NOTES AND COMMENTS

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ON THE SPREAD OF NEW GENE COMBINATIONS IN THE THIRD PHASE OF WRIGHT'S SHIFTING-BALANCE

N. H. BARTON
I.C.A.P.B., Division of Biological Sciences, University of Edinburgh, King's Buildings, Edinburgh EH9 3JT, UK

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Crow et al. (1990) recently presented one of the first explicit analyses of the third phase of Wright's (1931) "shifting-balance" theory of evolution: that is, of the spread of a new adaptive peak through a population. Their simulations were surprisingly favorable to the shifting-balance: very low levels of migration can ensure the spread of a new, favorable combination of genes, even when that set is continually broken up by recombination. In this note, I will set out a somewhat different interpretation, supported by a simple analytic model, and further simulations. I will argue that the new combination of genes succeeds because gene flow overwhelms selection, rather than because selection overcomes recombination. Because the argument is over the biological interpretation, rather than the mathematics, it may be helpful to begin with a brief summary of the issues involved in Wright's theory.

Fisherian Versus Wrightian Views of Adaptation

The most straightforward view of evolution is that it consists of the steady accumulation of advantageous alleles. Gene interactions and population structure then play only a minor role. This view is associated with Fisher, whose "Fundamental Theorem" describes the steady increase in mean fitness, equal to the additive genetic variance in fitness (though see Provine, 1986). In contrast, Wright (1931, 1980) argued that interactions in the effects of genes on fitness would lead to multiple stable equilibria, or "adaptive peaks." Natural selection leads a population up gradients of mean fitness to a nearby peak, but cannot take it to the global optimum: some means of escaping from inferior peaks would therefore speed progress.

Gene interactions of the kind emphasized by Wright are certainly widespread and do permit multiple equilibria. For example, stabilizing selection on an additive polygenic trait leads to multiple peaks: any combination of genes that brings the mean close to the optimum can be fixed (Wright, 1935). Selection against heterozygotes, or in favor of common genotypes, will maintain multiple equilibria in much the same way as epistatis: the alternative warning patterns in *Heliconius* butterflies are maintained by Mullerian mimicry, in which selection eliminates heterozygotes, recombinants, and rare alleles (Turner, 1977).

However, the prevalence of epistasis and multiple equilibria does not by itself decide between the "Fisherian" and "Wrightian" views: though populations may be trapped on inferior adaptive peaks, they may still adapt primarily by accumulation of favorable alleles. The usual two-dimensional illustrations of Wright's "adaptive landscape" are misleading, because populations are free to evolve along many dimensions—roughly equal to the number of alleles that could be produced by a single mutation (Provine, 1986). In many directions, populations might only be able to reach a fitter peak by crossing an "adaptive valley"; however, there might be many other directions in which they could evolve up a gradient of increasing mean fitness. Progress of this sort becomes more plausible if selection coefficients vary in space and time. Thus, even accepting the importance of gene interactions, it is still not clear whether peak shifts of the kind envisaged by Wright are significant in either adaptation or speciation (Barton and Charlesworth, 1984).

Wright proposed a "shifting-balance" between drift, intrapopulation selection, and interpopulation selection. He divided the process into three phases. In the first, random processes cause local populations to cross adaptive valleys into a new domain of attraction. In the second, mass selection takes each population to its new optimum. In the third phase, adaptive peaks compete with each other, and the fitter peaks spread through the whole species. This selection between peaks might occur through differential extinction and recolonization (Slatkin, 1981), through stochastic shifts triggered by immigration from higher peaks (Lande, 1985), or through the movement of "tension zones" through a continuous population (Rouhani and Barton, 1987; Barton and Hewitt, 1989). However, the process that Wright emphasized was that demes at higher peaks would send out more migrants, and would pull neighboring demes to the new peak without any need for stochastic shifts or extinctions (Wright, 1931, 1980). It is this process that was first modeled by Crow et al. (1990), and which concerns us here. It is important to note that it involves three distinct issues: first, whether new adaptive peaks can spread; second, whether the process is selective, favoring some adaptive peaks at the expense of others; and finally, whether this selection is based on individual or on group fitness (Lande, 1985; Barton and Hewitt, 1989; Barton and Clark, 1990).

Crow et al.'s Model of the Third Phase

Crow et al.'s model was chosen to be unfavorable to the "shifting-balance," and so to provide a conservative test of its plausibility. Selection acts on n loci, and favors just two complementary types. Individuals homozygous for recessive alleles at all n loci $\frac{abc\ldots}{abc\ldots}$ have fitness 1, while those carrying one or two copies of the dominant allele at all loci $\left(\frac{ABC\ldots}{-\,-\,-\ldots}\right)$ have fitness $1 + ks$. All other genotypes have fitness $1 - s$. In Crow et al.'s original model, k was taken to be positive, so that the new peak is fitter than the old; however, we will see that the results are qualitatively similar when $k = -1$, in which case the new alleles are simply deleterious. (Note that because dominance is complete, F_1 fitness is unimpaired: this favors the spread of the new type).

