Evolutionary principles for polynomial models of frequency-dependent selection

JAMES W. CURTSINGER

Department of Genetics and Cell Biology, University of Minnesota, 1445 Gortner Avenue, St. Paul, MN 55108

ABSTRACT   A one-locus two-allele deterministic model of frequency-dependent selection is analyzed, where genotypic fitnesses $[w_i(q)]$ are assumed to be nth-degree polynomial functions of allelic frequency (q). The model encompasses many modes of selection, including intraspecies competitive interaction, brood selection, meiotic drive, cyclical selection, and mixed models. Allelic frequencies converge monotonically to locally stable equilibria provided that $|dw_i(q)/dq|$ is not large. There exists a function $T(q)$ that is nondecreasing and locally maximized at locally stable equilibria. The rate of change of $T(q)$ per generation is approximately equal to the additive genetic variance in fitness. $T(q)$ is a simple function of the average effect of an allelic substitution and is closely related to Wright's "fitness function." These results define "evolutionary landscapes" for some complex selection processes and enlarge the scope of the classical methods embodied in Wright's "mean fitness principle" and Fisher's "fundamental theorem."

Many ecological observations suggest that genotypic fitness parameters in natural populations are not invariant but are instead dependent on the genetic composition of the population (1). A general advantage of rareness, a tendency for similar organisms to compete most intensely for limited resources, and an occurrence of genotype-specific behavioral interactions are three of the many possible factors that can cause fitness to vary with allelic or genotypic frequencies. Deterministic models that incorporate frequency variables in the fitness parameters do not generally conform to Wright's "mean fitness principle," invalidating the concept of "evolutionary landscape" (2). Although some particular frequency-dependent selection models can be analyzed on a case-by-case basis, there is no known general principle that governs the dynamics of frequency dependence. Thus, the subject of frequency-dependent selection has a high ratio of experimental interest to theoretical understanding.

A rather general class of one-locus two-allele deterministic frequency-dependent selection models is investigated here. Genotypic fitnesses are assumed to be nth-order polynomial functions of allelic frequency. This parameterization encompasses many modes of selection, including pairwise and higher-order organismal interaction, brood selection, reproductive compensation, aposematic selection, altruism towards sibs, selection under constant inbreeding, meiotic drive, gametic selection, cyclical selection, the classical case of constant viability selection coefficients, and mixed models incorporating constant and variable fitness components (3–9). It is shown that there are two principles that govern the model dynamics, one related to Wright's "mean fitness principle" and one related to Fisher's "fundamental theorem."

MATHEMATICAL ANALYSIS

The Model. Assume large population size, discrete generations, random mating, Mendelian segregation, and negligible mutation and immigration rates. In the parental generation, autosomal alleles A_1 and A_2 have relative frequencies p and q respectively, where $p + q = 1$. Viability, the relative probability of survival from zygote to adult stage, is an nth-order function of allelic frequency:

$$w_i(q) = \sum_{j=0}^{n} a_{i,j} q^j, \qquad [1]$$

where $i = 1$, 2, and 3, corresponding to genotypes A_1A_1, A_1A_2, and A_2A_2, respectively. The $a_{i,j}$ are constrained such that $w_i(q) \geq 0$ for all q on $(0,1)$. Denoting allelic frequencies in the offspring generation after selection by p' and q', transformation equations are

$$\overline{W}(q)q' = q^2 w_3(q) + pq w_2(q)$$

and

$$p' = 1 - q', \qquad [2]$$

where $\overline{W}(q) = p^2 w_1(q) + 2pq w_2(q) + q^2 w_3(q)$ is the average zygotic viability or "mean fitness." By suppressing the argument of the $w_i(q)$ and $\overline{W}(q)$, the change in frequency from parental to offspring generation is $\Delta q = q' - q$:

$$\overline{W}\Delta q = pq[q(w_1 - 2w_2 + w_3) + w_2 - w_1]. \qquad [3]$$

Equilibria $\hat{q} = 0$ and $\hat{q} = 1$ always exist. In addition, there may exist from 0 to $n + 1$ equilibria of the form:

$$\hat{q} = \frac{w_1 - w_2}{w_1 - 2w_2 + w_3}. \qquad [4]$$

The local stability of a particular equilibrium $\hat{q}_0$ depends on the sign and magnitude of $d\Delta q/dq$, evaluated at $\hat{q}_0$. There are in general six possibilities: (i) If $d\Delta q/dq > 0$, then $\hat{q}_0$ is unstable. After a perturbation, q diverges monotonically from $\hat{q}_0$. (ii) If $d\Delta q/dq = 0$, then $\hat{q}_0$ is neutrally stable. (iii) If $-1 \leq d\Delta q/dq < 0$, then $\hat{q}_0$ is stable. After a perturbation, q converges monotonically to $\hat{q}_0$. (iv) If $-2 < d\Delta q/dq < -1$, then $\hat{q}_0$ is stable. After a perturbation, q converges to $\hat{q}_0$ by damped oscillations. (v) If $d\Delta q/dq = -2$, then q exhibits stable oscillations about $\hat{q}_0$. (vi) If $d\Delta q/dq < -2$, then q exhibits increasing oscillations about $\hat{q}_0$.

