

Fundamental Theorems of Evolution

David C. Queller*

Department of Biology, Washington University in St. Louis, St. Louis, Missouri

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ABSTRACT: Evolutionary biology is undergirded by an extensive and impressive set of mathematical models. Yet only one result, Fisher's theorem about selection and fitness, is generally accorded the status of a fundamental theorem. I argue that although its fundamental status is justified by its simplicity and scope, there are additional results that seem similarly fundamental. I suggest that the most fundamental theorem of evolution is the Price equation, both because of its simplicity and broad scope and because it can be used to derive four other familiar results that are similarly fundamental: Fisher's average-excess equation, Robertson's secondary theorem of natural selection, the breeder's equation, and Fisher's fundamental theorem. These derivations clarify both the relationships behind these results and their assumptions. Slightly less fundamental results include those for multivariate evolution and social selection. A key feature of fundamental theorems is that they have great simplicity and scope, which are often achieved by sacrificing perfect accuracy. Quantitative genetics has been more productive of fundamental theorems than population genetics, probably because its empirical focus on unknown genotypes freed it from the tyranny of detail and allowed it to focus on general issues.

Keywords: fundamental theorem, evolution, Price equation, breeder's equation, average excess.

Fisher's fundamental theorem of natural selection states that natural selection increases the mean fitness at a rate equal to the additive genetic variance for fitness (Fisher 1930). The name he bestowed on it makes it clear that he viewed it as a very important result, as does his likening it to the second law of thermodynamics. Opinions about it have waxed and waned over the years or, more accurately, waned and waxed, with initially negative views (Kempthorne 1957; Li 1967; Crow and Kimura 1970; Karlin 1975; Nagylaki 1991) being supplanted by more favorable ones (Ewens 1989; Frank and Slatkin 1992; Frank 1997; Lessard 1997; Grafen 2003, 2015a; Plutynski 2006; Okasha 2008; Bijma 2010).

Evolution probably has the most elaborate and beautiful mathematical theories in all of biology. We have thousands

of results justified by mathematical deduction from specified assumptions, which could therefore be thought of as theorems. Which of these should be considered fundamental? Mathematical models, and scientific theories in general, serve multiple and often conflicting roles. Levins (1966) discussed how models have to trade off between generality, realism, and precision. Kuhn (1977) similarly noted that theories face conflicts between accuracy, consistency, scope, simplicity, and fruitfulness. Among these qualities, Fisher's fundamental theorem (Fisher 1930) excels in simplicity and scope. It does not cover all cases exactly (accuracy is what it sometimes sacrifices, and I say more about that below), but it does cover a very wide range of cases in a simple way.

As significant as it is, Fisher's fundamental theorem has been shown to be a special case of even more general theorems (Frank 1997, 2012; Rice 2004; Walsh and Lynch, forthcoming) that are arguably just as fundamental, in the sense of having similar simplicity and scope. This may not be well known among evolutionary biologists, so part of the purpose of this article is to summarize and synthesize this work. The synthesis will include proposals for fundamental-theorem status for several well-known equations, a brief review their domains and relationships to each other, and suggestions for names that reflect those relationships (summarized in fig. 1). Finally, I include some reflections on the nature of fundamental theorems in evolution.

The Fundamental Theorem of Evolution

At the top of the hierarchy of candidates for fundamental theorem status is Price's equation or theorem:

$$\Delta \bar{\phi} = \frac{1}{\bar{w}} (\text{Cov}(w_i, \phi_i) + E(w_i \delta_i)) \quad (1)$$

(Price 1970, 1972a; Grafen 1985; Frank 1997, 2012; Rice 2004; Walsh and Lynch, forthcoming). Though initially derived in a somewhat limited form (Price 1970), it is a general mathematical identity that applies to any trait ϕ of entities i that can be tracked through time, either by following i itself or by tracking from i to its descendants (Price 1972a, 1995; Grafen 1985; Frank 1995, 1997, 2012; Rice 2004; Luque 2017; Walsh and Lynch, forthcoming). Though couched in statistical terms,

* E-mail: queller@wustl.edu.

ORCID: Queller, <http://orcid.org/0000-0002-5464-1984>.

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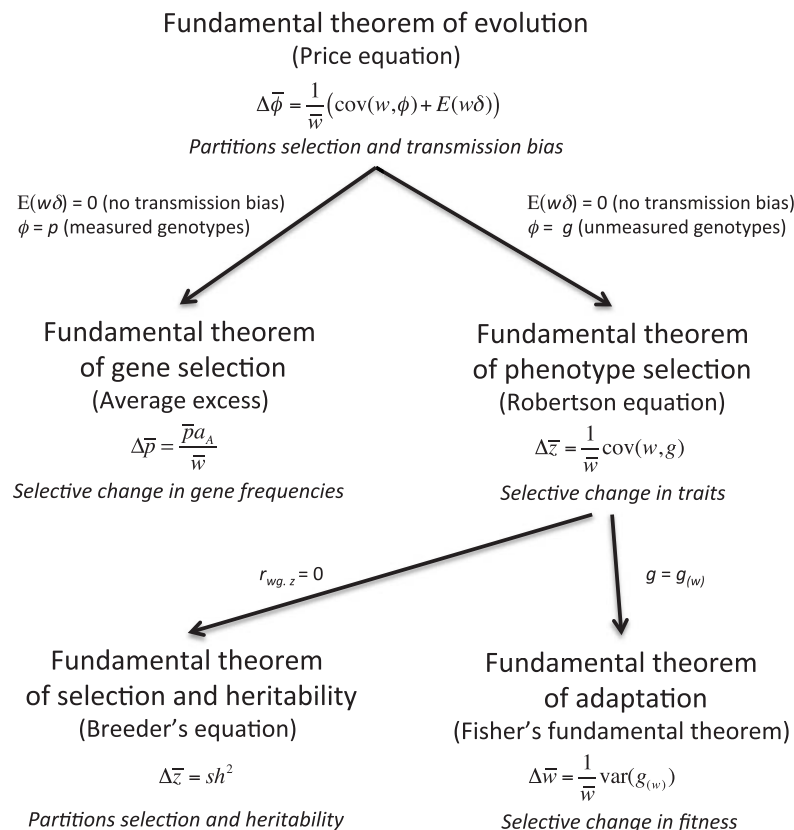


