Evolution, 47(6), 1993, pp. 1733–1743

PEAK SHIFTS AND POLYMORPHISM DURING PHASE THREE OF WRIGHT'S SHIFTING-BALANCE PROCESS

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Abstract.—The third phase of Wright's shifting-balance theory involves the export of adaptive gene combinations from one subpopulation to another. Previous results have demonstrated that this can occur at very low migration rates, but it has been argued that this simply reflects the ability of migration to overcome selection and fix any (even deleterious) alleles. Here, previous analyses are extended by concentrating on the critical balance between forward and reverse migration rates that still allows phase III to proceed. It is shown that selective advantage, dominance, recombination rate, and the number of loci all affect the ability of a genotype to invade and become fixed in a new subpopulation, but it is unlikely that phase III will occur in the absence of differential migration unless the invading genotype consists of a few dominant loci with a large selection advantage, spreading into a few populations of lower fitness. Therefore, as was envisioned by Wright, differential migration from more to less fit populations will be necessary for phase III to occur under most circumstances.

Key words.—Gene flow, group selection, population subdivision, Wright's shifting-balance theory.

Received July 30, 1992. Accepted December 28, 1992.

Over 60 yr ago Sewall Wright proposed his shifting-balance theory of evolution as a solution to the conundrum that alleles that are individually deleterious but advantageous in combination cannot become fixed in a large population because they are selected against when at low frequencies (Haldane 1931; Wright 1931, 1932, 1977, 1988). In terms of Wright's familiar peaks and valleys metaphor, natural selection by itself is incapable of reaching the global fitness optimum (or peak) generated by the new alleles, because selection always acts to move the population towards a local optimum. If population size is restricted, however, genetic drift can randomly increase the frequency of the deleterious alleles until such a point that they are found more often in combination than separately (i.e., the population passes through the adaptive valley). This constitutes phase I of Wright's process. After reaching this frequency, mass selection then drives the alleles toward fixation (phase II).

In a single population, phase I can take a very long time unless the population is very small, in which case it is then susceptible to extinction caused by demographic fluctuations. To overcome this problem, Wright imagined a network of many semiisolated demes connected through the exchange of migrants. If the advantageous alleles become fixed in one of these demes, the mean fitness of that deme will be increased, and it should therefore send out more migrants into surrounding demes. These migrants then invade the surrounding demes, upgrading their fitness, and so on until the alleles become fixed in the species as a whole. It is this upgrading of fitness through differential migration (phase III) that will be the subject of this paper.

The difficulty with phase III is that an advantageous allelic combination carried by incoming migrants is likely to be rapidly broken up by recombination when these migrants mate with resident genotypes. This problem led Haldane (1959) to conclude that phase III was therefore the weakest part of Wright's argument. Contrary to the expectation of difficulties with phase III, however, Crow et al. (1990) demonstrated that very little migration was sufficient to complete this final phase of the process. Indeed, they showed that phase III can occur under some circumstances even when the migration rate from the low fitness population is greater than that from the high fitness population. They therefore concluded, "whatever weaknesses the Wright theory may have, they are not in phase III (p. 233)." Barton (1992) disagreed with this interpretation, arguing instead that small migration rates can easily overcome the effects of selection to drive even deleterious alleles to fixation: "while populations may well diversify through a 'shifting balance,' it is difficult to see that this process leads to significant adaptation (p. 556)."

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Here, I extend the analyses of both Crow et al. (1990) and Barton (1992) by concentrating primarily on the balance in migration rates between high fitness and low fitness demes that results in one deme upgrading (or downgrading) the fitness of the other deme. This balance is described by the *invasiveness* of a genotype; that is, how easily a genotype from one deme can invade and become fixed in another deme in the face of reverse migration from that deme (Lande 1985). In general, phase III will depend on differential migration between a single high fitness subpopulation and several surrounding low fitness subpopulations (interdemic selection) unless the invading genotype is highly advantageous and dominant and the number of other subpopulations is not too large.

The Model

Recursion Equations.—Following Crow et al. (1990), consider two subpopulations that are initially fixed at different fitness optima and subsequently exchange migrants. For simplicity, I assume that selection occurs only through differences in viability and that selection precedes migration [the "adult migration" model of Crow et al. (1990); this is less favorable to Wright's theory than a "zygote migration" model]. In addition, mating is assumed to be at random, and generations are discrete and nonoverlapping. The two populations are labeled by the symbols x and y, such that the frequency of gamete i in each of the two populations is represented by x_i and y_i, respectively. Migration from y to x occurs at a rate m, and that from x to y at a rate m^*. I will focus on the y population and ask under which combination of migration rates do the gametes originally fixed in y become fixed in x.

A multilocus model with n loci and two alleles at each locus (2^n possible gametes) will be used. The allelic composition of each gamete and each possible recombinational outcome can be represented by a vector of length n, whose elements come from the set (0, 1). For example, the vector 11001 denotes the gamete ABcdE or recombinational outcome MMPPM. Letting w_{ij} be the fitness of a zygote formed from gametes i and j,

$$\bar{w}_x = \sum_{i,j} x_i x_j w_{ij}, \quad \text{and} \quad \bar{w}_y = \sum_{i,j} y_i y_j w_{ij},$$

the frequency of gamete i after one generation of selection and migration is

$$x_i' = \frac{(1 - m)}{\bar{w}_x} \sum_{j,k,\rho} x_j x_k w_{jk} P(\rho) + \frac{m}{\bar{w}_y} \sum_{j,k,\rho} y_j y_k w_{jk} P(\rho)$$