It can be shown that $d\Delta q/dq \geq -1$ for an interesting class of models, indicating that convergence is monotonic. The proof follows. Let $\hat{w}_i \equiv w_i(\hat{q})$ and $\Delta w_i \equiv w_i(q') - w_i(q)$. Then, by evaluating at equilibrium and suppressing allelic

frequency arguments,

$$\frac{d\Delta q}{dq} = \frac{\hat{p}\hat{q}}{\overline{W}} \times$$

$$\left[\hat{w}_1 - 2\hat{w}_2 + \hat{w}_3 + \hat{q} \frac{d(w_1 - 2w_2 + w_3)}{dq} + \frac{d(w_2 - w_1)}{dq}\right]. \quad [5]$$

For $d\Delta q/dq < -1$, it is necessary that

$$Z \equiv \hat{p}\hat{q}\left[\hat{w}_1 - \hat{p}\frac{dw_1}{dq} + \hat{w}_3 + \hat{q}\frac{dw_3}{dq}\right]$$

$$+ \hat{p}^2\hat{w}_1 + \hat{q}^2\hat{w}_3 + \hat{p}\hat{q}(\hat{p} - \hat{q})\frac{dw_2}{dq} < 0. \quad [6]$$

However, Eq. 6 cannot be satisfied if $\hat{w}_i \geq |dw_i/dq|$, meaning that the frequency-dependent component of fitness cannot change rapidly relative to net genotypic fitness. Under this condition the term in brackets in Eq. 6 is nonnegative. There are four conditions under which the last term of Eq. 6 can be negative:

(*i*) If $\hat{w}_1 - 2\hat{w}_2 + \hat{w}_3 > 0$, $\hat{w}_3 > \hat{w}_1$, and $dw_2/dq < 0$, then $\hat{w}_1 > \hat{w}_2$ and $\hat{w}_1 + dw_2/dq > 0$. Thus, $Z \geq \hat{p}^2[\hat{w}_1 + \hat{q}(dw_2/dq)] > 0$.

(*ii*) If $\hat{w}_1 - 2\hat{w}_2 + \hat{w}_3 > 0$, $\hat{w}_3 < \hat{w}_1$, and $dw_2/dq > 0$, then $\hat{w}_3 > \hat{w}_2$ and $\hat{w}_3 - dw_2/dq > 0$. Thus, $Z \geq \hat{q}^2[\hat{w}_3 - \hat{p}(dw_2/dq)] > 0$.

(*iii*) If $\hat{w}_1 - 2\hat{w}_2 + \hat{w}_3 < 0$, $\hat{w}_3 > \hat{w}_1$, and $dw_2/dq > 0$, then $\hat{w}_2 > \hat{w}_3$. $Z > \hat{p}\hat{q}[\hat{w}_3 + (\hat{p} - \hat{q})dw_2/dq] \geq \hat{p}\hat{q}[\hat{w}_3 + (\hat{p} - \hat{q})\hat{w}_2] = \hat{p}\hat{q}(\hat{w}_3 - \hat{w}_2)(\hat{w}_1 + \hat{w}_3)/(\hat{w}_1 - 2\hat{w}_2 + \hat{w}_3) > 0$.

(*iv*) If $\hat{w}_1 - 2\hat{w}_2 + \hat{w}_3 < 0$, $\hat{w}_3 < \hat{w}_1$, and $dw_2/dq < 0$, then $\hat{w}_2 > \hat{w}_1$. $Z > \hat{p}\hat{q}[\hat{w}_1 + (\hat{p} - \hat{q})dw_2/dq] \geq \hat{p}\hat{q}[\hat{w}_1 - (\hat{p} - \hat{q})\hat{w}_2] = \hat{p}\hat{q}(\hat{w}_1 - \hat{w}_2)(\hat{w}_1 + \hat{w}_3)/(\hat{w}_1 - 2\hat{w}_2 + \hat{w}_3) > 0$.

Thus $Z > 0$, $d\Delta q/dq \geq -1$, and convergence is monotonic near locally stable equilibria.

