Alternative Fitness Models With the Same Allele Frequency Dynamics

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ABSTRACT

For any set of one- or two-locus genotypic fitnesses there are alternative sets, usually frequency-dependent and often with quite different biological meanings, that give rise to the same equations for change of allele or haplotype frequencies. Therefore, it is not possible to distinguish among alternative fitness models from allele or haplotype frequency trajectories or equilibrium distributions. For a single locus and for two loci when linkage equilibrium can be assumed, a simple procedure generates some of the alternative fitness sets.

Sewall Wright (see Wright and Dobzhansky 1946) noted that two different fitness models, with quite disparate biologic interpretations, led to approximately the same trajectories of allele-frequency change. He could equally well explain population cage experiments involving inversions in Drosophila pseudoobscura by fitness overdominance or by additive fitnesses with selection favoring the rare type. Takahata and Nei (1989) have made a similar point for multiple alleles at the MHC loci, pointing out that the equations of allele frequency change are the same with symmetrical overdominance as with a multiplicative, frequency-dependent fitness model.

The equivalence of two biologically quite different models can be illustrated by a simple example, a slight extension of that of Takahata and Nei. If the \( A_i A_j \) homozygote has fitness \( w(A_i A_j) = 1 - s_i \) relative to heterozygotes, \( A_i A_j \), which all have fitness 1, then with discrete generations, random mating, and viability selection the equation for change of frequency, \( p_i \) of allele \( A_i \), is

\[
p_i' = \frac{p_i(1 - s_i p_i)}{\bar{w}}, \quad \bar{w} = 1 - \sum s_i p_i^2
\]

in which a prime indicates the next generation. An alternative, multiplicative, frequency-dependent scheme, \( w(A_i A_j) = (1 - s_i p_i)(1 - s_j p_j) \), leads to the same equation. Thus, the trajectory of allele-frequency change or the equilibrium frequency distribution cannot distinguish between the two models; ancillary information is required.

The purpose of this article is to show that there are always alternative fitness sets, often with quite different properties, that lead to the same equations, and to provide a procedure for finding some such transformations. Ordinarily only relative fitnesses are of interest; but since it is often possible to transform absolute fitnesses as well, this is included.

ONE LOCUS

The general principle: Here, and throughout, we assume a model with discrete generations, random mating, and viability selection (or multiplicative fertilities). Let the absolute fitness of genotype \( A_i A_j \) be \( w_{ij} \). Then the fitness of allele \( A_i \), and the mean fitness are given by

\[
w_i = \sum_j p_j w_{ij}, \quad \bar{w} = \sum_j p_j w_i = \sum_j p_i p_j w_{ij}
\]

in which \( p_i \) is the proportion of allele \( A_i \). The equations for change of allele frequency and total population number, \( N \), are

\[
p_i' = \frac{p_i w_i}{\bar{w}} \quad (3a)
\]

\[
N' = N \bar{w}. \quad (3b)
\]

If the transformed allelic fitness, \( w_i' = w_i \), then (3a) is preserved and so is (3b), since \( \bar{w}' = \bar{w} \). Hence the transformed fitnesses lead to the same allele-frequency and population number dynamics as the untransformed. Usually in population genetics the interest is in allele frequencies, and not in the total population size. In this case it is sufficient that \( w_i' / \bar{w}' = w_i / \bar{w} \). Henceforth, we shall designate transformations that preserve the population growth rate as well as the equations of allele frequency change by primes. Those that preserve only allele frequency change are unprimed.