Figure 1: Fundamental theorems and their relationships. Arrows indicate derivation, with required assumptions or domain restrictions written beside them. ϕ = any trait value; δ = the change in ϕ from parent to offspring; w = fitness; p = allele frequency; a_A = average excess; g = breeding value; z = phenotype value; r = partial correlation; s = selection differential, h^2 = heritability. The i subscripts for individuals used in the text are omitted for economy.

the basic Price equation is concerned not primarily with estimation but rather with the population parameters and causal interpretation (Frank 2012).

Both ϕ and i are very flexible. For example, I use ϕ variously to track either gene counts, phenotypic values, or breeding values. I usually take i to index individuals, but the equation can also work for alleles, groups, or classes of various kinds. As w_i stands for fitness, the first term of equation (1) is usually taken as representing change due to selection on ϕ . Technically it also includes drift (Rice 2004), although in most applications this is ignored. Here δ_i is the change in the value of ϕ_i during the time period in question, which could be a change in the individual itself but is more often a change from individual i to its offspring. Thus, the second term is often described as representing biased transmission. In biological terms, this transmission change could be due to a change in environment, regression on the mean, mutation, selection within (rather than between) the parental entities, or any other force not incorporated in the covariance term (Frank 2012).

The Price equation is at the top of the hierarchy for several reasons. First, it requires the fewest assumptions. It is essentially a mathematical identity, given trait measurements ϕ and a mapping from one time to the next of entities possessing those traits (Frank 1997, 2012; Rice 2004; Walsh and Lynch, forthcoming), although extensions may be required to incorporate complexities such as uncertainty (Grafen 2000; Rice 2008), migration (Kerr and Godfrey-Smith 2009), and class structure (Grafen 2015b). Indeed, it is applicable outside of evolutionary biology, for example in ecology (Fox 2006) and epidemiology (Day and Gandon 2006). Second, it is fundamental in a sense that Fisher's theorem is not: all the other equations, including Fisher's theorem, can be easily derived from it with additional assumptions. Third, the Price equation covers not just selection but all forces affecting evolutionary change. As such, it merits being called the fundamental theorem of evolution.

It is not my goal to review the many applications of the Price equation, which has been done better elsewhere (Rice 2004; Luque 2017), but to trace its relations to other funda-

mental selection theorems. The derivations shown below reflect logical relationships but not historical ones—all of the fundamental theorems considered below actually predated the Price equation and were initially derived by other means. The Price equation helps show how to unify them and what their assumptions are (Luque 2017). The other fundamental theorems follow from Price’s equation using three kinds of steps (fig. 1). One is to restrict the domain, considering not the universe of entities covered by ϕ_i but more specific ones, such as allele counts, breeding values, phenotypes, or fitness. Second, they may add assumptions, especially about causes of either fitness or phenotype, often as linear equations substituted into the Price equation (Queller 1992a, 1992b; Frank 1997, 1998). Finally, all of these theorems, in their usual forms, require the assumption that the second term of equation (1) is near 0 or at least that it can usefully be set aside as being of secondary interest. This is the move that allows the simplification that is a hallmark of the fundamental theorem, and I revisit this critical assumption later in the article.

The Fundamental Theorem of Gene Selection

The Price equation’s role as a parent equation to other fundamental results applies to both of the major traditions of evolutionary biology: population genetics and quantitative genetics. When we know, or assume that we know, how genes exert their effects on phenotypes, we have the measured-genotype approach that leads to population-genetic models of gene frequency change; if instead the effects of genes are unknown, then we apply unmeasured-genotype approaches to obtain quantitative-genetic models of phenotype change (Templeton 2006). I begin with a single theorem from the measured-genotype approach.