The population consists of two demes. One is fixed for the recessive alleles, while the other has shifted to fixation for the dominant alleles, and sends out migrants to its neighbor. Crow et al. found that a very low rate of immigration—one or two orders of magnitude smaller than the selection coefficient—ensures the spread of the new peak. This holds even when many unlinked genes are involved (so that the new combination is difficult to assemble in the face of random segregation), and even when migration occurs in both directions (i.e., when both demes have the same group fitness). Their results were also insensitive to the model of selection: low migration rates still suffice when the new peak consists of the entirely recessive genotype, or when fitness is a quadratic function of the number of A versus a alleles. Crow et al. therefore argued that "whatever weaknesses [the shifting-balance theory] may have are not in the third phase."

Here, I will argue that the new gene combination spreads not because it is fitter, but because a low rate of immigration can swamp selection, and establish even a deleterious genotype. This is because migration is intrinsically a stronger force than selection, especially when selection is spread over many loci. I will support this argument with a simple analytic model, which applies when selection is weak enough that linkage disequilibria can be ignored, and with simulations of systems composed of more loci than were considered by Crow et al. (1990).

Migration Versus Selection at a Single Locus

The power of migration can be illustrated by the simplest model of multiple peaks: selection against heterozygotes at a single locus. Suppose that genotypes *PP*: *PQ*: *QQ* have frequencies p^2: $2pq$: q^2 immediately after random mating, and are then selected, with fitnesses 1: $1 - s$: 1. After selection, a fraction m of the population is replaced by migrants from a population fixed for P:

$$\Delta p = mq - (1 - m)\left[\frac{spq(q - p)}{1 - 2spq}\right] \qquad (1a)$$

This formula is exact. It describes migration of adults after selection; however, when selection is weak, this will give similar results to selection after migration of zygotes.

The population can always reach an equilibrium at $q = 0$: fixation for P is clearly stable. If migration is weak enough relative to selection, two other equilibria are possible: the lower is stable, and corresponds to a balance between immigration and elimination of heterozygotes:

$$\frac{m}{1 - m} = \frac{sp(q - p)}{1 - 2spq} \qquad (1b)$$

As p increases, the function on the right increases from zero, through a maximum, and then becomes negative when $p = \frac{1}{2}$. The polymorphic equilibria correspond to the points where this curve cuts a horizontal line of height $m/(1 - m)$; if migration is too high, this line will pass above the maximum, and no polymorphism can be maintained: the incoming allele will be fixed (see Fig. 1b, which gives the analogous curve for Crow et al.'s model). When selection is weak, the maximum is at $p = \frac{1}{4}$, and (to leading order in s) corresponds to a critical migration rate of $m^* = s/8$. Thus, immigration at a much lower rate than selection will fix the incoming allele. The same argument applies even when the new allele is simply deleterious (fitnesses 1: $1 - s$: $1 - 2s$): then, $m^* = s$ (Haldane, 1931).

Migration Versus Selection at Many Loci

The calculation can be extended to many loci, provided that linkage disequilibria are neglected. This will be a good approximation if selection is weak relative to recombination. In general, the rate of change of allele frequencies caused by selection is proportional to the gradient of log mean fitness with respect to allele frequency:

$$\Delta p_i = mq_i + (1 - m)\frac{p_i q_i}{2}\frac{\partial \log(\overline{W})}{\partial p_i} \qquad (2a)$$

Suppose that all loci have the same effect on fitness, and all have the same allele frequencies (p, q) at equilibrium. (Symmetric selection does not necessarily lead to symmetric equilibria—for example, stabilizing selection on an additive trait leads to alternative asymmetric equilibria (Wright, 1935). However, this is unlikely for the disruptive selection considered here). With these assumptions, we need only consider $\overline{W}$ as a function of p:

$$\Delta p = mq + (1 - m)\frac{pq}{2n}\frac{\partial \log(\overline{W})}{\partial p} \qquad (2b)$$

The factor of n appears because the effect on mean fitness of changing allele frequency at a single locus is smaller than the effect of changing the frequency at *all* loci: given the assumption of symmetry across loci, it is true in general that $\partial\log(\overline{W})/\partial p_i = [\partial\log(\overline{W}/\partial p]/n$. As before, there is always an equilibrium when P is fixed ($q_i = 0$ for all i). If migration is low enough, other equilibria are possible:

$$\frac{m}{1 - m} = -\frac{p}{2n}\frac{\partial \log(\overline{W})}{\partial p} = -\frac{1}{2n}\frac{\partial \log(\overline{W})}{\partial \log(p)} \qquad (2c)$$

TABLE 1. Ratio between the critical migration rate and selection (m^*/s), calculated assuming weak selection and hence negligible linkage disequilibrium. When the number of loci is large, this should approach $1/(2en)$.

n	$k = -1$	$k = 2$	$1/(2en)$
2	0.1055	0.0302	0.0920
3	0.0670	0.0493	0.0613
4	0.0491	0.0461	0.0459
5	0.0387	0.0384	0.0368
10	0.0189	0.0189	0.0184
20	0.00931	0.00931	0.00920

This formula depends only on the assumption that linkage disequilibria are negligible, which will be accurate when selection is weak. Then, the critical migration rate is proportional to the maximum of $\partial\log(\overline{W})/\partial\log(p)$, and inversely proportional to the number of loci.