$$y_i' = \frac{(1 - m^*)}{\bar{w}_y} \sum_{j,k,\rho} y_j y_k w_{jk} P(\rho) + \frac{m^*}{\bar{w}_x} \sum_{j,k,\rho} x_j x_k w_{jk} P(\rho), \quad (1)$$

where $\bar{w}_x$ and $\bar{w}_y$ are the mean fitnesses in each population before migration, and $P(\rho)$ is the probability of obtaining ρ as a recombinational outcome, given the bit-wise comparison $i = (j \cap \rho) \cup (k \cap \bar{\rho})$ (for details see Crow et al. 1990, eq. 4). $P(\rho)$ is determined by the recombination rate, r. For fitness models in which the specific composition of a gamete is irrelevant (e.g., gamete 1001 is equivalent to gamete 0101), equation (1) can be reformulated simply in terms of the frequency of the "1" alleles, as suggested by Barton (1992). Use of this simplification also requires that the initial populations begin with either all or no "1" alleles and that there is free recombination among loci ($r = 0.5$). In this case, x_i and y_i then represent the frequency of individuals with i "1" alleles, and $P(\rho)$ is a composite probability of recombinational outcome (see the Appendix for details). This greatly increases the speed of calculations because it involves keeping track of only $n + 1$ rather than 2^n frequencies.

Fitness Model.—The fitness model employed here is similar to the multilocus model used by Crow et al. (1990), with the additional feature of some scaling between dominant and recessive gene action. Consider a model of gene action in which the products of n loci each make an equal and necessary contribution to some final outcome. Two separate combinations of alleles at these loci produce a successful outcome, although one combination is superior to the other. However, any break in the chain of compatible alleles disrupts the pathway and results in individuals with lowered fitness. Epistasis among loci is therefore complete, and the effect of having just one mismatched allele is identical to having two or more such alleles. Because this is a diploid model, dominance of one allele over another can either restore or disrupt the pathway, depending on which alleles are present at other loci. To reduce the number of possible parameters, it is assumed that all loci display the same level of dominance (h). These considerations lead to the following fitness classes.

Individuals that are homozygous for one set of alleles at each locus $\left(\text{i.e., } \frac{000..0}{000..0}\right)$ have fitness 1.0,

whereas individuals homozygous for the other set of alleles $\left(\text{i.e., } \frac{111..1}{111..1}\right)$ have fitness $1 + ks$. Individuals that are heterozygous at every locus $\left(\text{e.g., } \frac{100..1}{011..0}\right)$ have a fitness that depends on the dominance of the alleles from the high fitness set, $1 + hks$. Individuals homozygous for alleles that are all from the same fitness set at some loci and heterozygous at the other loci will have fitnesses that are also dependent on the degree of dominance. For instance, individuals whose loci are either heterozygous or homozygous for alleles from the high fitness set $\left(\text{e.g., } \frac{011..1}{101..1}\right)$ have fitness $1 + hks - (1 - h)s$, while those who are either heterozygous or homozygous for alleles from the lower fitness set $\left(\text{e.g., } \frac{010..0}{100..0}\right)$ have fitness $1 - hs$. Finally, individuals that do not have complete representations of either set $\left(\text{e.g., } \frac{101..1}{100..1}\right)$ have a reduced fitness, $1 - s$. This model corresponds to the "dominant favored" and "recessive favored" models of Crow et al. (1990) when $h = 1$ and $h = 0$, respectively.

Phase III.—Phase III can be considered to have occurred when either of the two populations becomes fixed for the genotype initially present in the other population. Note that this includes cases in which the low fitness population converts the high fitness population, as well as the opposite case. The final outcome of the migration process was therefore determined by iterating equation (1) until the mean fitnesses in both populations changed less than 10^{-8}. Phase III was determined to have occurred when the equilibrium frequency of the genotype initially fixed in a population was less than 10^{-5}.

I will first present results illustrating some typical dynamics for mean fitness under different levels of migration. I will then examine in detail the genetic factors that interact with migration rate to determine the outcome of phase III.

Results

Consider first the dynamics of gene frequency change for the two-population migration equations (eq. 1). Because the fitness model has two distinct peaks, one population is initially fixed at the higher fitness of optimum and the other at the lower fitness optimum. The migration rate from the high fitness to the low fitness population is given by m, and that in the opposite direction by m^*. The change in mean fitness can be used as an indicator of the underlying multilocus dynamics. Several sample trajectories of mean fitness are shown in figure 1. When the migration rate from both populations is low, each population remains in the vicinity of its respective peak and reaches an equilibrium between migration and selection (fig. 1A). Increasing the migration rate from the high fitness to low fitness population (m), causes both populations to equilibrate at the high fitness peak (fig. 1B). In this example, both populations go to the high peak even though the reverse migration rate is somewhat larger than the forward migration rate ($m^* > m$). Alternatively, increasing the reverse migration rate (m^*) causes both populations to go towards the lower fitness peak (fig. 1C). Simultaneously increasing m and m^* can result in the populations ending up at either the high peak or the lower peak, depending on the details of the model (such as the number of loci involved; fig. 1D). Note that regardless of the outcome, both populations experience a period of reduced mean fitness before they reach an equilibrium.