Multiplicative fitness transformation: The appropriate multiplicative transformation is \( w_i^{\text{Mult}} = w_i \bar{w} / \bar{w} \). Using Equations 2, we find that \( w_i^{\text{Mult}} = w_i \), and therefore \( \bar{w}^{\text{Mult}} = \bar{w} \). Hence the allele frequencies and population number change according to (3) as do the untransformed fitnesses. If the \( w_i \)'s are interpreted as

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relative fitnesses, (3b) is unnecessary. Then the transformation, \( w^{\text{Add}}_i = w_i \), is sufficient because \( w^{\text{Multi}}_i / w^{\text{Add}}_i = w_i / \tilde{w}_i \), and therefore (3a) is the same for both. This is usually less cumbersome to apply. Furthermore, any multiple of \( w^{\text{Add}}_i \) also leads to the same equation since only relative fitnesses matter. A two-allele example, using \( w^{\text{Multi}}_i \), is the fitness transformation \( \{1, 1, 0\} \rightarrow \{1, p_1, p_1\} \), in which the fitness order is \( A_1 A_1, A_1 A_2, A_2 A_2 \). Here, a set of fitnesses in which one genotype is lethal or sterile and the other two are equally fit gives the same allelic trajectory as a frequency-dependent set of multiplicative fitnesses, with a greatly different biological interpretation.

**Additive fitness transformation:** In this case the transformation is \( w^{\text{Add}}_i = w_i + w_j - \tilde{w} \). As before, \( w^{\text{Add}}_i = w_i \) and \( \tilde{w}^{\text{Add}}_i = \tilde{w} \), and equations 3 describe the allele frequency and population number change. The same example as above now gives the transformation \( \{1, 1, 0\} \rightarrow \{p_1^2 + 2p_2, p_1^2 + p_2, p_2^2\} \). Note that, as expected with multiplicative and additive models, in the first example the heterozygote is the geometric mean of the homozygotes while in the second it is the arithmetic mean. For any set of fitnesses, one can always find a multiplicative and an additive set of transformed fitnesses that produce the same gene frequency trajectories.

If allele frequency change is the only consideration and the total number is irrelevant, any multiple of \( w^{\text{Add}}_i \) is appropriate.

**Linear combination:** If multiplicative and additive transformations exist, it is not surprising that a linear combination of the two does also. The transformation \( w^{\text{Lin}}_i = (A w^{\text{Multi}}_i + B w^{\text{Add}}_i) \), where \( A \) and \( B \) may be functions of allele frequencies, has the property that \( w^{\text{Lin}}_i = w_i (A + B) \); hence relative fitnesses are preserved and equation (3a) is appropriate. An example, using \( A w^{\text{Multi}}_i + B w^{\text{Add}}_i \) with \( A = B = 1 \), is \( \{1, 1, 0\} \rightarrow \{1 + p_1^2, 1 + p_1^2, 2p_2^2\} \). Note that, as expected, these values are the sums of the examples in the two preceding sections. We can use any combination of primed and unprimed multiplicative and additive transformations and any values of \( A \) and \( B \), provided the fitnesses are nonnegative. Since there are infinitely many ways of choosing \( A \) and \( B \), there are infinitely many transformed fitness sets that lead to the same equations for allele frequency change.

**Other transformations:** The three transformations might suggest that only multiplicative and additive transformations, or a linear combination of these, are possible. These are the only ones for which we have found a simple rule giving the transformed fitnesses. Many other possibilities are easily found, however.

One procedure is to set \( w^{\text{Multi}}_i = w_i \) (or \( w^{\text{Add}}_i / w^{\text{Multi}}_i = w_i / \tilde{w}_i \)) for all \( i \). Since there are fewer equations than unknowns, there are multiple solutions. As a multiple allele example, a fitness transformation for the genotypes \( A_1 A_1 \) and \( A_1 A_2 \) is \( \{1 - s \sum p_i^2, 1 \rightarrow \{1 - sp_i^2, 1 - sp_i^2\} \). These two fitness sets have the same values of \( w_i \) (and \( \tilde{w}_i \)), and hence the same equations of allele frequency change (and of change of total population size). The original fitnesses show simple heterosis with all heterozygote fitnesses equal and all homozygous fitnesses also equal, although dependent on the total homozygote frequency. The transformed fitnesses are also frequency dependent, but are functions of individual genotype frequencies.