Besides ignoring the second term of the Price equation, I restrict the domain by letting ϕ equal an allelic score p , scored as $p = 1$ for the allele of interest and $p = 0$ for alternative alleles. Here I make an exception to my usual practice and interpret i as allele copies, not individuals. Therefore, the covariance is taken over all n allele copies in the population, and $\Delta\bar{p} = (1/\bar{w})\text{Cov}(p_i, w_i) = (1/\bar{w}n)\sum_i p_i(w_i - \bar{w}) = (1/\bar{w}n)\sum_{i|p_i=1}^n (w_i - \bar{w})$, where the last step eliminates zero terms and switches to summing only over the n_1 terms where $p_i = 1$. Multiplying and dividing by n_1 yields $(1/\bar{w})(n_1/n) \times (1/n_1)\sum_{i|p_i=1}^n (w_i - \bar{w})$, or

$$\Delta\bar{p} = \frac{\bar{p}a_A}{\bar{w}}, \tag{2}$$

where $\bar{p} = n_1/n$ is the population frequency of the allele and $a_A = (1/n_1)\sum_{i|p_i=1}^n (w_i - \bar{w})$ is Fisher’s average excess for the allele, the extent to which the fitness experienced by copies of this allele differs from the average for all alleles

(Fisher 1930, 1941). See Frank (1997) and Rice (2004) for related treatments. The sign of the average excess is sufficient to tell whether the allele will increase or decrease in frequency and captures the essence of selection in the measured-genotype population-genetic tradition. Templeton (2006) recognized its fundamental status, calling it the “fundamental equation of natural selection for a measured genotype” (p. 408). For brevity and better comparison to the other theorems treated here, I call it the “fundamental theorem of gene selection.”

The Fundamental Theorem of Phenotype Selection

Fisher’s fundamental theorem (Fisher 1930) does not consider selection on alleles; it considers selection on fitness. As fitness can be viewed as a special phenotypic trait, I begin by considering selection on any phenotypic trait, now assuming no knowledge of exactly how the underlying genes specify that trait—the unmeasured-genotype approach.

If we use Price’s equation on phenotypes directly, letting ϕ be a phenotypic value z , then $\Delta\bar{z} = (1/\bar{w})(\text{Cov}(w_i, z_i) + E(w_i\delta_i))$. Here and henceforth, i indexes individuals. The covariance expression is the selection differential, the effect of selection within a generation before reproduction and transmission (Arnold and Wade 1984). It would be foolish and inaccurate to ignore the second term here, because it includes the often-major effect of imperfect heritability or transmission (Walsh and Lynch, forthcoming). Selected parents will tend to have less extreme offspring because their genes are recombined with those of less extreme mates and because environmental effects are not generally inherited.

Fisher developed additional concepts to address this issue, the average effect and the sum of average effects, the breeding value (Fisher 1930, 1941). An individual’s breeding value is that portion of its phenotype that it passes on to its offspring. It can be estimated by studying resemblance among relatives. Given that the Price equation applies to anything that can be measured in parents and offspring, we can simply let ϕ be the breeding value g (Queller 1992b), and the first term of the Price equation becomes

$$\Delta\bar{z} = \Delta\bar{g} = \frac{1}{\bar{w}}\text{Cov}(w_i, g_i), \tag{3}$$

a result that can also be derived more rigorously from an alternative form of the Price equation (Rice 2004). Now that the covariance term uses only the heritable part of phenotype g_i , the expected regression on the mean is moved into the covariance term, and it is now more reasonable to ignore the second term of the Price equation.

Equation (3) is due to Robertson (1966, 1968) and has been called Robertson’s secondary theorem of natural selection (there are actually two related versions of it; Walsh and Lynch, forthcoming). Robertson sometimes receives credit for the Price equation itself, but Robertson’s re-

sults omit the second term and are thus less general. He did, however, anticipate the key first term.

Li (1967) provided population-genetic versions of both Robertson's result and Fisher's fundamental theorem. The great advantage of Robertson's approach is that it is a quantitative-genetic result that can be applied to phenotypes without knowing the underlying genes. As it captures the general effect of selection on phenotypes, I call it the "fundamental theorem of phenotype selection."

Fisher's Fundamental Theorem of Adaptation

Fisher's fundamental theorem is a special case of the fundamental theorem of phenotypic selection; in equation (3), let the phenotype z_i be fitness w_i , so that g_i becomes $g_{(w)i}$, the breeding value for fitness (Frank 1997; Rice 2004). Then write the breeding-value prediction for fitness, $w_i = \alpha + \beta_{w,g_{(w)}} g_{(w)i} + \varepsilon_i$. This is equivalent to the standard quantitative-genetic model $z_i = g_i + e_i$ for fitness, with the regression coefficient equaling 1, but I retain the coefficient for a moment to illustrate a general procedure that will be applied again below. Substitution into equation (3) yields three covariances. Since α is a constant, $\text{Cov}(\alpha, g_{(w)i}) = 0$, and it drops out of this and all subsequent models. The third covariance, $\text{Cov}(\varepsilon_i, g_{(w)i})$ is also 0 in this case (but not always), because a residual is always uncorrelated with a predictor variable. The remaining term is $\text{Cov}(\beta_{w,g_{(w)}} g_{(w)i}, g_{(w)i}) = \beta_{w,g_{(w)}} \text{Cov}(g_{(w)i}, g_{(w)i}) = \text{Var}(w_{(w)i})$, so we are left with

$$\Delta \bar{w} = \frac{1}{\bar{w}} \text{Var}(g_{(w)i}). \quad (4)$$

Fisher's fundamental theorem required no additional assumptions, just the domain restriction of viewing fitness as the phenotype of interest. Because the other fundamental theorems also deal with natural selection, it would be more accurate to call this one the "fundamental theorem of fitness selection" or the "fundamental theorem of adaptation."