Clearly, the dynamics of change can be quite complex. Focusing only on the outcome of the process, however, greatly simplifies the analysis. For two populations and two optima, there are three possible outcomes: both populations end at the higher optimum, both populations end at the lower optimum, or both populations remain near the optimum at which they began. These three outcomes can be summarized in a phase diagram that differentiates the regions in parameter space associated with each end point. For example, the outcomes generated in figure 1 for the three-locus case can be predicted from the phase diagram shown in figure 2a. This figure illustrates the general form taken by all phase diagrams of this model. First, there are two large areas of monomorphic equilibria in which both populations go to a single peak. Whether the populations go to the higher or the lower peak for a given model depends on an approximately linear function of the ratio between the forward and reverse migration rates. Second, a small region in the lower left hand corner of the diagram corresponds to a polymorphic equilibrium maintained by a balance between migration and selection within each population. The size of this area is determined by the strength of selection, and comprises the region of parameter space in which $m/s \ll 1$ (Karlin and McGregor 1972; Bazykin 1973; for a discussion of the implications this region has for the maintenance of ge-

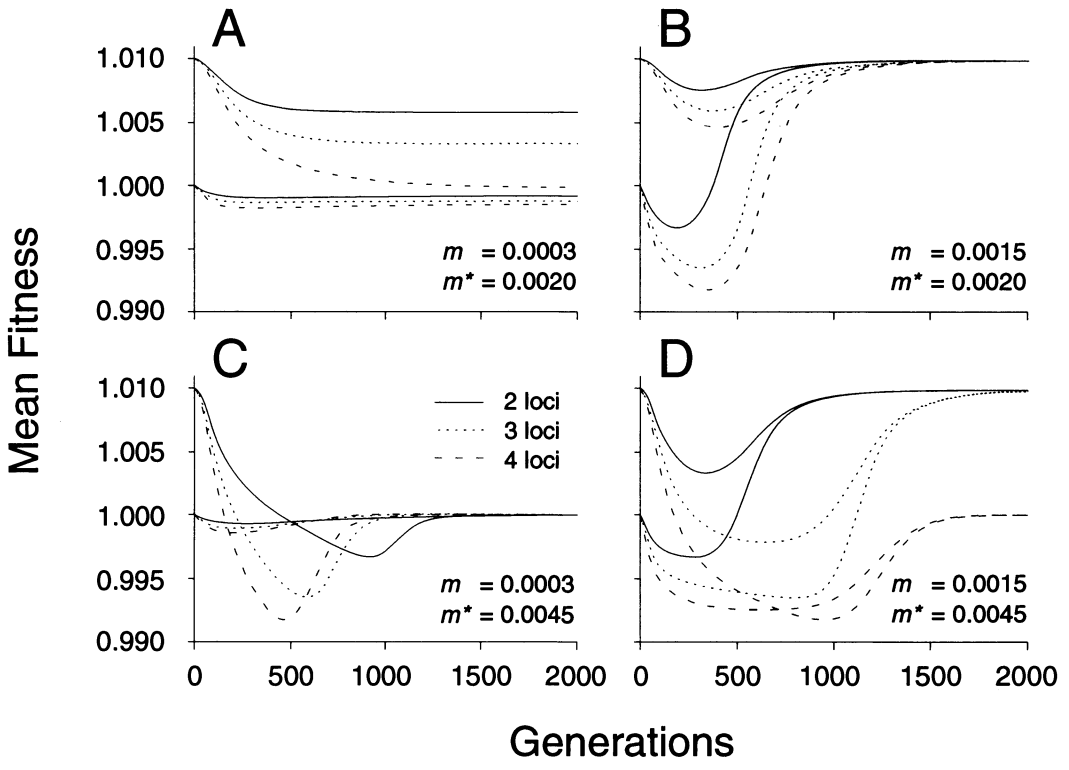

FIG. 1. Change in mean fitness through time. The mean fitness of the population that begins at the higher peak is shown by the line starting at 1.01; the mean fitness of the population that begins at the lower peak is shown by the line starting at 1.0. Different line styles show the trajectories for two-, three-, and four-locus models. The graphs show four combinations of two different migration rates in each direction, where m is the migration rate from the high fitness to the low fitness population, and m^* is the migration rate in the opposite direction. (A) Low migration both ways: both populations go to polymorphic equilibria with reduced mean fitness. (B) Increased migration high→low: both populations go to the higher peak. (C) Increased migration low→high: both populations go to the lower peak. (D) Higher migration in both directions: which peak the populations go to depends on the number of loci. Note that both populations go through a period of reduced mean fitness. For all graphs, s = 0.01, k = 1, r = 0.5, and h = 1 (complete dominance).

netic variance, see Phillips 1994). Any point on the line dividing two regions in the phase plot also represents a polymorphic equilibrium. Outside the lower-left corner, however, this equilibrium is unstable. The intersection of the line of polymorphic equilibria with the x-axis is the critical migration rate extensively discussed by Crow et al. (1990) and Barton (1992).

Point of No Return.—An inexorable approach to the monomorphic equilibria commences at the point of no return, the time at which stopping migration between the populations leads to the same outcome as continued migration (Crow et al. 1990). Stopping migration one generation before the point of no return causes both populations to return to their original optima. In the region of polymorphic equilibria, the point of no return is effectively infinite because stopping migration always leads to redifferentiation of the populations. As can be seen in figure 3, for a fixed amount of reverse migration, the point of no return slowly increases as division between the polymorphic and monomorphic equilibria is approached, and then rapidly grows to infinity at the division. Thus, the overall rate of approach to the monomorphic equilibria is relatively constant across most combinations of forward and reverse migration, except very near the boundaries between different classes of equilibria.