It is important to note that there exist polynomial frequency-dependent viability functions that generate oscillatory convergence to stable equilibria, but such functions violate the condition on dw_i/dq. For instance, if $w_1 = q^3$, $w_2 = 1$, and $w_3 = (1 - q)^3$, then there is a stable polymorphic equilibrium at $\hat{q} = 0.5$, where $d\Delta q/dq < -1$. Functions that generate oscillatory behavior are characterized by a large change in w_i over small frequency changes; these may be of biological interest but are excluded from the present analysis. A peculiarity of this restriction is that the model behavior is sensitive to linear changes in the w_i. If, for instance, we add a constant equal to unity to each w_i above, then the monotonic convergence is restored. This situation contrasts sharply with the usual observation that model behavior is qualitatively invariant under linear transformation of the genotypic fitnesses.

A Maximization Function. Under the present assumptions, the w_i are "weights" as defined by Lewontin (4). That is, given allelic frequencies p and q in the parental generation, there exist U_i such that genotypic frequencies in the offspring generation after selection are proportional to p^2U_1, $2pqU_2$, and q^2U_3. For models in which the weights can be defined, there may exist a maximization function "$T(q)$" (10) provided that Eq. 7 is integrable:

$$T(q) \equiv 2\int[q(U_1 - 2U_2 + U_3) + U_2 - U_1]dq. \quad [7]$$

The maximization function consists of an "additive" and a "dominance" effect of the allele A_2. For frequency-dependent viability selection as specified in Eq. 1,

$$T(q) = 2\sum_{j=0}^{n}$$

$$\left[\frac{1}{j+1}(a_{2,j} - a_{1,j})q^{j+1} + \frac{1}{j+2}(a_{1,j} - 2a_{2,j} + a_{3,j})q^{j+2}\right] \quad [8]$$

plus a constant of integration. For the special case of constant viability selection coefficients, $T(q)$ differs from $\overline{W}$ by a constant of integration. Note that, from Eqs. 7 and 3,

$$\Delta q = \frac{pq}{2\overline{W}}\frac{dT(q)}{dq}. \quad [9]$$

Eq. 9 shows that there is a one-to-one correspondence between critical points of $T(q)$, which is continuous, and polymorphic equilibria. Differentiating Eq. 9 shows that the condition for local stability of an equilibrium implies $d^2T(q)/dq^2 < 0$. Thus, locally stable polymorphic equilibria occur at local maxima of $T(q)$, and unstable equilibria occur at local minima of $T(q)$. Given the additional fact that allelic frequencies converge monotonically, it follows that $T(q)$ is nondecreasing through time.

A "Fundamental Theorem." For the classical model of constant viability selection coefficients, the average effect of allele "i," denoted α_i, is defined as the difference between two quantities: the average viability of the population and the average viability of a subset that receives allele "i" from one parent, the other gamete being drawn at random (11, 12). This definition can be extended to frequency-dependent viability selection as defined in Eq. 1:

$$\alpha_1 = pw_1 + qw_2 - \overline{W}$$

$$= \sum_{j=0}^{n}[(a_{1,j} - a_{2,j})q^{j+1} - (a_{1,j} - 2a_{2,j} + a_{3,j})q^{j+2}], \quad [10a]$$

$$\alpha_2 = pw_2 + qw_3 - \overline{W}$$

$$= \sum_{j=0}^{n}[(a_{2,j} - a_{1,j})q^{j} + (2a_{1,j} - 3a_{2,j} + a_{3,j})q^{j+1}$$

$$- (a_{1,j} - 2a_{2,j} + a_{3,j})q^{j+2}]. \quad [10b]$$

Now define the average effect of an allelic substitution $\alpha \equiv \alpha_2 - \alpha_1$, and the additive genetic variance, $V_a \equiv 2pq\alpha^2$.

The change in $T(q)$ from generation to generation is $\Delta T = T(q') - T(q)$:

$$\Delta T = 2\sum_{j=0}^{n}\left[\frac{1}{j+1}(a_{2,j} - a_{1,j})(q'^{j+1} - q^{j+1})\right.$$

$$\left. + \frac{1}{j+2}(a_{1,j} - 2a_{2,j} + a_{3,j})(q'^{j+2} - q^{j+2})\right]$$

$$= \frac{2pq\alpha^2}{\overline{W}}\left[1 + \frac{pq}{\overline{W}}(E_1 + E_2)\right],$$

where

$$E_1 = \sum_{j=0}^{n}\sum_{k=2}^{j+2}\left[(a_{1,j} - 2a_{2,j} + a_{3,j})\left(\frac{1}{j+2}\right) \times \right.$$

$$\left. \binom{j+2}{k}(\Delta q)^{k-2}(q^{j+2-k})\right],$$

and

$$E_2 = \sum_{j=1}^{n}\sum_{k=2}^{j+1}\left[(a_{2,j} - a_{1,j})\left(\frac{1}{j+1}\right) \times \right.$$

$$\left. \binom{j+1}{k}(\Delta q)^{k-2}(q^{j+1-k})\right]. \quad [11]$$

For the case of constant selection coefficients, Eq. 11 is identical to the expression for $\Delta \overline{W}$ given by Crow and Kimura (13). Provided that selection is not very intense, the quantity in brackets is ≈ 1, hence $\Delta T \approx V_a/\overline{W}$ for many cases.