The Fundamental Theorem of Selection and Heritability

The breeder's equation (Lush 1937) is also a direct descendant of the phenotypic theorem (3). It can be derived in several ways (Queller 1992b; Rice 2004; Walsh and Lynch, forthcoming); I continue to use the regression method for consistency. Starting with theorem (3), plug in the linear description of fitness from phenotype z_i ($w_i = \alpha + \beta_{w,z_i} z_i + \varepsilon_i$), and simplify to $\Delta \bar{z} = \frac{1}{\bar{w}} \beta_{w,z_i} \text{Cov}(z_i, g_i)$, assuming $\text{Cov}(g_i, \varepsilon_i) = 0$, which we return to in a moment. Now substitute the linear description of phenotype z_i from breeding value ($z_i = \alpha + \beta_{z,g_i} g_i + \varepsilon_i$), where $\beta_{z,g_i} = 1$, and because these residuals are necessarily uncorrelated with g_i , we have $\Delta \bar{z} = \beta_{w,z_i} \text{Var}(g_i) / \bar{w}$. Multiplying and dividing by $\text{Var}(z_i)$ gives the breeder's equation:

$$\Delta \bar{z} = \frac{1}{\bar{w}} \text{Cov}(w_i, z_i) \frac{\text{Var}(g_i)}{\text{Var}(z_i)} = sh^2. \quad (5)$$

This neatly separates selection into the phenotypic selection differential $s = \text{Cov}(w_i, z_i) / \bar{w}$ and the narrow-sense heritability $h^2 = \text{Var}(g_i) / \text{Var}(z_i)$.

With each of the two substitutions of a regression model, we required that $\text{Cov}(g_i, \varepsilon_i) = 0$. In the second case this is necessarily true, because g_i was a predictor in the model, but in the first regression ($w_i = \alpha + \beta_{w,z_i} z_i + \varepsilon_i$) it was not. Here our assumption that $\text{Cov}(g_i, \varepsilon_i) = 0$ is equivalent to assuming that $r_{wg-z} = 0$, or that the relationship between breeding value and fitness is mediated entirely by a linear effect of the phenotype (Queller 1992b; Rice 2004; Morrissey et al. 2010; Walsh and Lynch, forthcoming). This does not mean that z_i fully explains w_i —only that once z_i 's effect is accounted for or removed, g_i has no further relationship with w_i . Queller (1992b) called this assumption the "separation condition," but it is an example of the broad concept of d-separation (for dependence separation) developed for causal modeling (Shibley 2000; Pearl 2009) in a tradition rooted in Wright's path analysis (Wright 1921). Two variables, such as w_i and g_i in the Price equation, are d-separated when conditioning on one or more other variables (our substituted model) makes them independent (zero covariance).

Thus, here we are making a true modeling assumption, and when it is violated the equation can be inexact (Rice 2004; Morrissey et al. 2010; Walsh and Lynch, forthcoming). But the name "breeder's equation" points to its practical use for short-term predictions of response to selection. It is also important in a conceptual sense, for how it shows that the selection response depends on both phenotypic selection and heritability. In the context of the other fundamental theorems, it could be called the "fundamental theorem of selection and heritability."

Additional Fundamental Theorems?

Like Fisher's theorem, the other fundamental theorems are simple and have wide scope. Each highlights a particular core issue of evolution. But where to draw the line is inevitably a judgment call. Of course, there is no absolute need to bestow the term "fundamental" on any theorem, but since Fisher started the practice, it is useful to ask what else might be equally fundamental. I have been conservative by choosing results that are already widely considered to be important and are in some sense at least as general as Fisher's theorem. Here I will mention a few more borderline candidates. These can be more accurate for a broader range of cases than the fundamental theorems discussed above, at some cost in the dimensions of simplicity and scope.

An obvious candidate, which one might call the "fundamental theorem of multivariate selection," is the multivar-

iate result of Lande and Arnold (1983), extending insights from Pearson (1903). As expected, it too emerges easily from the Price equation (Lande and Arnold 1983; Rice 2004). If correlated traits are under selection, then the d-separation assumption that we used for deriving the breeder's equation fails; our focal trait does not fully explain why the genes covary with fitness, and we need a more complex model that can do so.

For single-trait models we have been able to index both individuals and traits by i . Now we must distinguish: each individual i will have j traits measured. Starting from the phenotypic Price equation (3) for the change in trait j , $\Delta \bar{z}_j = \text{Cov}(w_i, g_{ij})/\bar{w}$, we parallel the derivation of the breeder's equation, but with a multiple-regression prediction of i 's fitness from all of its measured traits, $w_i = \alpha + \sum_j \beta_{w_i z_{ij}} z_{ij} + \varepsilon_i$, where the β 's must now be read as partial-regression coefficients that hold all other effects constant. Substituting this into the Price equation for trait $j = 1$, this yields $\Delta \bar{z}_1 = \sum_j \beta_{w_i z_{ij}} \text{Cov}(g_{i1}, z_{ij})$, provided $\text{Cov}(g_{i1}, \varepsilon_i) = 0$, meaning that the more complex regression is now good enough to d-separate g_{i1} and w_i . Now for each phenotype z_{ij} in the covariances, substitute its breeding-value prediction ($z_{ij} = \alpha + \beta_{z_{ij} g_{ij}} g_{ij} + \varepsilon_{ij}$) and, assuming for each equation that $\text{Cov}(g_{i1}, \varepsilon_{ij}) = 0$ (that the genes for trait 1 g_{i1} and any other phenotype z_{ij} are d-separated by the genes for that trait g_{ij}), we have

