Estimates and bounds on the rate and extent of allele frequency change

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Two approximations are provided to the frequency of an autosomal allele after any number of generations of selection and, conversely, to the number of generations required for any given frequency change. These estimates are accurate over a wide range of selection coefficients and initial conditions, and have the added advantage of providing strict upper and lower bounds to the true values under quite general conditions. The approach employed here, of finding exact solutions to approximating difference equations, could easily be applied to models with migration, mutation, etc. and, indeed, to any non-linear difference equation. In such applications, it offers several advantages over traditional methods from approximation theory.

Keywords: allele frequencies, approximations, modelling, population genetics, selection.

Introduction

One of the basic questions of microevolutionary theory is how do allele frequencies change through time in response to selection and other forces. Haldane first addressed this question in a series of papers on single-locus models, assuming various mating systems and inheritance patterns (Haldane, 1932a, for review). Much of the current research in population genetics remains focused on this question, although the models now include the complicating effects of, for example, multi-locus interactions, spatially varying selection regimes, and population dynamics (e.g. Feldman, 1989). Haldane found that even the simplest models for populations with discrete generations often yielded 'formidable' non-linear difference equations whose solutions could only be approximated. The accuracy of these approximations varies, depending on the allele frequencies and parameter values. Of course, where greater accuracy is needed, the original equations can now be solved numerically by computer. Nevertheless, it is often useful to have simple, approximate solutions, as a check on the numerical solutions and, more importantly, as components in larger genetics models such as those incorporating population dynamics.

This paper presents simple, explicit estimates on the rate and extent of change in the frequency of an autosomal allele under selection. These estimates are extremely accurate over a wide range of selection coefficients and initial conditions, and have the added

advantage of providing strict upper and lower bounds to the true values under fairly general conditions. They may rival in accuracy and utility the more complex approximations by Haldane (1932a) and Wright (1931) under certain conditions. The approach employed here, of finding exact solutions to approximating difference equations, could easily be applied to models with migration, mutation, and so on.

Consider a large, panmictic population of sexually reproducing organisms, with discrete generations. Suppose that A_1 and A_2 are two alleles at an autosomal locus which occur at frequencies p and $1 - p$. Suppose also that the relative fitnesses of the three genotype A_1A_1 , A_1A_2 and A_2A_2 are, respectively, 1, r_1 , and r_2 . Then, in the absence of other factors, selection will change the frequency of A_1 from p_0 to p_1 in one generation, where

$$p_1 = \frac{p_0^2 + r_1 p_0 (1 - p_0)}{p_0^2 + 2r_1 p_0 (1 - p_0) + r_2 (1 - p_0)^2}. \quad (1)$$

The problem is to find p_n , the frequency of A_1 alleles after n generations, as a function of p_0 , r_1 , r_2 and n . Alternatively, one can ask how many generations, n , are required for the frequency of A_1 alleles to change from p_0 to p_n , given r_1 and r_2 .

Equation (1) has been solved in closed form for only two special cases. First, if the homozygote A_2A_2 has zero fitness ($r_2 = 0$), then $p_n/(1 - p_n) = 1 + (1/r_1)(p_{n-1})/$

$(1 - p_{n-1})$ exactly, which yields

$$p_n = \frac{(1 - r_1)p_0 + (1 - p_0)r_1(1 - r_1^n)}{1 - r_1 + (1 - p_0)(2r_1 - 1)(1 - r_1^n)} \quad (2)$$

The solution has been discovered several times (see Li, 1976, pp. 413–414). In the limit $r_1 \rightarrow 1$ (using l'Hopital's rule, Li, 1976), it reduces to $p_n = [p_0 + n(1 - p_0)]/[1 + n(1 - p_0)]$. In addition, an exact solution is known when the A_1 alleles have multiplicative effects on fitness so that the effect of two doses, relative to none, is the square of the effect of one dose: $1/r_2 = (r_1/r_2)^2$ (Li, 1959, and see below).

When the selection coefficients do not satisfy either condition, then one can always solve equation (1) numerically by iteration. This will yield a value for p_n or n that is correct, but which may be tedious to obtain and which reveals nothing of its dependence on the parameters and initial conditions. A more satisfying approach is to use closed form approximations which may sacrifice little in accuracy in exchange for a greater ease of use and transparency. This paper presents two such approximations for the case of an autosomal allele under selection, and illustrates a general approach that can be applied more broadly to population genetics models with discrete generations and, indeed, to any non-linear difference equations.