Relevance to Phase III.—Phase III of Wright's process occurs when both populations equilibrate at the higher peak. The relevant question here is under what conditions one population can upgrade (or downgrade) the fitness of another population. Clearly, anything that increases the slope of the line separating the monomorphic

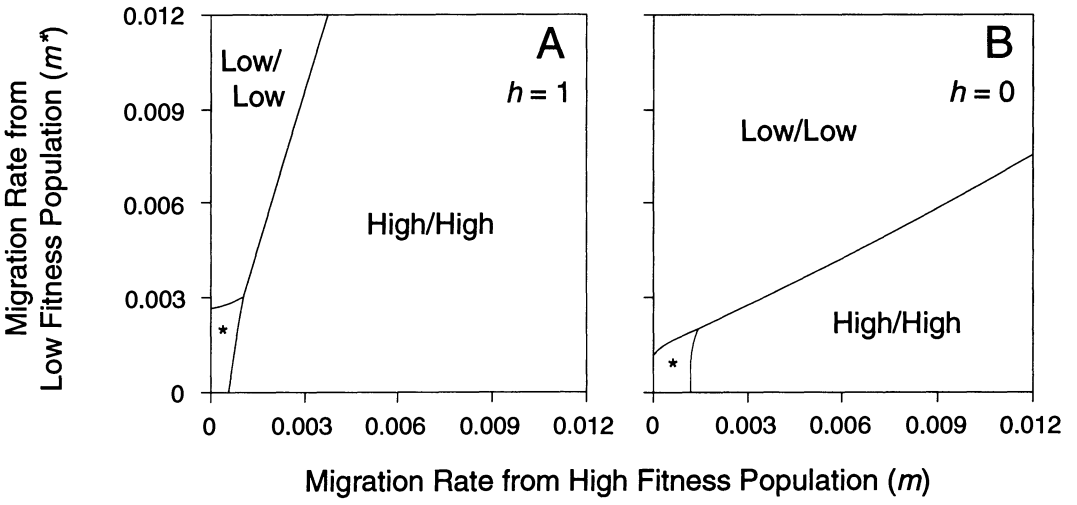

FIG. 2. Regions of equilibria for different combinations of forward and reverse migration rates. This graph represents the possible outcomes for a three locus model with parameters as in figure 1, except where noted. Three different equilibria are possible: both populations go to the high fitness peak (high/high), both population go to the low fitness peak (low/low), or both populations go to a polymorphic equilibrium in the vicinity of their original peaks (*). The slope of the line separating the low/low and high/high regions gives the invasiveness of the higher peak. A) Dominant favored, $h = 1$. B) Recessive favored, $h = 0$.

equilibria shown in figure 2 will facilitate phase III. I will call the slope of this line the *invasiveness* (I) of a peak, because the slope gives the amount of reverse migration a population can endure while still converting the other population. In some cases differential migration between the populations will be necessary to cross this line, in other cases, it will not.

Invasiveness

Defining invasiveness solely in terms of the slope ignores the area of polymorphic equilibria, which also partly influences the division between monomorphic equilibria. However, the slope is the major determinant of the outcome. As selection becomes weak, the area of polymorphic equilibrium becomes small (Phillips 1994), and the slope completely determines the division between equilibria.

Roughly then invasiveness is given by the ratio between the reverse and forward migration rates (m^*/m) at the point of transition from both populations going to the higher peak to both populations going to the lower peak. An invasiveness value of 1.0 therefore means that both peaks are balanced and, in the absence of differential migration, neither peak would be expected to overtake the other. An invasiveness value greater than 1.0 means that the genotype can invade even if the reverse migration rate is I times larger than the forward rate. The reciprocal is true when invasiveness is less than 1.0.

Analytical Approximation.—An approximation for invasiveness can be obtained using Barton's (1992) description of the shift between peaks when selection is weaker than migration. Because of the high migration rates, mixing between populations causes the allele frequencies in both populations to rapidly reach values of $y = m/(m + m^*)$. Which peak the populations eventually move toward then depends on whether this frequency lies within the domain of attraction of the higher or lower peak. Viewed in this way, the conversion process consists of two, somewhat independent steps: the initial attainment of the between-population migration equilibrium and the subsequent movement toward the selective equilibrium or peak. Separating the process into these two steps greatly simplifies the analysis.

The domains of attraction of the two peaks are separated by the valley between the peaks. The location of the valley can, in turn, be found by locating the point at which mean fitness takes its minimum value. Following Barton (1992), if it is assumed that all loci are at the same allele frequency (as would be the case if migration initially swamps selection) and that they are in linkage equilibrium, mean fitness can be written as

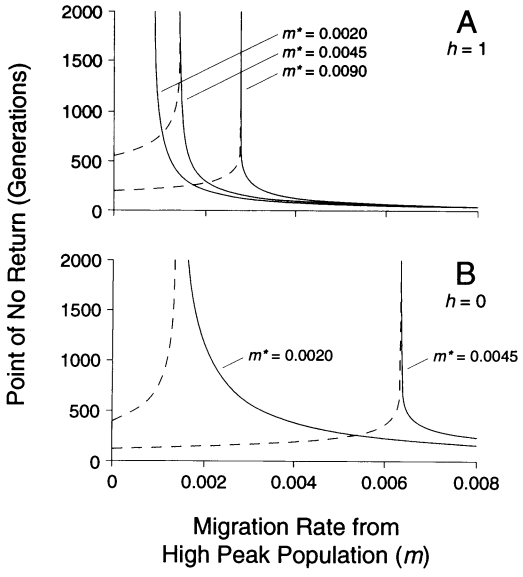

FIG. 3. Point of no return for the three locus case shown in figure 2. The solid line gives the point of no return obtained while approaching the high/high equilibrium, whereas the dotted line gives the same for the low/low equilibrium. Areas of polymorphic equilibria represent an effectively infinite point of no return. The different sets of lines show the point of no return for different levels of reverse migration. A) Dominant favored, $h = 1$. B) Recessive favored, $h = 0$. Parameters as in figure 1.