$$\Delta \bar{z}_1 = \beta_{w_i z_{i1}} \text{Var}(g_{i1}) + \sum_{j \neq 1} \beta_{w_i z_{ij}} \text{Cov}(g_{i1}, g_{ij}), \quad (6)$$

which is Lande and Arnold's (1983) result for trait 1, more often expressed in matrix form for all traits. The focal character is affected not just by direct selection on it but also by selection on other characters $\beta_{w_i z_{ij}}$ when they are genetically correlated ($\text{Cov}(g_{i1}, g_{ij}) \neq 0$). Though less concise than the breeder's equation, it is often far more accurate. For example, even when there is no direct selection on trait 1, the genes underlying the trait will still be under selection if they contribute to other selected traits, and therefore trait 1 will change.

We can also ask how a single party evolves when it is affected by others. Hamilton's inclusive-fitness rule (Hamilton 1964) does this, and it could serve as a fundamental theorem of social evolution. Hamilton's rule was one of the first applications of the Price equation (Hamilton 1970; Seger 1981; Grafen 1985; Wade 1985; Queller 1992a; Marshall 2015). Again, it is needed when the d-separation condition of the breeder's equation fails, because there are additional correlated effects, this time from kin. Now, to our primary index for individuals, i , we need to add a second, k , for kin, to index all individuals affecting its fitness (including itself when $i = k$). Let individual i 's fitness be described by a multiple regression, $w_i = \alpha + \sum_k \beta_{w_i z_k} z_k + \varepsilon_i$ (Queller 1992a; Marshall 2015), and follow steps exactly analogous to those

in the previous paragraph to get $\Delta \bar{z} = \beta_{w_i z_i} \text{Var}(g_i) + \sum_{k \neq i} \beta_{w_i z_k} \text{Cov}(g_i, g_k)$ or, factoring out $\text{Var}(g_i)$,

$$\Delta \bar{z} = \text{Var}(g_i) (\beta_{w_i z_i} + \sum_{k \neq i} \beta_{w_i z_k} \beta_{g_i g_k}), \quad (7)$$

where $\beta_{g_i g_k}$ is a regression relatedness coefficient and the partial regressions on fitness are the direct (due to self) and indirect (due to others) selection gradients, so the part inside parentheses is a direct-fitness version of the inclusive-fitness effect. Note that kin selection is not just Hamilton's inequality; there is a full equation for degree of change (e.g., Gardner et al. 2011). A corresponding version of Fisher's fundamental theorem shows that it is actually inclusive fitness that increases under selection (Bijma 2010). Kin selection is really a special case of correlated selection where the correlated traits are in other individuals. There are also more-general versions for when correlations that arise from factors other than relatedness, even for partners of different species (Queller 1985, 2011; Frank 1994, 1998; Fletcher and Zwick 2006).

Multilevel selection provides an alternative view of social selection that could also provide fundamental theorems, using either a partition due to Price or one due to contextual analysis (Price 1972a; Hamilton 1975; Wade 1985; Heisler and Damuth 1987; Goodnight et al. 1992; Okasha 2006). The contextual-analysis approach parallels equation (7), but with the predictor being mean group phenotype rather than individual phenotypes.

Similarly, the replicator equation (Taylor and Jonker 1978; Schuster and Sigmund 1983) could be viewed as a fundamental theorem of frequency-dependent selection. It too is closely related to the Price equation (Page and Nowak 2002).

Another modification is to study joint phenotypes, traits that are affected by more than one organism. For example, virulence can be affected by both pathogen and host. Equations describe both rate of change of the phenotype and rate of change of fitness, the latter giving a version of Fisher's fundamental theorem (Queller 2014). Here the "deterioration of the environment" (Fisher 1930, p. 41) caused by the evolution of antagonists, which would normally be in Price's second term, is brought into the covariance selection term.

Price's Second Term and Fighting the Last War

In general, I have concentrated on the selection part of the Price equation. I leave open whether there might also be candidates for fundamental-theorem status derived from the second term, but here I consider the implications of ignoring it entirely. When fundamental theorems ignore it, they will be inexact to the extent that there are forces other than selection, such as mutation or environmental change.

But the value of the theorems does not primarily lie with their exactness; it rests on their capturing broad features of selection in a simple way. Fisher realized this and spoke of increase in fitness being opposed by a “deterioration of the environment” that he did not quantify (Fisher 1930, p. 41). Early critics of Fisher’s theorem may have accepted this much, but they argued that even so, the theorem did not capture selection fully. For example, Li (1967) showed that, even without mutation or changes in the environment, simple allelic dominance appeared to cause deviations from the fundamental theorem. This kind of work (Kempthorne 1957; Crow and Kimura 1970; Karlin 1975; Nagylaki 1991) led to the early negative view of the fundamental theorem.

It was George Price who finally explained what Fisher meant (Price 1972*b*) and shifted the tide more in favor of the view that Fisher’s theorem was important (Ewens 1989; Frank and Slatkin 1992; Frank 1997; Lessard 1997; Grafen 2003, 2015*a*; Plutynski 2006; Okasha 2008; Bijma 2010). Curiously, Price did not use his own theorem to show this, but it must have allowed him to see the solution, as both theorems rest on similar partitions. Fisher viewed changes in gene frequency as a special case of a change in the environment (Fisher 1941; Price 1972*b*), a view that seems odd at first but one that comes naturally in a gene-centered viewpoint (Dawkins 1982). Specifically, Fisher’s equation represents the selective change if breeding values are unchanged in the next generation. It is inexact when breeding values do change.

