = C_{i \in I_t}[p_{t,i}, v_{t,i}] + E_{i \in I_t}[v_{t,i} \Delta p_{t,i}]$$

$$E_{\omega:t}[p_{t+1} - p_t] = C_i[p_{t,i}, E_{\omega:t}[v_{t,i}]]. \tag{5}$$

Adding over t, we obtain the difference for given states of nature, and the expected difference, in mean p-score over T generations as

$$p_T - p_0 = \sum_{t=0}^{T-1} C_{i \in I_t}[p_{t,i}, v_{t,i}] + \sum_{t=0}^{T-1} E_{i \in I_t}[v_{t,i} \Delta p_{t,i}]$$

$$E_{\omega:(0 \ldots T-1)}[p_T - p_0] = \sum_{t=0}^{T-1} E_{\omega:(0 \ldots t-1)}[C_{i \in I_t}[p_{t,i}, E_{\omega:t}[v_{t,i}]]]. \tag{6}$$

Thus the (expected) difference in mean p-score over T generations equals the sum of the (expected) covariances between individual p-scores and the (expected) reproductive success.

Employing the subsitution (3), we obtain the formulations

$$p_T - p_0 = \sum_{t=0}^{T-1} E_{i \in I_t}[p_{t,i}(v_{t,i} - v_t)] + \sum_{t=0}^{T-1} E_{i \in I_t}[v_{t,i} \Delta p_{t,i}]$$

$$E_{\omega:(0 \ldots T-1)}[p_T - p_0] = \sum_{t=0}^{T-1} E_{\omega:(0 \ldots t-1)}[E_{i \in I_t}[p_{t,i} E_{\omega:t}[v_{t,i} - v_t]]]. \tag{7}$$

These equations show a direct relationship between the change in p-score and the individuals' 'reproductive-success discrepancies', that is, the difference between an individual's reproductive success and the average in that generation (which is always unity).

A further development is possible for the special case in which p_i is the frequency of a single allele A, but in which the number of offspring w_i depends not only on the frequency of A, but depends in general on the genotype as a whole. Let G be the set of possible genotypes, which may include multiple loci with arbitrary linkage patterns, and may distinguish between maternally and paternally derived alleles. Let q^g for $g \in G$ be the value of p_i for individuals with genotype g, f_t^g be the frequency of individuals with genotype g, and the mean reproductive success of individuals with genotype g be v_t^g in generation t. As before, the values of everything in generation t are

random variables that depend on the sequence of states of nature up to generation $t-1$. Then it follows that

$$p_T - p_0 = \sum_{t=0}^{T-1} \sum_{g \in G} q^g f_t^g (v_t^g - v_t)$$

$$E_{\omega:(0 \ldots T-1)}[p_T - p_0] = \sum_{t=0}^{T-1} E_{\omega:(0 \ldots t-1)}\left[\sum_{g \in G} q^g f_t^g E_{\omega:t}[v_t^g - v_t]\right]. \tag{8}$$

These equations show that the (expected) change in the frequency of A over T generations equals the (expected) weighted sum of the difference between the (expected) average reproductive success of bearers of the gene minus the average reproductive success of individuals in the same generation. The weights provide that each individual in each generation is weighted according to its own p-score, in this case, the fraction of A at the relevant locus.

Further forms look directly at the summed reproductive successes, as follows:

$$p_T - p_0 = \sum_{t=0}^{T-1} \sum_{g \in G} q^g f_t^g v_t^g - \sum_{t=0}^{T-1} \sum_{g \in G} q^g f_t^g v_t$$

$$E_{\omega:(0 \ldots T-1)}[p_T - p_0] = \sum_{t=0}^{T-1} E_{\omega:(0 \ldots t-1)}\left[\sum_{g \in G} q^g f_t^g E_{\omega:t}[v_t^g]\right]$$

$$- \sum_{t=0}^{T-1} E_{\omega:(0 \ldots t-1)}\left[\sum_{g \in G} q^g f_t^g E_{\omega:t}[v_t]\right]. \tag{9}$$

Here the change in the frequency of A equals a weighted sum of the reproductive successes of the bearers of A minus the same weighted sum of the average reproductive successes in corresponding generations.