Approximations to p_n

Equation (1) can be rewritten

$$p_1 = \frac{r_1 p_0 + (1 - r_1)p_0^2}{r_1 p_0 + r_2(1 - p_0) + (r_1 - r_2)p_0(1 - p_0) + (1 - r_1)p_0^2} \quad (3)$$

If the A_1 allele is dominant, then $(1 - r_1)p_0^2$ vanishes; if A_2 is dominant, $(r_1 - r_2)p_0(1 - p_0)$ disappears. More generally, if p_0 is small, and r_1 and r_2 are not enormously different in value, then these terms are much smaller than the leading terms in the ratio and can be set equal to zero. This yields an approximation u_1 to p_1

$$u_1 = \frac{p_0}{p_0 + R(1 - p_0)} \quad (4)$$

where $R = r_2/r_1$, provided the A_2 allele is neither fully dominant ($r_1 \neq r_2$) nor lethal ($r_2 \neq 0$). One can show by direct substitution that $U_i = u_i/(1 - u_i)$ obeys the recursion relation $U_n = U_{n-1}/R = U_0/R^n$ which on rearrangement yields

$$u_n = \frac{p_0}{p_0 + R^n(1 - p_0)} \quad (5)$$

This provides a simple approximation u_n to p_n , the frequency of A_1 alleles in generation n , as a function of p_0 , r_1 , r_2 and n .

This approximation has several useful features. First, u_n is bounded between 0 and 1 for all $n = 1, 2, \dots$, r_1 and $r_2 > 0$, and $0 < p_0 < 1$. Second, it returns the exact solution in the special case that the A_1 alleles have multiplicative effects on fitness, when $r_1^2 = r_2$ (Li, 1959). Finally, when $r_1^2 \neq r_2$, u_n provides not only an estimate but also a bound on the true value of p_n . In particular, $u_1 > p_1$, hence $u_n > p_0$ for all p_n and n if and only if $r_1^2 > r_2$. Therefore, this approximation provides a strict upper bound on the actual gene frequency p_n after n generations if $r_1^2 > r_2$, and a strict lower bound if $r_1^2 < r_2$.

A second approximation to equation (1) can be obtained by setting all terms in $p_0^2 = 0$, valid when the A_1 allele is rare. This yields

$$l_1 = \frac{p_0}{2p_0 + R(1 - 2p_0)} \quad (6)$$

again where $R = r_2/r_1$ and the A_2 allele is neither fully dominant nor lethal. This equation can be linearized by the transformation $L_n = l_n/(1 - 2l_n) = L_{n-1}/R = L_0/R^n$ to yield

$$l_n = \frac{p_0}{2p_0 + R^n(1 - 2p_0)} \quad (7)$$

This approximation is well-behaved if $p_0 < 0.5$, and converges monotonically to 0.5 or 0 depending on whether $r_1 > r_2$ or $r_1 < r_2$. It provides a strict lower or upper bound on p_1 according to whether $(r_1 - r_2)p_0 + r_2(1 - r_1)(1 - p_0) > 0$ or < 0 , respectively. For p_0 small, this condition effectively reduces to $r_1 < 1$ or > 1 , independent of r_2 . More generally, the condition simplifies and becomes independent of p_0 provided either allele is strictly favoured under selection. If A_1 is favoured ($1 \geq r_1 > r_2$), then $l_1 < p_1$ and therefore $l_n < p_n$ for all n as the two series increase to 0.5 and 1, respectively. Conversely, if A_1 is strictly opposed ($1 \leq r_1 < r_2$), then $l_1 > p_1$ hence $l_n > p_n$ as both measures decrease to 0.

These approximations can be used separately or in concert. Several cases are considered.

One possibility is that the A_1 allele is fully dominant. Haldane considered this case to be the simplest, though perhaps the most important, of a large number' (1932b, p. 247), and he discussed it in two separate papers (1924, 1932b, see below). In this case, $r_1 = 1$, and equation (1) can be written

$$p_1 = \frac{p_0}{1 - (1 - r_2)(1 - p_0)^2} \quad (8)$$

The two approximations [equations (4) and (6)] correspond respectively to replacing the $(1 - p_0)^2$ term by the slightly larger $(1 - p_0)$ or smaller $(1 - 2p_0)$. Here u_n overestimates the actual change in p each generation, and l_n underestimates the change, regardless of whether p is increasing or decreasing. Therefore, if the dominant allele is favoured under selection ($r_2 < 1$), then its true frequency after n generation is bracketed by the simple estimates $u_n > p_n > l_n$, as the three series converge respectively to 1, 1, and 0.5. Conversely, if the dominant allele is deleterious ($r_2 > 1$), then the inequalities are reversed, $u_n < p_n < l_n$, as all three converge to 0.