$$\bar{W} = 1 - s + (1 - h)s[(k + 1)y^{2n} + (1 - y^2)^n] + hs[(1 - y)^{2n} + (k + 1)(2y - y^2)^n], \quad (2)$$

where n is the number of loci and y is the allele frequency at each locus. Equation (2) takes its minimum with respect to y when

$$(1 - h)\tilde{y}[(k + 1)\tilde{y}^{2(n-1)} - (1 - \tilde{y}^2)^{n-1}] = h(1 - \tilde{y})[(1 - \tilde{y})^{2(n-1)} - (k + 1)(2\tilde{y} - \tilde{y}^2)^{n-1}]. \quad (3)$$

In general, it is necessary to find the largest real root ($\tilde{y}$) to (3) numerically, but in the special cases of $h = 1$ and $h = 0$,

$$\tilde{y} = 1 - \frac{1}{\sqrt{1 + (k + 1)^{-1/(n-1)}}}, \quad \text{and} \quad (4a)$$

$$\tilde{y} = \frac{1}{\sqrt{1 + (k + 1)^{+1/(n-1)}}}, \quad (4b)$$

respectively (Barton 1992, eq. 5). Invasiveness can then be calculated as

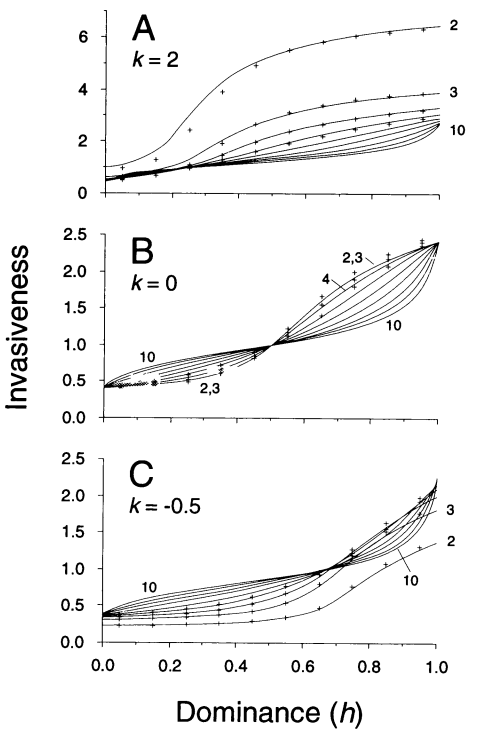

FIG. 4. Effect of dominance on invasiveness. Dominance scales between $h = 0$ (completely recessive) through $h = 0.5$ (additive) to $h = 1$ (completely dominant). Solid lines give the predicted results based on the approximation (eq. 6), while the +'s represent the exact results calculated from equation (1) for up to five loci (results for up to 10 loci were also calculated and agreed with the approximations but are omitted for clarity). The different lines within each figure indicate the results for models with different numbers of loci. A) Invading genotype is at a higher peak, $k = 2$. B) Invading genotype has same fitness as resident genotype, $k = 0$. C) Invading genotype is at a lower peak, $k = -0.5$. Note the change of scale in (B) and (C). For all graphs, $s = 0.01$ and $r = 0.5$.

$$I = m^*/m \quad (5)$$

$$\approx (1 - \tilde{y})/\tilde{y}. \quad (6)$$

This approximation will be compared to exact results obtained by iterating equation (1).

Effects of Dominance and Peak Height Asymmetry.—The more dominant a group of alleles are the easier it is for them to invade another population (figs. 4, 5). This can be most easily seen in figure 4B, in which both peaks are of the same height ($k = 0$). When alleles act additively ($h = 0.5$), neither peak has an advantage, and $I = 1$. Any increase in dominance ($h > 0.5$) enhances invasiveness ($I > 1$), while recessive alleles ($h < 0.5$) are at a disadvantage ($I < 1$).

Indeed, for any value of k, invasiveness increases with dominance, but whether it exceeds 1.0 depends on the particular value of k (fig. 4). A similar result has been found in the analysis of continuous populations, in which tension zones between hybrids tend to move in favor of dominant alleles (Mallet 1985; Johnson et al. 1990).

Populations that begin at higher peaks ($k > 0$) usually tend to be at an advantage, unless the higher peak is generated by very recessive alleles (fig. 5). Similarly, populations at lower peaks ($k < 0$) may overtake those at higher peaks if the low-peak alleles are strongly dominant over high-peak alleles (Figs. 4C and 5). No population that begins with a mean fitness that is below the value of the fitness of hybrids ($k \leq -1$) can ever invade another population with which it is exchanging migrants. Above this value, however, there will usually be some critical level of dominance at which the population can invade, even in the face of stronger reverse migration. In summary, then, for any fixed level of migration between two populations, more recessive alleles can invade if they produce a sufficiently higher peak, and allelic combinations that generate low peaks can invade if they are sufficiently dominant over other alleles.

Effect of the Number of Loci.—Increasing the number of loci dilutes the effects of any differences between the peaks by decreasing the invasiveness of high fitness peaks and enhancing the invasiveness of low fitness peaks (figs. 4, 5). With many loci, the likelihood that an advantageous migrant genotype will be reconstructed after recombining with resident genotypes becomes small, and thus the impact of the selective advantage of one peak over another is obscured (Barton 1992). With many loci, then, the influence of dominance and selection are reduced, and the outcome of the process is determined primarily by differences in migration rate between the populations ($I = 1$). At the extreme values of dominance, however, the limiting situation is somewhat different. Here alleles are either always expressed ($h = 1$) or always obscured ($h = 0$) in heterogeneous genetic backgrounds, and thus in the limit, completely dominant alleles always have an invasiveness greater than one ($I \approx 2.41$ from eq. 4A), whereas completely recessive alleles always have an invasiveness less than one ($I \approx 0.41$ from eq. 4b; see also Barton 1992).