5. DISCUSSION OF GENERAL RESULTS

In each pair of results of equations (6)–(9), the first member is an exact equation that relates the change in p-value during T generations to individual reproductive successes. The second equation, on the assumption only of fair meiosis and no gametic selection, relates the expected change in p-value over T generations to the arithmetic average over uncertainty of the reproductive success of individuals. It is important that these equations hold exactly without needing to include terms that relate to the mating system, or linkage, or linkage disequilibrium. Pairs (6) and (7) apply to the frequency of a single allele as well as to arbitrary weighted sums of alleles, and to p-values involving one or many loci that may be linked or unlinked. All the pairs apply to arbitrary and even mixed ploidies, to asexual and sexual or mixed populations. They hold in the presence of genomic imprinting. Nothing has been assumed about frequency dependence or the nature of interactions, so the formulae apply where evolutionary games are being played, and where interactions are between relatives and/or within groups. Additionally, the equations hold for arbitrary forms of uncertainty (subject to the existence of the relevant expectations), and it has not been necessary to state whether the Ω_t (or indeed the I_t) are finite or infinite sets.

What is impressive about Price's 'covariance selection mathematics' is not merely that these cases are all covered, but that they are all covered by a simple single notation that precisely abstracts the essentials of selection and inheritance from the profound variety of other circumstances.

It is important to stress that although the additive genetic value for a trait in one generation is a p-value in which each allele has a certain weight, the set of weights may change from one generaton to the next. So the multi-generational forms applying to a p-value will apply exactly to a character only to the extent that those weights remain fixed over time.

These precise genetic results are therefore close in form to game theory models in which individual 'fitnesses' are modelled and genetic details disregarded. This holds out hope for a formal link with game theory models, but this is beyond the scope of the present paper. Two points may be made now, however. The definition of v_i ensures that, as its average is always unity, the tendency of natural selection to favour p-scores associated with higher values of v_i cannot be confused with what would clearly be a nonsensical tendency to maximize the mean reproductive success. Also, there are reconciliations to be made with population genetics models, which appear to show that selection lacks a maximizing tendency.

There are, of course, some assumptions. We have assumed discrete non-overlapping generations, though this can be finessed by treating the survival of an individual as a special kind of reproduction. We assume discrete events of population-wide reproduction, though we could extend the previous finesse and define the moments t as occurring at each moment at which any individual reproduces. We have more substantively assumed that all the alleles involved in the p-score have the same mode of inheritance. Thus the analysis applies to autosomes in humans, and to the X chromosome in humans and to the Y chromosome in humans; but not to a p-score that combines genes from more than one of these locations. Other substantive assumptions for the 'expectation' forms are that segregation of alleles is fair in a Mendelian sense and that there is no gametic selection, which together set the expectation of the second summand in equation (1) to zero.

It is well recognized that the Price equation is not dynamically sufficient. For example, we need to know the whole array of genotype frequencies f_t^g for all $g \in G$ in equation (8), but can calculate only one gene frequency p_{t+1} for the next generation. Thus the Price approach does not suffice to deduce the outcome of an evolutionary process. The primary role of the Price approach is to provide an interpretation of selective processes, and this it can do using the exact equations shown above. It is unfortunate in this respect that the term 'exact' has been used in population genetics as a synonym for 'dynamically sufficient', presumably reflecting a historical situation in which dynamically insufficient equations led to approximate and therefore potentially erroneous results. The Price equation is exact in the ordinary sense, and the interpretations of selection in terms of individual reproductive successes given in equations (6)–(9) are in no way prejudiced by the dynamic insufficiency of the approach.

The general results obtained so far may seem unsurprising to many biologists, who have assumed that genes spread or not according to the average fitnesses of their bearers. However, one particular area in which geometric means have seemed to represent better the workings of natural selection is that of stochastic environments, to which we now turn.

6. AN EXAMPLE WITH STOCHASTIC ENVIRONMENTS

Here a very simple model will show how the formulations just derived are consistent with the traditional population genetics approach to stochastic environments, but offer a new interpretation.