To take a simple case, consider frequency-dependent selection on the sex ratio. An excess of females in one generation gives higher fitness to mothers who produce more males. This fitness gain is captured by Fisher’s theorem. But when more males are produced, this constitutes a deterioration of the environment for males (more competitors), and the total fitness gain will not be as large. A similar phenomenon occurs with other nonadditive effects, such as dominance and epistasis; when gene frequencies change, the partition between additive genetic variance, dominance variance, and interaction variance can change, so what constitutes breeding value for fitness shifts from one generation to the next. Fisher and Price chalk these effects up to a change in the genetic environment rather than to selection.

In one sense, this is a bit of a cheat, since this change was also caused by selection. But it also makes sense (Grafen 2003). There are two different consequences of selection. The first term captures the primary effect of selection that leads to adaptation. It shows that selection “at all times acts to increase the fitness of a species to live under the conditions that existed an instant earlier” (Price 1972*b*, p. 131). Selection is like the generals who are said to always fight the last war. This is not the best possible strategy, given that the next war occurs under altered conditions, including the fact that opposing generals have learned from the last war. In spite of this, learning from the last war does lead to steady

improvements in military technology and strategy, and that is the kind of improvement Fisher had in mind. The second term includes secondary knock-on effects of selection; these are due not to selective sorting itself but instead to the population’s response to selection—the change in frequencies and consequent recalculation of breeding values. These changes are more idiosyncratic and typically smaller and could either decrease or increase mean fitness. For example, in contrast to the decreasing component in fitness in negative frequency-dependent selection on the sex ratio, positive frequency-dependent selection can cause an extra increase in fitness.

Dropping the second term is what allows us to capture the universal adaptive effect of selective sorting, setting aside the secondary effects that change in frequencies can have on calculation of breeding values. Note that this applies not just to Fisher’s theorem but to all the fundamental theorems derived by ignoring Price’s second term. It is precisely this move that makes the theorems fundamental. I believe that this same issue underlies much of the recent debate over the merits of inclusive fitness, with some preferring more exact and more complicated models (Nowak et al. 2010) while other prefer the simplicity and scope of Hamilton’s rule.

Although most fundamental theorems discussed here drop the second term, they need not do so. We could simply keep the second term in the other fundamental theorems to make them more accurate. In fact, this has often been done in particular cases. Models of selection-mutation balance can be viewed as using equation (1) with a second term for the effect of mutation that can easily be framed in terms of Price’s second term. And the models that criticized Fisher’s theorem did so by finding out what has to be added to Fisher’s first term in order to make things more exact—in other words, by including effects of the second term (Kempthorne 1957; Li 1967; Crow and Kimura 1970; Karlin 1975; Nagylaki 1991). This is valuable when what we most desire is accuracy rather than simplicity and scope.

Conclusions

I have argued that there is a set of fundamental theorems of evolution and that they are marked by high degrees of simplicity and scope. If my selection of fundamental theorems is a reasonable one, one conclusion that follows is that the unmeasured-genotype approach of quantitative genetics has been more productive of fundamental theorems than the measured-genotype approach of population genetics. This may seem odd, since population genetics is generally considered to be more rigorous, or at least more complete, because of more detailed assumptions of how genes combine and how these combinations translate into phenotypes or fitness. The

explanation is probably that the greater accuracy possible in the measured-genotype approach has focused population geneticists on results that are more exact but less fundamental in the sense used here. Practitioners of the unmeasured approach, on the other hand, have been forced into using summary measures such as variances, covariances, and regressions. This constraint frees them from the tyranny of detail and can lead to generalities that are valuable, even if inexact. I suspect that the reason Fisher's fundamental theorem was initially pilloried, while the equally inexact breeder's equation was not, is that only the former was treated as a population-genetic result to be held to population-genetic standards, while the latter was recognized as an acceptable approximation for doing practical quantitative genetics.

In this connection, it is worth noting that unmeasured-genotype models are generally not dynamically sufficient. That is, one cannot necessarily iterate the equation generation after generation, and so it cannot be used for fixation probabilities. To reconstitute the changed breeding values would require the understanding of the precise relationship between genes and phenotype that the unmeasured-genotype methods were designed to circumvent. We are thus left with a more limited result but one that is useful for short-term prediction and one that can have great intuitive explanatory power.

Note, however, that although many population-genetic models are dynamically sufficient, the single fundamental theorem of this type, equation (2), is not. Although it gives an exact result for the change in allele frequency due to selection, by itself it contains no information about how alleles are to be combined in the next generation. So unless everything is additive, so that the fitness effects of alleles are unchanged by context, we cannot predict the following generation exactly (Frank 2012). This lack of dynamic sufficiency in our fundamental theorems is not a function of the Price equation itself; it depends on what additional information we elect to put into the equation (Frank 1995, 2012). The Price equation is an identity, simply a partition of evolutionary change, so all results, whether measured or unmeasured, dynamically sufficient or insufficient, should be expressible in terms of it. Rather, it seems that dynamic sufficiency, because it depends on precise details, is something that we may need to sacrifice to achieve results of the level of simplicity and scope that we seek for fundamental theorems.