More generally, if the A_1 allele is strictly favoured in selection such that $1 \geq r_1^2 > r_2$ (which includes full dominance as a special case) then $u_n > p_n > l_n$ for all n as the three series converge respectively to 1, 1 and 0.5.

Alternatively, if the A_1 allele is strictly opposed such that $1 \leq r_1^2 < r_2$, the order of the three values is reversed, $u_n < p_n < l_n$, as all three converge to 0.

If the heterozygote is at a selective advantage ($1 < r_1 > r_2$), then p_n will approach a stable, intermediate value $p^* = (r_1 - r_2)/(2r_1 - 1 - r_2)$. In this case, the two approximations (5) and (7) cannot reproduce the full range of behaviours of equation (1) but can only increase, since $r_1 > r_2$, ultimately converging to 1 and

0.5. However, if A_1 is initially rare, then the two approximations will increase with p_n , and provide accurate estimates of the latter until it asymptotes at p^* . In addition, p_n will always be bounded from above by u_n (and p^*), although whether l_n simultaneously provides a lower bound on p_n depends on the precise values of r_1 , r_2 , and p_0 , and is not assured.

Alternatively, the heterozygote may be at a selective disadvantage ($1 > r_1 < r_2$); here, p^* is an unstable equilibrium, and p_n will go to 1 or 0 depending on which allele has the initial advantage. Again, approximations (5) and (7) cannot reproduce the full range of possibilities (both always converge to 0) although they provide accurate approximations to p_n when it too converges to 0 (that is, if $p_0 < p^*$). In this case, u_n is always a lower bound to p_n although whether l_n is simultaneously an upper bound is more complex.

All these applications are for A_1 rare and not fully recessive. As alleles can be labelled arbitrarily, the approximations can be used whenever the rarer allele, whichever it is, is not fully recessive.

Accuracy

Figure 1 illustrates the accuracy of these two approximations. At the upper left is a contour plot showing the

Fig. 1 Accuracy of the approximations given by equations (4) and (6) as a function of r_1 and r_2 , given $p_0 = 10^{-5}$ (top row) and $p_0 = 10^{-2}$ (bottom row). In each row, the left contour plot shows the allele frequency p_1 after one generation of selection. The middle and right contour plots respectively show how well u_1 and l_1 approximate p_1 as measured by $(u_1 - p_1)/p_1$ and $(l_1 - p_1)/p_1$.

value of p_1 as a function of r_1 and r_2 , when $p_0 = 10^{-5}$. This is the surface to be approximated. To the right are contour plots of the accuracy with which u_1 and l_1 respectively approximate p_1 . Here accuracy is measured by $(u_1 - p_1)/p_1$ or $(l_1 - p_1)/p_1$, so that a contour line labelled -10^{-5} would indicate values of r_1 and r_2 for which the approximation underestimates p_1 by a factor of 10^{-5} , or 0.001 per cent. The lower set of plots provide similar information for the case in which $p_0 = 0.01$.

Note that for all p_0 , the first approximation u_1 equals p_1 along the line $r_1^2 = r_2$ and underestimates or overestimates the actual allele frequency above or below that line, thereby always providing a strict bound. The accuracy is greater near this line, and varies systematically with p_0 . In particular, when $p_0 = 10^{-5}$, u_1 is itself within a fraction 10^{-5} (0.001 per cent) of p_1 inside a large and broadening band about the line, and within a fraction 10^{-4} for essentially all values of the selection coefficients that were considered. However, when p_0 is increased 1000-fold, so is the error. Therefore, for any p_0 , u_1 is within a fraction p_0 of p_1 for moderate values of r_1 and r_2 , and within a larger fraction $10p_0$ for essentially all other r_1 and r_2 .