Table 1 gives some additional two-allele examples. These preserve allele-frequency equations but not necessarily total population changes. Example (a) transforms a constant-fitness model with complete dominance to a frequency dependent one. When \( s = 1 \) the transformation is \( \{1, 1, 0\} \rightarrow \{1 - p_1, 1, p_1\} \), which reverses the dominance. Example (b) transforms a gene frequency-dependent model into a genotype frequency-dependent one. In example (c) a gene frequency-dependent model is transformed into a constant fitness, multiplicative model and in (d) to an additive model. Example (e) shows a frequency-dependent, multiplicative model that is transformed into a frequency-independent additive one.

**Nonrandom mating:** If \( P_i \) is the frequency of the genotype \( A_i A_j \) and \( \theta_i = P_i / \theta_j \), the transformations \( w^{\text{Multi}}_i = w_i / \theta_j \) and \( w^{\text{Add}}_i = (w_i + w_j - \tilde{w}) / \theta_j \) and all linear combinations preserve equations 3. A simple example of a multiplicative transformation, with genotype frequencies, \( P_{11}, 2P_{12} \) and \( P_{22} \), is \( \{1, 1, 0\} \rightarrow \{1/\theta_{11}, 1, (p_1 \theta_{12})^2 / \theta_{22}\} \). In this case Equations 3 are not complete; there must be an additional rule for the change in the \( \theta_{i j} \).

**TWO LOCI**

With two loci, each with two alleles, we designate the four haplotypes, \( AB, Ab, aB \) and \( ab \), by 1, 2, 3 and 4 and their frequencies by \( x_1, x_2, x_3 \) and \( x_4 \). Then

\[
\tilde{w} \alpha' = x_i (w_i + k_c wD / x_i)
\]

\[
w_j = \sum_j x_j w_{ij}
\]

(4)

in which \( w_{ij} \) is the fitness of the zygote formed from gametes \( i \) and \( j \). \( c \) is the proportion of recombinants between the \( A \) and \( B \) loci, \( D = (x_1 x_4 - x_2 x_3) \), \( w \) is the fitness of the double heterozygote, and \( k_c = 1 \) when \( i = 2 \) or \( 3 \) and \( -1 \) when \( i = 1 \) or \( 4 \) [see for example EWENS (1979, p. 56)].

We now assume that \( w = w_{14} = w_{25} \) is the same before and after transformation. This means that only relative frequency changes are preserved, not the change of total population number. We then let

\[
w_i' + k_c wD / x_i = w_i + k_c wD / x_i,
\]

(5)
Alternative Fitness Models

TABLE 1
Genotypic fitnesses under different models, A and B, that lead to the same equation for allele frequency change

<table>
<thead>
<tr>
<th></th>
<th>Model A</th>
<th>Model B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$A_A A_A$</td>
<td>$A_A A_B$</td>
</tr>
<tr>
<td>(a)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>(b)</td>
<td>$p_2$</td>
<td>1</td>
</tr>
<tr>
<td>(c)</td>
<td>$a - p_2$</td>
<td>1</td>
</tr>
<tr>
<td>(d)</td>
<td>$2a - (a - b + 1)p_2$</td>
<td>1</td>
</tr>
<tr>
<td>(e)</td>
<td>$a + b p_1$</td>
<td>1</td>
</tr>
</tbody>
</table>

or

\[ w_i^{tr} = w_i. \] (6)

Since \( w \) is unchanged by the transformation, this yields 4 equations and 8 unknowns. Four fitnesses can be chosen arbitrarily and the others are then determined. An example of a transformation obtained in this way is given in Table 2. The quantities, \( a, b, c \) and \( d \), are arbitrary and can be functions of haplotype frequencies, but must be chosen so that none of the fitnesses is negative.

An alternative is to use pseudo-fitnesses (DENNISTON 1978). The “fitness,” \( r_{ij} \), of genotype \( A_i A_j \) is the relative proportion of this genotype next generation. Thus \( P_i = P_j r_{ij} / \bar{r} \) and the change of allele or haplotype frequency is given by Equation 3a. Thus the same methods as were used for a single locus are applicable. Although this shows that appropriate transformations of pseudo-fitnesses exist, it does not demonstrate that transformations exist for traditional fitnesses.