A haploid population with discrete non-overlapping generations has two alleles at its one locus, and two types of environment. Allele A leaves one offspring in environment I, and no offspring in environment II. Allele B leaves k offspring in both environments. The environment in each generation is I with probability $1 - \pi$, independently in each generation. The simple population genetic analysis calculates the weighted geometric mean for A as $1^{1-\pi}0^\pi$, which equals zero if $\pi > 0$ and unity if $\pi = 0$. For B, we have $k^{1-\pi}k^\pi = k$. Hence A dies out if $\pi > 0$. If $\pi = 0$, then A invades, is neutral, and dies out, according to whether $k < 1$, $k = 1$ or $k > 1$.

To apply equation (5), we need the covariance in generation t. This will depend on the mean p-score in that generation, p_t, as follows

$$\frac{p_t((1-k)(1-p_t) - \pi)}{k(1-p_t) + p_t}. \tag{10}$$

It is a straightforward exercise to calculate the probability distribution of p_t to be $p_0/(p_0 + k^t(1-p_0))$ with probability $(1-\pi)^t$ and otherwise zero. Notice that this calculation does not use the Price equation, and here the dynamic insufficiency comes into view even in an extremely simple case. The sum of the sequence of expected values of expression (10) up to generation t is readily found as

$$\frac{p_0((1-\pi)^{t+1} - p_0 - k^{t+1}(1-p_0))}{p_0 + k^{t+1}(1-p_0)}. \tag{11}$$

The limit as t increases when $\pi > 0$ is simply $-p_0$. The expected sum of the changes in gene frequency therefore equals minus the original gene frequency, and so the expected eventual value of the gene frequency equals zero, indicating extinction. Note that in the case $\pi = 0$, the limit is $1 - p_0$ when $k < 1$, corresponding to the spread of A, but tends to $-p_0$ again when $k > 1$, and equals zero indicating no change of gene frequency when $k = 1$. Thus the accounting provided by the extended Price equation is precise and correct even when it is not the shortest or most natural modelling tool.

The partial sums of the sequence show how the expected fraction of A changes over the generations. The expected fraction increases initially if $1 - \pi > k$. At later stages the expected change is a mixture of the increasingly likely event that A has already gone extinct and so the covariance is zero, and the event that A has reached an increasingly high frequency in the population, which leads to a negative covariance. The real significance of

the later frequency dependence, in which the frequency of A reduces its own reproductive success, is brought out by this approach.

It is interesting to look at the form of equation (8) in this simple case in which $G = \{A,B\}$, $q^A = 1$, $q^B = 0$, $f_t^A = p_t$ and $f_t^B = 1 - p_t$. v_t^A depends on p_t, and equals $(1 - \pi)/(p_t + k(1 - p_t))$ until a generation of type II occurs, and is zero thereafter, but this substitution would obscure. The formulae become, for exact and expected values, respectively,

$$p_T - p_0 = \sum_{t=0}^{T-1} p_t(v_t^A - 1)$$

$$E_{\omega:(0 \dots T-1)}[p_T - p_0] = \sum_{t=0}^{T-1} E_{\omega:(0 \dots t-1)}[p_t(E_{\omega:t}[v_t^A] - 1)].$$

Even in this simple example in which the geometric mean analysis is the fastest way to work out whether A spreads, the Price formulae are exact and correct and have simple and appealing interpretations of the spread or extinction of A in terms of arithmetic averages of individual reproductive successes. It is noteworthy that, in a parallel analysis of whether B would be invaded by A, the weights for the generations would be different, depending on the frequency of B not A. Thus the same sequence of partial sums (11) can be interpreted as a sum of covariances, a sum of reproductive success differences for A weighted by the frequency of A, and a sum of reproductive success differences for B weighted by the frequency of B.

7. CONCLUSIONS

This paper presents a simple and very general demonstration that, on the understanding that reproductive success is measured relative to the population average, natural selection acts on the arithmetic average of reproductive success. It also shows that this principle continues to hold when the calculation of expected relative reproductive success becomes complex. These results bode well for the use of the Price equation to derive appropriate notions of reproductive value in more sophisticated and inclusive models, for the construction of formal links between population genetics and optimizing methodologies, and for capturing in formal terms the biologically commonsense notion of an individual's Darwinian fitness.

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