The second approximation (right-hand plots) has similar properties. The error is 0 along a line (here a hyperbola) in the (r_1, r_2) plane, and is smallest for values of r_1 and r_2 near this line. One important difference, however, is that because of the orientation of the hyperbola, unless r_2 is small the accuracy essentially depends only on r_1 and p_0 , increasing as $r_1 \rightarrow 1$ and as $p_0 \rightarrow 0$. A comparison of the plots with $p_0 = 10^{-5}$ and $p_0 = 0.01$ shows that l_1 is within a fraction p_0 of the true value provided $r_1 > 0.5$, and within $10p_0$ for essentially all $r_1 > 0$. This second approximation is therefore comparable to the first in accuracy, though for a larger region in the (r_1, r_2) plane. It is also comparable in

behaviour, as for any given fitness values the accuracy increases roughly 10-fold for each 10-fold reduction in p_0 . One consequence is that when p is increasing from small values, neither approximation will suffer from the compounding of large errors incurred when p was small.

Figure 2 illustrates these points in the special case of complete dominance. Here, p_1 is always strictly bounded between u_1 and l_1 , with the order depending on whether $r_2 > 1$ or < 1 . Both approximations are most accurate when $r_2 \rightarrow 1$ and $p_0 \rightarrow 0$. There is an important difference between them, however; when $r_2 > 0.5$, the first approximation u_1 is within a fraction p_0 of the true value of p_1 while the second, l_1 , is within the smaller fraction p_0^2 . Therefore, near $r_1 = 1$, the second approximation increases 100-fold in accuracy with each 10-fold reduction in p_0 , increasing from four-decimal place accuracy (0.01 per cent) when $p_0 = 10^{-2}$ to ten-decimal place accuracy when $p_0 = 10^{-5}$. Clearly, the second approximation is superior when r_1 is near 1 and r_1^2 is not near r_2 (near-full dominance), while the first approximation is particularly accurate when r_1^2 is near r_2 (approximately multiplicative effects).

Figure 3 illustrates the accuracy of both estimates after 10 generations of selection for all $r_1, r_2 \leq 2$, starting with $p_0 = 10^{-5}$. Note that both u_{10} and l_{10} are still within 10^{-4} (0.01 per cent) of the actual value almost everywhere that $r_2 > 0.5$ and $r_2 > r_1$, and l_{10} is within 4 per cent provided only $r_2 > 0.5$. Both remain accurate, therefore, where there is weak or moderate selection for or against A_1 , and strong selection against it. They are less accurate when there is strong selection favouring the allele (r_1 and r_2 small, p_{10} close to 1), and when there is strong heterosis (r_1 large, r_2 small, p_n converging on an intermediate value).

Fig. 2 Accuracy of the approximations given by equations (4) and (6) when there is complete dominance ($r_1 = 1$), as a function of p_0 and r_2 . As before, accuracy is measured by $(u_1 - p_1)/p_1$ (a) and $(l_1 - p_1)/p_1$ (b).

Fig. 3 Accuracy of the approximations given by equations (5) and (7) after 10 generations of selection, starting at $p_0 = 10^{-5}$, as a function of r_1 and r_2 . (a) Shows the allele frequency p_{10} , while (b) and (c) respectively show how well u_{10} and l_{10} approximate p_{10} , as measured by $(u_{10} - p_{10})/p_{10}$ and $(l_{10} - p_{10})/p_{10}$.

Approximations to n

The approximations (5) and (7) above can be manipulated to yield estimates of the number of generations n required for A_1 to change in frequency from p_0 to some specified value p_n , given r_1 and r_2 .

$$n_u = \frac{1}{\ln(R)} \ln \left[\frac{p_0(1 - p_n)}{p_n(1 - p_0)} \right] \quad (9)$$

$$n_l = \frac{1}{\ln(R)} \ln \left[\frac{p_0(1 - 2p_n)}{p_n(1 - 2p_0)} \right] \quad (10)$$

As before, the second approximation is restricted to the case in which p_0 and $p_n < 0.5$.

Note that whenever u_n or l_n provides a bound on the amount of allele frequency change in n generations, then n_u or n_l will place the opposite bound on the number of generations required to achieve that change. Under certain conditions the two approximations can be combined to bracket the exact solution. In particular, if $1 \geq r_1^2 > r_2$, then since u_n and l_n respectively overestimate and underestimate the rate of increase in p , the actual number of generations required for any specified change in p will be bracketed by $n_u < n < n_l$. If the direction of selection is reversed and the fitness values obey $1 \leq r_1^2 < r_2$, then u_n overestimates the rate of decline in p , and l_n underestimates it, and again the actual n for any specified change is bounded by $n_u < n < n_l$.