Two loci at linkage equilibrium: It is clear that the major complication in writing a simple two-locus transformation is linkage disequilibrium. When \( D = 0 \), as is approximately true for most pairs of loci in many natural populations, the situation is much simpler.

Assume random mating proportions and let \( p_i p_j p_k p_l \) and \( w_{ijkl} \) be the frequency and fitness of genotype \( A_i A_j B_k B_l \); we also assume, as usual, that cis and trans heterozygotes have equal fitnesses. The equation for change of allele \( A_i \) is

\[ p_i' = \frac{p_i w_i}{\bar{w}} \] (7)

in which \( w_i = \Sigma_{ijkl} p_i p_j p_k p_l w_{ijkl} \) and \( \bar{w} = \Sigma_{ijkl} p_i p_j p_k p_l w_{ijkl} \). The multiplicative and additive transformations are:

\[ w_{ijkl}^{mult} = w_{ijkl} w_i / \bar{w} \] (8)

\[ w_{ijkl}^{add} = w_i + w_j + w_k + w_l - \bar{w} \] (9)

With these transformations, \( w_i^{mult} = w_i^{add} = w_i \), and the allele frequency changes are described by (7) or (3a), and population number, if of interest, can be obtained from (5b).

A transformation that preserves dominance relations: Suppose there are two loosely linked loci, each with two alleles, complete dominance, random mating, and linkage equilibrium. We then choose a transformation that leaves the dominance unchanged. The model is:

\[
\begin{align*}
\text{Genotype} & \quad A_A A_A \quad A_A A_B \quad A_B A_B \quad A_B a_b \\
\text{Frequency} & \quad (1 - p)^2 \quad (1 - q)^2 \quad (1 - p^2) \quad (1 - q^2) \\
\text{Fitness} & \quad w_{A_A A_A} \quad w_{A_A A_B} \quad w_{A_B A_B} \quad w_{A_B a_b}
\end{align*}
\]

The single-locus, genotypic fitnesses are

\[ w_{A_A} = (1 - q^2) w_{A_A A_B} + q^2 w_{A_A A_B} + q^2 w_{A_B a_b}, w_{a_B} = (1 - p^2) w_{a_A A_B} + p^2 w_{a_A a_b} - w_{a_B a_b}, w_{A_B} = (1 - p^2) w_{A_A A_B} + p^2 w_{a_A A_B} + p^2 w_{a_B a_b} \]

The equations of allele frequency change are

A locus:

\[ \Delta p = - \frac{(1 - p)(1 - q^2) w_{A_A A_B} + q^2 w_{A_B a_b} - \bar{w})}{\bar{w}} \] (10a)

B locus:

\[ \Delta q = - \frac{(1 - q)(1 - p^2) w_{A_A A_B} + p^2 w_{a_B a_b} - \bar{w})}{\bar{w}} \] (10b)

The desired transformations are

Multiplicative: \( w_{ijkl}^{mult} = w_i = w_{ijkl} / \bar{w} \), etc.

Additive: \( w_{ijkl}^{add} = w_i + w_j + w_k + w_l - \bar{w} \), etc.

The transformed fitnesses lead to (10), as expected.

HALDANE (1931, p. 191) considered the case where \( w_{A_A A_B} = 1, w_{a_B a_b} = 1 - 4k, w_{a_A A_B} = 1 - k, \) and \( w_{a_b A_B} = 1 + 11k \). If \( k \) is small and positive this leads to an unstable equilibrium at \( p = 0.516 \) and \( f = 0.258 \). The transformations are multiplicative or additive between loci and the fitnesses are functions of the phenotype frequencies. For example, the multiplicatively trans-
formed relative fitnesses of the four phenotypes are:

\[
A - B = 1 \rightarrow [1 - 4kq^2][1 - kp^2]
\]

\[
A - bb: 1 - 4k \rightarrow [1 - 4kq^2][1 - 4k(1 - p^2) + 11kp^2]
\]

\[
aaB - 1 - k \rightarrow [1 - k(1 - q^2) + 11kq^2][1 - kp^2]
\]

\[
aabb: 1 + 11k \rightarrow [1 - k(1 - q^2) + 11kq^2] \cdot [1 - 4k(1 - p^2) + 11kp^2].
\]

The trajectories, including the point of metastable equilibrium, are preserved.