In general, the approximation provides a good quantitative and qualitative description of the

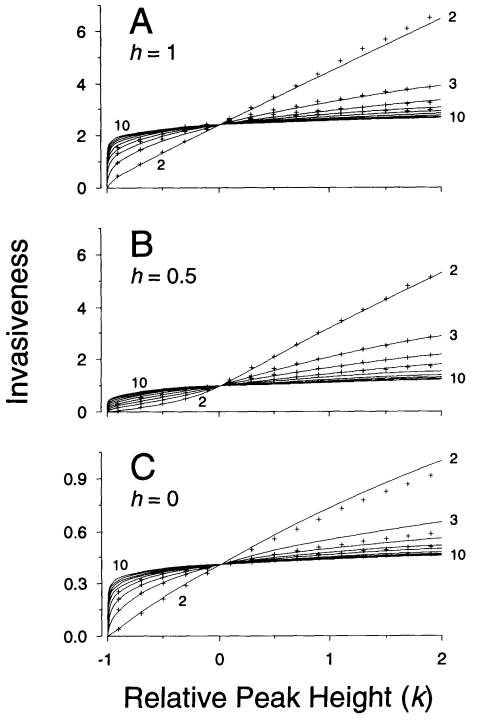

FIG. 5. Effect of peak height on invasiveness. This figure and figure 4 are slices of the same set of three-dimensional surfaces. A) Invading genotype is completely dominant, $h = 1$. B) Invading genotype is additive, $h = 0.5$. C) Invading genotype is completely recessive, $h = 0$. Note the change of scale in (C).

effects of dominance, relative peak height, and the number of loci on invasiveness, indicating that the process is well described simply by the domains of attraction of the peaks, as suggested by Barton (1992; see also Barton and Rouhani 1993). The error in the approximation seems to be amplified in the cases of a few recessive loci ($h \approx 0$), but otherwise is quite small. The basic idea behind the approximation is shown schematically in figure 6. Using the one-dimensional representation of the adaptive landscape provided by equation (2), it can be seen that the domain of attraction of the higher peak is much larger when the alleles are dominant than when they are additive or recessive. If a balance between migration rates leaves the gene frequency in the populations on the high fitness side of the adaptive valley, phase III will proceed. Under this interpretation, invasiveness does not depend on the depth of the adaptive valley, only on its location. As will be shown below, this is true only when selection is weak and the recombination rate is not too small.

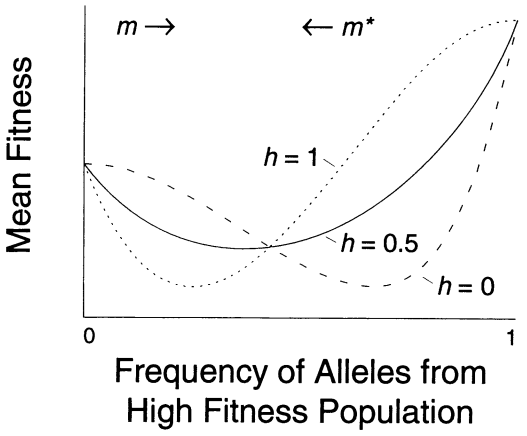

FIG. 6. One dimensional representation of several adaptive landscapes showing how the domain of attraction of the higher peak expands with an increase in dominance. If the balance between migration rates is on the right-hand side of the adaptive valley, the high fitness genotype will be fixed. Lines are based on equation (2) with $k = 1$, $s = 0.01$, and $n = 4$.

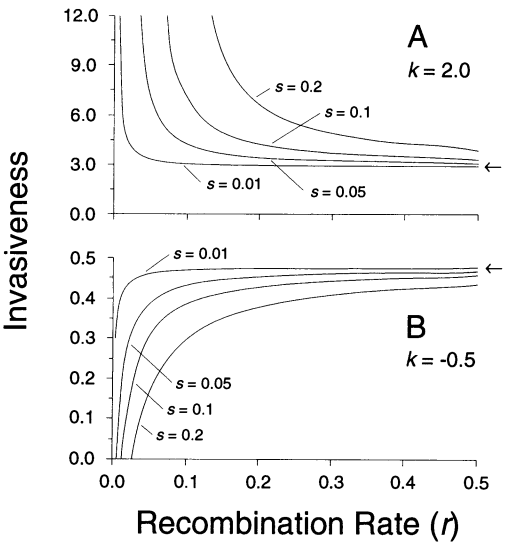

FIG. 7. Effect of recombination rate on invasiveness. The different lines show results of different recombination rates on invasiveness for a three locus model with varying amounts selection (s). A) Invading genotype is advantageous, $k = 2$. B) Invading genotype is disadvantageous, $k = -0.5$. Arrows indicate the values given by the analytical approximation (eq. 6).

Effect of Recombination.—Reducing the rate of recombination between loci opposes the breakup of advantageous genotypes and should make it easier for these genotypes to invade. This is indeed the case, as linkage among loci increases the invasiveness of advantageous genotypes ($k > 0$) and decreases the invasiveness of disadvantageous genotypes ($k < 0$; fig. 7). When selection is weak, invasiveness is little affected by the recombination rate unless linkage is very tight ($r \approx 0$), and the approximation given earlier works well. As selection increases, however, the recombination rate has a greater influence on invasiveness. This is primarily caused by the fact that, in this model, as the depth of the valley (s) increases, the advantage (or disadvantage) of the invading genotype (ks) also increases. When selection is sufficiently strong ($s > 0.1$), invasiveness depends almost entirely on the produce ks rather than on k and s separately. Therefore, the approximation is not valid when selection is strong and linkage is tight.