The accuracy of these two approximations is illustrated in Table 1, which presents the exact number of generations required for specific changes in p as calculated by iteration, and the estimates obtained with equations (9) and (10). In all but one case, the selection regimes considered satisfy the requirements that n is bounded on either side by $n_u < n < n_l$, although often

the error is so small as to vanish on rounding off to the nearest generation. Both approximations are essentially exactly correct whenever the beginning and final allele frequencies do not exceed 0.1, regardless of whether the A_1 allele is fully or incompletely dominant, favoured or opposed in selection. In some cases, the accuracy remains high even at higher frequencies, with the best predictor depending on the selection coefficients. Thus when $r_1 = 1$ and $r_2 = 0.99$, there is weak selection favouring the dominant allele, and the second approximation is expected to be more accurate. In fact, it predicts that 1036 generations are required for p to increase from 10^{-5} to 0.2, and is high by only three generations, whereas the first approximation is low by 24. Similarly, in the two cases in which r_1^2 is near r_2 , the second approximation is close but the first gives the exact solution over the entire range of allele frequencies considered: 205 generations to increase from 10^{-5} to 0.4 when $r_1 = 0.95$ and $r_2 = 0.90$, and 239 generations to decrease from 0.4 to 10^{-5} when $r_1 = 1.05$ and $r_2 = 1.10$.

Alternative approximations

The approximations first offered here are intermediate in complexity and accuracy to others already in the literature. At one extreme is the estimate $p_n \approx p_0/R^n$, obtained by setting all terms in both p_0 and p_0^2 equal to 0 in the formula for p_1/p_0 (e.g. Jacquard, 1974). Although crude, this returns accurate solutions when p_0 and p_n are both small. The corresponding estimate for the number of generations required to pass from p_0 to p_n is $n \approx \ln(p_0/p_n)/\ln(R)$.

At the other extreme are quite complicated formulas obtained from differential equation approximations to the difference equation (1). Haldane (1926) obtained an approximate solution to (1) which he had written

Table 1 Number of generations required for the A_1 allele to change in frequency from p_0 to p_n given r_1 and r_2 as specified below, as calculated exactly by iteration of equation (1), and as estimated by equation (9) n_u and (10) n_l . Note that in all but the last case, the fitness values satisfy the conditions that ensure $n_u \leq n_{\text{exact}} \leq n_l$

$p_0 \rightarrow p_n$	$10^{-5} \rightarrow 10^{-2}$	$10^{-2} \rightarrow 0.1$	$0.1 \rightarrow 0.2$	$0.2 \rightarrow 0.4$	$p_0 \rightarrow p_n$	$0.4 \rightarrow 0.2$	$0.2 \rightarrow 0.1$	$0.1 \rightarrow 10^{-2}$	$10^{-2} \rightarrow 10^{-5}$
$r_1 = 1, r_2 = 0.99$					$r_1 = 1, r_2 = 1.01$				
n_u	688	239	81	98	n_u	99	81	241	695
n_{exact}	689	249	95	139	n_{exact}	140	95	251	696
n_l	689	249	98	178	n_l	180	99	252	696
$r_1 = 1, r_2 = 0.90$					$r_1 = 1, r_2 = 1.10$				
n_u	66	23	8	9	n_u	10	9	25	73
n_{exact}	66	24	9	13	n_{exact}	15	10	26	73
n_l	66	24	9	17	n_l	19	10	26	73
$r_1 = 0.95, r_2 = 0.90$					$r_1 = 1.05, r_2 = 1.10$				
n_u	128	44	15	18	n_u	21	17	52	149
n_{exact}	128	44	15	18	n_{exact}	21	17	52	149
n_l	128	46	18	33	n_l	39	21	54	149

$$U_1 - U_0 = U_0 [KU_0 - K + k] / [(1 - K)U_0 + 1 - k],$$

where $U = p/(1 - p)$, $K = 1 - r_1$ and $k = 1 - r_2$. Assuming selection to be weak, he approximated the denominator by $U_0 + 1$ and the difference $U_1 - U_0$ by dU/dn to yield

$$n = \frac{1}{r_1 - r_2} \ln \left[\left(\frac{p_n}{p_0} \right) \left(\frac{1 - p_0}{1 - p_n} \right)^{1/(R_1 + 1)} \left(\frac{R_1 p_0 + 1}{R_1 p_n + 1} \right)^{R_1/(R_1 + 1)} \right], \quad (11)$$