The elevation of several results to fundamental theorems might seem to imply a demotion for Fisher's fundamental theorem. If so, Fisher's reputation as a giant of both evolutionary biology and statistics can certainly withstand it. There might even be some justice to a demotion in that Fisher, but not everyone else, had the cheek to self-nominate his result for fundamental status. But there are several important senses in which this is not a demotion. First, embedding Fisher's

theorem within the other fundamental theorems makes more transparent what Fisher's theorem accomplished. Although it may not strictly be about natural selection in general, it is about systematic change in fitness or adaptation, and that is very important (Grafen 2003). Adaptation is the feature that makes biology different from inanimate chemistry and physics, so to have captured its essence in a simple equation is a tremendous feat. Second, we should remember that it was Fisher who provided the concepts necessary for other fundamental theorems—the average excess, the average effect, and the breeding value—along with the critical strategy of ignoring the deterioration of the environment. Finally, besides providing us with his own valuable theorem, Fisher demonstrated the general value of simplifying and sacrificing a bit of accuracy in order to capture and highlight fundamental issues in a simple and elegant way.

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Literature Cited

- Arnold, S. J., and M. J. Wade. 1984. On the measurement of natural and sexual selection: theory. *Evolution* 38:709–719.
- Bijma, P. 2010. Fisher's fundamental theorem of inclusive fitness and the change in fitness due to natural selection when conspecifics interact. *Journal of Evolutionary Biology* 23:194–206.
- Crow, J. F., and M. Kimura. 1970. An introduction to population genetics theory. Harper & Row, New York.
- Dawkins, R. 1982. *The extended phenotype*. W. H. Freeman, Oxford.
- Day, T., and S. Gandon. 2006. Insights from Price's equation into evolutionary epidemiology. Pages 23–44 in Z. Feng, U. Dieckmann, and S. A. Levin, eds. *Disease evolution: models, concepts, and data analyses*. American Mathematical Society, Providence, RI.
- Ewens, W. J. 1989. An interpretation and proof of the fundamental theorem of natural selection. *Theoretical Population Biology* 36:167–180.
- Fisher, R. A. 1930. *The genetical theory of natural selection*. Oxford University Press, Oxford.
- . 1941. Average excess and average effect of a gene substitution. *Annals of Eugenics* 11:53–63.
- Fletcher, J. A., and M. Zwick. 2006. Unifying the theories of inclusive fitness and reciprocal altruism. *American Naturalist* 168:252–262.
- Fox, J. W. 2006. Using the Price equation to partition the effects of biodiversity loss on ecosystem function. *Ecology* 87:2687–2696.