The parameterization in terms of average effects makes it possible to simplify $T(q)$ as defined in Eq. 8:

$$T(q) = 2\int \alpha \, dq. \qquad [12]$$

Thus, the maximization function is a simple function of the average effect of an allelic substitution.

DISCUSSION

Wright (14) showed that there exists a function that is maximized at equilibrium for certain frequency-dependent selection models. The major result of this study is that the class of nth-degree polynomial frequency-dependent selection models is "well-behaved" in a dynamic sense: one can define a maximization (Lyapunov) function that is nondecreasing and that changes at a rate approximately proportional to the additive genetic variance. The proof consists of demonstrating that local maxima of $T(q)$ correspond to locally stable equilibria, that local minima of $T(q)$ correspond to unstable equilibria, and that allelic frequencies converge monotonically; it follows that the change in $T(q)$ associated with nonzero Δq is positive within the domain of a locally stable equilibrium. Knowledge of the maximization function allows one to determine the number, location, and stability of all equilibria and to predict allelic frequency trajectories. Thus, there exist "evolutionary landscapes" for a special but biologically significant class of models that subsumes the classical case of constant selection coefficients.

The critical feature that allows this generality is that selective coefficients for many modes of selection are "weightable"—i.e., given allelic frequencies p and q in the parental generation, there exist U_i such that postselection progeny genotypic frequencies are proportional to p^2U_1, $2pqU_2$, and q^2U_3. Many modes of selection involving organismal interactions fall into the "weightable" category, but there are obvious exceptions, such as fertility selection. The analytical method developed here has some generality, but is it not universal. The convergence proof is subject to the limitations of local equilibrium analysis. A further limitation of the meth-od, discussed elsewhere (10), is its restriction to one-locus two-allele models.

The maximization function $T(q)$ includes as a special case the usual mean fitness function $\overline{W}$, but it is not similarly interpretable as a measure of zygotic fitness, except for the special case of constant selection coefficients. $T(q)$ is most concisely defined as a function of the average effect of an allelic substitution, as shown in Eq. 12. Templeton (15) has noted that many of the classical formulae for Δq, derived for various modes of natural selection, can be regarded as special cases of a general formulation that includes an average excess parameter. Average effect, closely related to average excess, appears to play a similar role in generalizing the formulation of maximization functions. Whether there exists some other intuitively appealing interpretation of the function remains to be determined and is in any case of secondary importance to the issue of generality. Intuition evolves under the influence of theoretical advances.

1. Clarke, B. (1979) *Proc. R. Soc. London Ser. B* **205**, 453–474.
2. Li, C. C. (1967) *Biometrics* **23**, 397–484.
3. Li, C. C. (1955) *Am. Nat.* **89**, 281–296.
4. Lewontin, R. C. (1958) *Genetics* **43**, 421–433.
5. Clarke, B. & O'Donald, P. (1964) *Heredity* **19**, 201–206.
6. Wright, S. (1969) *Evolution and the Genetics of Populations* (Univ. of Chicago Press, Chicago), Vol. 2.
7. Cockerham, C. C., Burrows, P. M., Young, S. S. & Prout, T. (1972) *Am. Nat.* **106**, 493–515.
8. Templeton, A. R. (1979) *Am. Nat.* **114**, 515–524.
9. Hoekstra, R. F. (1975) *Genet. Res.* **25**, 1–15.
10. Curtsinger, J. W. (1984) *Evolution*, in press.
11. Fisher, R. A. (1958) *The Genetical Theory of Natural Selection* (Dover, New York), 2nd Ed.
12. Falconer, D. S. (1981) *Introduction to Quantitative Genetics* (Longman, London), 2nd Ed.
13. Crow, J. F. & Kimura, K. (1970) *An Introduction to Population Genetics Theory* (Harper & Row, New York), p. 208.
14. Wright, S. (1955) *Cold Spring Harbor Symp. Quant. Biol.* **20**, 16–24.
15. Templeton, A. R. (1982) in *Perspectives on Evolution*, ed. Milkman, R. (Sinauer, Sunderland, MA), pp. 15–31.