where $R_1 = (1 - 2r_1 + r_2)/(r_1 - r_2)$. Wright (1931) obtained this answer multiplied by r_2 from a differential equation approximation in p ,

$$dp/dn \approx p_1 - p_0 \approx [1/r_2]p(1 - p)[(1 - 2r_1 + r_2)p + r_1 - r_2],$$

where the denominator had been set equal to 1 after assuming weak selection. In the special case of complete dominance, these formulas simplify somewhat (e.g. Haldane, 1924), and Haldane (1932) even obtained an exact solution, although in the form of an infinite series which itself must be approximated. All these estimates are extremely accurate over a wide range of parameter values and initial conditions. However, they are unwieldy and therefore difficult to calculate, interpret, and incorporate into larger models. Moreover, unlike the approximations introduced here, they cannot be manipulated to yield estimates of p_n that are explicit functions of p_0 , r_1 , r_2 and n .

Discussion

To the extent that equations (5) and (7) provide accurate descriptions of the effect of selection on allele frequencies, several additional quantitative relations can be noted. First, it is clear from either equation that

n generations of selection with fitness 1, r_1 , and r_2 is approximately equal to one generation of selection with fitnesses 1, r_1^n , r_2^n . (It is slightly more or less, according to whether $r_1^n < r_2^n$.) This generalizes a point by Li (1959), who noted the exact equivalence when $r_1^n = r_2^n$. Alternatively, one generation of selection with fitnesses 1, r_1 , and r_2 is equivalent to x generations at 1, r_1^* , and r_2^* , where x is defined by $(r_2/r_1) = (r_2^*/r_1^*)^x$. Thus for example the degree to which being recessive protects deleterious rare alleles can be quantified. If the fitnesses are 1, $r_1 = 1.98$ and $r_2 = 2$, where the deleterious allele is effectively protected in heterozygote form, then 29 generations of selection are required to effect the same decrease in p as 1 generation of selection without dominance, $r_1 = 1.5$.

Finally, while equations (4) and (6) are rational approximations to (1), in that they are ratios of polynomials, they were not obtained through the normal machinery of rational approximation theory (e.g. Newman, 1979). The usual approach to approximate a function such as (1) over an interval is to select a class of approximating functions, for example, polynomials (e.g. Taylor's series) or trigonometric functions (Fourier expansions), and a measure of distance between the function and its approximation (absolute value, squared deviation, etc.) to be minimized. Once the problem is defined, one considers the existence, uniqueness, characteristics, and construction of its solution, which consists of the coefficients that achieve a good or best fitting function of the class, as measured by the metric (e.g. Rice, 1964; Lorentz, 1966).

The approximations proposed here were selected instead on the basis of three considerations. First it was necessary to approximate equation (1) for all r_1 and r_2 , and not merely a specific case such as when $r_1 = 0.95$

and $r_2=0.9$. This could be viewed as a multivariate approximation problem in r_1 , r_2 , and p_0 . Second, the result had to be a difference equation in p that could be solved in closed form, as the goal is to find p_n , not merely p_1 . Other approximations that were considered either could not be solved or were less accurate than the two selected. Third, the accuracy had to be greater at lower values of p_0 : an error of 10^{-2} or even 10^{-4} when $p_0=10^{-5}$ is unacceptable and, when iterated, would grow even larger. The identification of the 'best' rational approximation to equation (1) under these constraints may be a non-trivial problem, and might not provide any further advantage over the 'good' approximations given by equations (4) and (6).

The approximations introduced here satisfy all three criteria above, and offer several additional advantages as well. In particular, they provide simple, explicit, and transparent estimates for either n or p_n , unlike the more complex approximations available which can only estimate n . In addition, these estimates are especially accurate (certainly within measurement error) for fitness values near 1 that are most often encountered. Finally, the first approximation always places a strict bound on p_n or n , and the second approximation often provides the other bound. Therefore, one can not only estimate p_n or n , but also know the sign of the error and, in some cases, its maximum value. The more-complex estimates by Haldane and Wright are available when greater accuracy is required, especially at higher allele frequencies; however, these equations may be unwieldy for some applications, for example, as components in models with population dynamics, and they

cannot be manipulated to yield p_n as an explicit function of p_0 .

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