DISCUSSION

The main result obtained in this study is that excess migration from the fitter deme is not always required for phase III to proceed, but under most realistic circumstances, it probably is. Dominant, tightly linked, highly advantageous genotypes can invade almost any deme, even in the face of strong reverse migration. Recessive alleles and adaptive gene combinations made up of more than a few loci do not invade as easily, however, especially if migration involves more than a few populations. In these cases, excess migration is necessary if the new gene combination is to be fixed deterministically in other demes. These conclusions are consistent with the results of both Crow et al. (1990) and Barton (1992).

The ability of a genotype to spread from one deme to another depends on both demographic and genetic characteristics of the demes. The former consist of the migration rate and population size, whereas the latter include the recombination rate, the number of loci, and the effects of dominance and epistasis on fitness. These genetic attributes determine the effectiveness of individual selection in driving the invading genotype to fixation in a new deme. Therefore, the ability of a genotype to overcome the counteracting effects of migration, which I have called invasiveness (sensu Lande 1985), is an intrinsic property of that genotype, although it is conditioned on the genetic constitution of the other deme.

Invasiveness (I) is a measure of resistance (or susceptibility) to reverse migration. This can be thought of in two ways. First, for two demes that begin at different peaks, given a fixed amount of

migration from one of the demes, I gives the maximum amount of reverse migration from the other deme that can occur and still permit the first deme to overtake the second (i.e., $m \geq m^*/I$ from eq. 5). Second, if $n + 1$ demes are exchanging migrants at equal rates, with n of the demes beginning at one peak and one of the demes beginning at another peak, I gives the maximum size that n can be and still have the one deme convert the fitnesses of the other n demes. If n is larger than I, then there must be a proportional increase in the migration rate from the single deme for the process to proceed. This interpretation is valid only when the n demes all start at the same fixed state, and ignores complications caused by random drift, especially when there are many peaks (see below).

If differential migration is necessary, how large must it be for phase III to proceed? If the advantageous type is recessive, the differential between migration rates must be larger (on the order of twice as large for exchange between only two demes; fig. 5), whereas if the advantageous type consists of a few, dominant loci there need not be any differential migration unless many demes are involved (> 5). As Barton (1992) has pointed out, this can work against the spread of adaptive types with a less fit genotype spreading if it is sufficiently dominant. This scenario is limited to exchange among only a few demes, however, because the effect of dominance on invasiveness is bounded ($I \approx 2.41$), whereas that of selective advantage is not. Clearly, phase III cannot proceed in a deterministic fashion if hundreds of demes that are all exchanging migrants are involved. Spatial structuring of the pattern of migration will be essential when many demes are involved (Wright 1941; Kimura and Weiss 1964; Rouhani and Barton 1987). The success of phase III will be greatly facilitated if most demes tend to exchange migrants with only a few neighbors. Even if some migrants are exchanged over a long distance, if most migration is with adjacent demes, phase III will proceed given the proper genetic parameters. The effectiveness of differential migration in this context has been demonstrated empirically by Wade and Goodnight (1991).

The treatment of phase III in this study has been entirely deterministic. Wright envisioned that the spread of a new gene combination would be deterministic during phase III, in contrast to its stochastic fixation during phase I. In this way, phase III would inexorably drive the new combination to fixation in the species as a whole. The balance between the isolation required to allow phase I and the migration required for phase III could be tenuous, however. One possibility is that the migration rate is low during phase I until a deme approaches the new peak when the migration rate increases, and phase III then proceeds deterministically (Crow et al. 1990).

When all three phases occur simultaneously, the shifting-balance process may work better than would be predicted by an analysis of phase III by itself. This is because drift can fix the adaptive gene combination in many demes simultaneously; thus, migration is more likely to include demes with the new combination. This helps overcome the limitation, imposed by the deterministic approach, on the number of demes that can exchange migrants. Migration also then simply initiates the drift process, rather than causing fixation by itself (see Barton and Rouhani 1993). In this case, the success of the shifting-balance process is determined more by the rate of transition between peaks (phase I) than the export of the higher peak (phase III). Lande (1985), for example, has shown that the addition of interdemic selection via an extinction-recolonization process does not significantly increase the likelihood that an underdominant chromosome rearrangement will be fixed in a subdivided population. It is therefore likely that the shifting-balance process as a whole is limited more by phases I and II than phase III.

The same genetic factors that influence invasiveness during phase III will also affect the likelihood of fixation during phases I and II. Any genotypic attribute that makes it easier for a migrant to invade will also aid a new mutant to become fixed. All three phases also suffer from the fact that mean fitness is depressed during the shift from one peak to another by either drift or migration (e.g., fig. 1). The selective load on the population as a whole could therefore be quite large while the shifting balance process is operating (Kimura et al. 1963). The advantage of the new gene combination has to be weighed against this load.