- Frank, S. A. 1994. Genetics of mutualism: the evolution of altruism between species. *Journal of Theoretical Biology* 170:393–400.
- . 1995. George Price's contributions to evolutionary genetics. *Journal of Theoretical Biology* 175:373–388.
- . 1997. The Price equation, Fisher's fundamental theorem, kin selection, and causal analysis. *Evolution* 51:1712–1729.
- . 1998. *Foundations of social evolution*. Princeton University Press, Princeton, NJ.
- . 2012. Natural selection. IV. The Price equation. *Journal of Evolutionary Biology* 25:1002–1019.
- Frank, S. A., and M. Slatkin. 1992. Fisher's fundamental theorem of natural selection. *Trends in Ecology and Evolution* 7:92–95.
- Gardner, A., S. A. West, and G. Wild. 2011. The genetical theory of kin selection. *Journal of Evolutionary Biology* 24:1020–1043.
- Goodnight, C. M., J. M. Schwartz, and L. Stevens. 1992. Contextual analysis of models of group selection, soft selection, hard selection, and the evolution of altruism. *American Naturalist* 140:743–761.
- Grafen, A. 1985. A geometric view of relatedness. *Oxford Surveys of Evolutionary Biology* 2:28–89.
- . 2000. Developments of the Price equation and natural selection under uncertainty. *Proceedings of the Royal Society B* 267:1223–1227.
- . 2003. Fisher the evolutionary biologist. *Statistician* 52:319–329.
- . 2015a. Biological fitness and the fundamental theorem of natural selection. *American Naturalist* 186:1–14.
- . 2015b. Biological fitness and the Price equation in class-structured populations. *Journal of Theoretical Biology* 373:62–72.
- Hamilton, W. D. 1964. The genetical evolution of social behaviour. I. *Journal of Theoretical Biology* 7:1–16.
- . 1970. Selfish and spiteful behavior in an evolutionary model. *Nature* 228:1218–1220.
- . 1975. Innate social aptitudes in man: an approach from evolutionary genetics. Pages 133–155 in R. Fox, ed. *Biosocial anthropology*. Wiley, New York.
- Heisler, I. L., and J. Damuth. 1987. A method for analyzing selection in hierarchically structured populations. *American Naturalist* 130:582–602.
- Karlin, S. 1975. General two-locus selection models: some objectives, results and interpretation. *Theoretical Population Biology* 7:364–398.
- Kempthorne, O. 1957. *Introduction to statistical genetics*. Chapman & Hall, London.
- Kerr, B., and P. Godfrey-Smith. 2009. Generalization of the Price equation for evolutionary change. *Evolution* 63:531–536.
- Kuhn, T. S. 1977. *The essential tension*. University of Chicago Press, Chicago.
- Lande, R., and S. J. Arnold. 1983. The measurement of selection of correlated characters. *Evolution* 37:1210–1226.
- Lessard, S. 1997. Fisher's fundamental theorem of natural selection revisited. *Theoretical Population Biology* 52:119–136.
- Levins, R. 1966. The strategy of model building in population biology. *American Scientist* 54:421–431.
- Li, C. C. 1967. Fundamental theorem of natural selection. *Nature* 214:505–506.
- Luque, V. J. 2017. One equation to rule them all: a philosophical analysis of the Price equation. *Biology and Philosophy* 32:97–125. doi:10.1007/s10539-016-9538-y.
- Lush, J. L. 1937. *Animal breeding plans*. Iowa State College Press, Ames.
- Marshall, J. A. R. 2015. *Social evolution and inclusive fitness theory*. Princeton University Press, Princeton, NJ.
- Morrissey, M., L. Kruuk, and A. J. Wilson. 2010. The danger of applying the breeder's equation in observational studies of natural populations. *Journal of Evolutionary Biology* 23:2277–2288.
- Nagylaki, T. 1991. Error bounds for the fundamental and secondary theorems of natural selection. *Proceedings of the National Academy of Sciences of the USA* 88:2402–2406.
- Nowak, M. A., C. E. Tarnita, and E. O. Wilson. 2010. The evolution of eusociality. *Nature* 466:1057–1062.
- Okasha, S. 2006. *Evolution and the levels of selection*. Oxford University Press, Oxford.
- . 2008. Fisher's fundamental theorem of natural selection—a philosophical analysis. *British Journal of the Philosophy of Science* 59:319–351.
- Page, K. M., and M. A. Nowak. 2002. Unifying evolutionary dynamics. *Journal of Theoretical Biology* 219:93–98.
- Pearl, J. 2009. *Causality*. Cambridge University Press, Cambridge.
- Pearson, K. 1903. *Mathematical contributions to the theory of evolution*. XI. On the influence of natural selection on the variability and correlation of organs. *Philosophical Transactions of the Royal Society A* 200:1–66.
- Plutynski, A. 2006. What was Fisher's fundamental theorem of natural selection and what was it for? *Studies in History and Philosophy of Biological and Biomedical Sciences* 37:59–82.
- Price, G. R. 1970. Selection and covariance. *Nature* 227:520–521.
- . 1972a. Extension of covariance selection mathematics. *Annals of Human Genetics* 35:485–490.
- . 1972b. Fisher's fundamental theorem made clear. *Annals of Human Genetics* 36:129–140.
- . 1995. The nature of selection. *Journal of Theoretical Biology* 175:389–396.
- Queller, D. C. 1985. Kinship, reciprocity and synergism in the evolution of social behaviour. *Nature* 318:366–367.
- . 1992a. A general model for kin selection. *Evolution* 46:376–380.
- . 1992b. Quantitative genetics, inclusive fitness, and group selection. *American Naturalist* 139:540–558.
- . 2011. Expanded social fitness and Hamilton's rule for kin, kith, and kind. *Proceedings of the National Academy of Sciences of the USA* 108:10792–10799.
- . 2014. Joint phenotypes, evolutionary conflict and the fundamental theorem of natural selection. *Philosophical Transactions of the Royal Society B* 369:20130423. doi:10.1098/rstb.2013.0423.
- Rice, S. H. 2004. *Evolutionary theory: mathematical and conceptual foundations*. Sinauer, Sunderland, MA.
- . 2008. A stochastic version of the Price equation reveals the interplay of deterministic and stochastic processes in evolution. *BMC Evolutionary Biology* 8:262. doi:10.1186/1471-2148-8-262.
- Robertson, A. 1966. A mathematical theory of the culling process in dairy cattle. *Animal Production* 8:95–108.
- . 1968. The spectrum of genetic variation. Pages 5–16 in R. Lewontin, ed. *Population biology and evolution*. Syracuse University Press, Syracuse, NY.
- Schuster, P., and K. Sigmund. 1983. Replicator dynamics. *Journal of Theoretical Biology* 100:533–538.
- Seger, J. 1981. Kinship and covariance. *Journal of Theoretical Biology* 91:191–213.
- Shipley, B. 2000. *Cause and correlation in biology*. Cambridge University Press, Cambridge.
- Taylor, P. D., and L. B. Jonker. 1978. Evolutionary stable strategies and game dynamics. *Mathematical Biosciences* 40:145–156.

Templeton, A. R. 2006. Population genetics and microevolutionary theory. Wiley, Hoboken, NJ.
Wade, M. J. 1985. Soft selection, hard selection, kin selection, and group selection. *American Naturalist* 125:61–73.
Walsh, B., and M. Lynch. Forthcoming. Evolution and selection of quantitative traits. Sinauer, Sunderland, MA.

Wright, S. 1921. Correlation and causation. *Journal of Agricultural Research* 20:557–585.

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“The animal, from which I have made the drawings, is now developing his fourth pair of horns. The second pair of horns were about three inches longer than the first, and the same difference existed between the second and third pair.” From “The Prong-Horn Antelope” by W. J. Hays (*The American Naturalist* 1868, 2:131–133).