**DISCUSSION**

The major conclusion of this article, perhaps not a surprising one, is that there are always transformations of the fitnesses that lead to the same equations of allele or haplotype frequency change. Hence it is not possible to distinguish among these models from the trajectories or from the distribution of frequencies at equilibrium. For a single locus it is always possible to find a transformation of the fitnesses that is multiplicative, or additive, or a linear combination of these. Additional transformations can be obtained by equating the allelic fitnesses (or gametic in the case of two loci) before and after transformation.

Perhaps the most striking conclusion is that an overdominant, single-locus fitness set can be transformed into a set with no dominance (additive) or one with multiplicative fitnesses. For the latter, heterozygotes are always less than the mean of the corresponding homozygotes, since the geometric mean is less than the arithmetic. Furthermore, since a multiplicative model is equivalent to a haploid model (Li 1959; Nagylaki 1975), it is always possible to transform a diploid model into a frequency-dependent, haploid one with the same allele-frequency dynamics.

We have shown that for a single locus it is always possible to transform a set of frequency-independent fitnesses into one that is frequency-dependent. The converse is not generally true, as can be seen from the following example. With constant fitness coefficients the mean fitness always increases unless the population is at an equilibrium point (see, for example, Ewens 1979, pp. 40–42). If the allele frequencies cycle, they cannot be transformed into a set of frequency-independent fitnesses.

Our procedure is also applicable to the Wright-Fisher stochastic model. In this model, each genotype contributes in proportion to its fitness to an infinite gamete pool, then a finite sample of gametes is drawn to produce the next generation. Since the sampling process involves only gametes, it is not genotype-dependent. The transformations described here preserve equations based on this model. The Markov chains are identical.

Furthermore, mutation does not affect these transformations whether deterministic or stochastic. Since mutation is gene-dependent and does not depend on zygotic properties, it does not affect the transformations that preserve relative allelic fitnesses.

A stochastic model in which our fitness transformations do not preserve the Markov process is the Ether-Nagylaki model (see Nagylaki 1990). In this more realistic model, the stochastic element comes when the population number is reduced by density regulation, a process involving genotypes, not simply alleles. Nevertheless, this model leads to the same diffusion equations as the Fisher-Wright model. Since the diffusion term in the equation involves only allele frequencies and effective population number, and the mean change term is derived from (3a), the equations are unchanged under transformation. Thus, such properties as probability of and mean time to fixation (Kimura 1964) are preserved. Different models can lead to the same diffusion limit; any of these preserve the transition equations to the accuracy of the diffusion approximation.

Finally, we note that although the transformed fitnesses lead to the same equations of allele or haplotype frequency change as the original fitnesses, there may be other ways in which they can be distinguished. One possibility is direct measurement of genotypic fitnesses at different allele frequencies to determine frequency dependence directly. Another possibility is to count individuals at different stages of the life cycle. For example, transformation (a) in Table 1, when \( s = 1 \), reverses the dominance and converts a class with zero fitness into one with positive fitness. If the cause of the zero fitness is lethality, comparison of zygotic with adult frequencies could permit a distinction. It is also
possible that two sets of fitnesses that lead to equivalent deterministic equations may differ stochastically. As stated above, this will not happen with the diffusion equations if the stochastic element is caused by finite population size. But if the variance is dependent on genotype frequencies the stochastic equations could differ after transformation while the deterministic ones remained unchanged.

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