Barton (1992) attributed the results of Crow et al. (1990) solely to the ability of migration to swamp the effects of selection, arguing that migration pressure could as easily lead to nonadaptive as adaptive change. The results presented here, however, demonstrate that many different factors can affect the ability of one deme to upgrade (or downgrade) the fitness of another

deme (see also Kondrashov 1992). Some of Barton's (1992) criticisms may be based on the fact that he, as well as Crow et al. (1990), concentrated on the extreme case of complete dominance of either the high or low peak genotype. These extremes can lead to qualitatively different outcomes than more intermediate levels of dominance (fig. 4). Barton also emphasized the case of many loci, where selective advantage is diluted and the process does indeed become migration-driven. Phase III works best when only a few loci are interacting epistatically, but this is the type of genetic system that Wright believed was most suited to the shifting-balance theory.

These conclusions are based on several assumptions, the consequences of which should be addressed. First, one particular pattern of migration, adult migration, is assumed. Although other patterns of migration would yield different results, they should be qualitatively similar. Migration that occurs earlier in the life cycle facilitates phase III, because migrants enter the population before selection acts on them (Crow et al. 1990). This should lead to an increase in invasiveness for advantageous combinations.

The pattern of selection assumed is also somewhat limited, because it allows only two fitness optima. Wright favored fitness models in which many different peaks exist, such as under stabilizing selection on an additive character (Wright 1935; Barton 1986; Phillips 1994). In this model, some genotypes have higher fitnesses because of pleiotropic effects on both the character and fitness. While the stabilizing selection model allows for a continuous gradation between fitness classes, its important features are qualitatively captured by the two-peak model, because in both models heterozygotes involving optimal gametes have intermediate fitness (≥ 1.0), all other combinations have reduced fitness (< 1.0). Calculations of invasiveness for the stabilizing selection model in fact turn out to be very similar to those of the two-peak model with additive effects (results not shown). The real difference between these models is the number of different peaks they allow. In the deterministic model used here, each population always ends at one of the two original peaks. In a stochastic model, however, genetic drift could move one of the populations into the domain of attraction of another peak during the transition through the adaptive valley. A deterministic model can skirt the edge of an unstable equilibrium, whereas a stochastic model will be influenced by it. Much the same thing can happen in equations describing mutation-selection balance under stabilizing selection (Barton 1986, 1989). Invasiveness therefore provides an oversimplified measure of the ability of one deme to overtake other demes, because it ignores complications caused by multiple peaks and genetic drift. Nevertheless, this simplification allows insight into the factors that influence the success of phase III.

Conclusion

Whether Wright's process occurs depends on a balance among factors such as population size, migration rate, and the strength of selection; whether the process necessarily leads to adaptive change depends on a balance among other factors such as dominance, recombination rate, and the number of loci. Adding restrictions based on the details of the genetic system to those already imposed by the balance among demographic parameters can serve to only weaken the general applicability of the shifting-balance theory.

As envisioned by Wright, phase III involves the deterministic fixation of an adaptive gene combination by the differential migration from demes of high fitness into those of lower fitness. We do not currently know enough about the correspondence, if any, between excess fitness within a population and excess migration among population to know what levels of differential migration are reasonable. A positive, nonlinear relationship between fitness and migration rate will definitely facilitate phase III, but it seems unlikely that small differences at the individual level will translate into the manifold differences at the group level required under certain circumstances (Barton 1992). It is therefore conservative to consider conditions under which phase III will proceed without large degrees of differential migration. These conditions are several dominant loci with a large selective advantage spreading into a few populations of lower fitness. Phase III is much less likely to occur under different circumstances.

In the end, it is unlikely that phase III is the limiting step in the shifting-balance process in the sense that under reasonable conditions phase III should easily proceed (although phases I and II may not). The real question is how often do these conditions exist in nature, and even if they do exist, is the shifting-balance theory necessary to explain the evolution of novel genetic combinations.

Acknowledgments

I thank N. Barton, A. Kondrashov, P. Moore, S. Tonsor, M. Wade, M. Whitlock, and especially J. Crow for numerous helpful discussions and comments. B. Engels and N. Barton provided copies of computer programs for calculating multilocus allele frequency dynamics that greatly speeded the completion of this work. The study was funded by National Institutes of Health grant 1-F32-GM14612-01.

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Appendix

In Barton's (1992) method of calculating multilocus gene frequency change, $P(\rho)$ in equation (1) is replaced by $P(j, k; i)$, the proportion of gametes carrying i "1" alleles that are produced by diploids carrying j and k "1" alleles. This is given by

$$P(j, k; i) = \sum_{m=0}^{\min(i,k,j+k-i)} \frac{\binom{j}{m}\binom{n-j}{k-m}}{\binom{n}{k}} \cdot \binom{j+k-2m}{i-m}\left(\frac{1}{2}\right)^{j+k-2m}, \quad \text{(A1)}$$

where $k \leq j$, and $\max(0, j + k - n) < i < \min(j + k, n)$(Barton 1992, eq. A2). Calculating the composite fitness w_{ij} is complicated by dominance. Defining $p_1(i, j) = i!j!/[(i + j - n)!n!]$, the probability that recombination between i and j yields exactly $i + j - n$ "1" alleles, and $p_2(i, j) = (n - i)!(n - j)!/[(n - i - j)!n!)]$, the probability that recombination between i and j yields no "1" alleles, then the fitnesses are given by $w_{00} = 1.0$, $w_{nn} = 1 + ks$, and

$$w_{ij} = p_2(i, j)(1 - hs) + p_1(i, j)[1 + hks - (1 - h)s] + [1 - p_1(i, j) - p_2(i, j)](1 - s), \quad \text{(A2)}$$

if $i + j = n$, otherwise

$$w_{ij} = p_2(i, j)(1 + hks) + [p_1(i, j) - p_2(i, j)][1 + hks - (1 - h)s] + [1 - p_2(i, j)](1 - s). \quad \text{(A3)}$$