In Crow et al's model, mean fitness is:

$$\overline{W} = 1 - s + \mathrm{sq}^{2n} + (k + 1)s(1 - q^2)^n \qquad (3)$$

Here, q^{2n} is the chance that recessives will be homozygous at all loci (the original combination), and $(1 - q^2)^n$ is the chance that one or two dominant alleles will be found at all loci (the new combination). The mean fitness is plotted in Figure 1a, as an illustration of the method. Critical migration rates can be calculated numerically from Equation 2c; they are given in Table 1, and an example is shown in Figure 1b. When many genes are involved, the maximum of $\partial\log(\overline{W})/\partial\log(p)$ approaches $p = 1/(2n)$, and gives a critical migration rate of $m^* = s/(2en)$, where e = 2.71828. This threshold is independent of the advantage of the new peak, because migration overwhelms selection when the incoming alleles are so rare that the new combination hardly ever arises. Thus, a very low migration rate can spread the new gene combination even when it is deleterious ($k < -1$; see Table 1).

Similar results will be obtained with other models. For example, Crow et al. (1990 p. 242) consider fitness to be a quadratic function of the fraction of alleles from the donor population, x:

$$W = 1 - s + s\theta\left(x - \frac{1}{\sqrt{\theta}}\right)^2 \qquad (4)$$

If θ is chosen so that $k = \theta - 2\sqrt{\theta}$, fitness is 1 at the original peak ($x = 0$), $1 + ks$ at the new peak ($x = 1$), and has a minimum at $1 - s$: it is therefore comparable to the previous model. The mean fitness depends on the mean and variance of x; assuming linkage equilibrium, these are p and $pq/2n$, respectively. With many loci, the latter can be neglected: the population is clustered around $x = p$, and so Equation 4 gives the mean fitness. Applying Equation 2c shows that the critical migration rate is $m^* = s/4n$. It is remarkable that this is again independent of the relative advantage of the new peak, k: again, a deleterious genotype can be established by a very low rate of immigration.

Note that the threshold is very similar to the previous value ($s/4n$ versus $s/2en$), and as before, is inversely proportional to the number of loci. This is because a given total selection pressure is less effective when spread over many independently segregating loci. One might imagine that migration would be more effective in the first model, where only two out of many genotypes are favored by selection: the similarity with the quadratic model shows that this is not so.

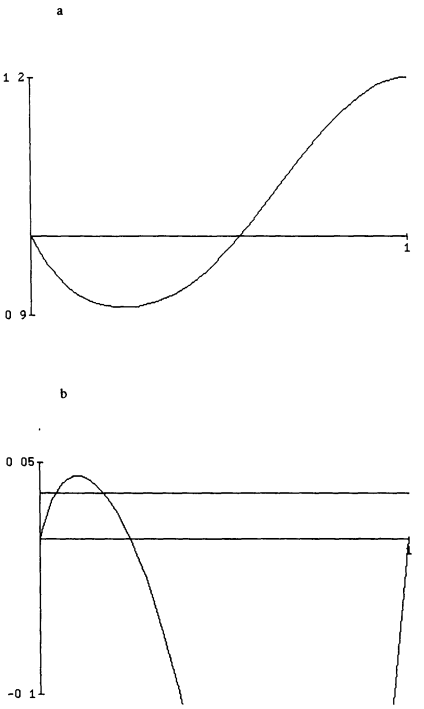

FIG. 1. a. Mean fitness as a function of allele frequency for Crow et al.'s model. $k = 2$, $n = 5$, $s = 0.1$; the new peak corresponds to dominant alleles. b. The gradient $\partial\log(\overline{W})/\partial\log(p)$, plotted against p, for the same parameters. This represents the force with which selection opposes migration. Polymorphic equilibria are given by the intersection of this curve with a horizontal line of height $2nm/(1 - m)$ (Eq. 2c). Here, the line corresponds to $m = 0.003$; it gives a stable equilibrium at $p = 0.04$, and an unstable equilibrium at $p = 0.17$. The critical migration rate, above which such equilibria are impossible, is determined by the peak of the curve.

For a given depth of the adaptive valley, there is no bound on the critical migration rate: the gradient $\partial\log(\overline{W})/\partial\log(p)$ could be made arbitrarily large or small. However, for a given dependence of fitness on degree of introgression, $W(x)$, the critical migration rate will be inversely proportional to the number of loci, and proportional to the strength of selection.

Exact Simulations

These analytic results neglect linkage disequilibria. To find whether selection can aid the spread of favorable combinations by building up associations between alleles, and to check against Crow et al.'s simulations, exact calculations are needed. It will also be useful to obtain results for large n, to bring out the dependence on numbers of loci. In general, deterministic simula-

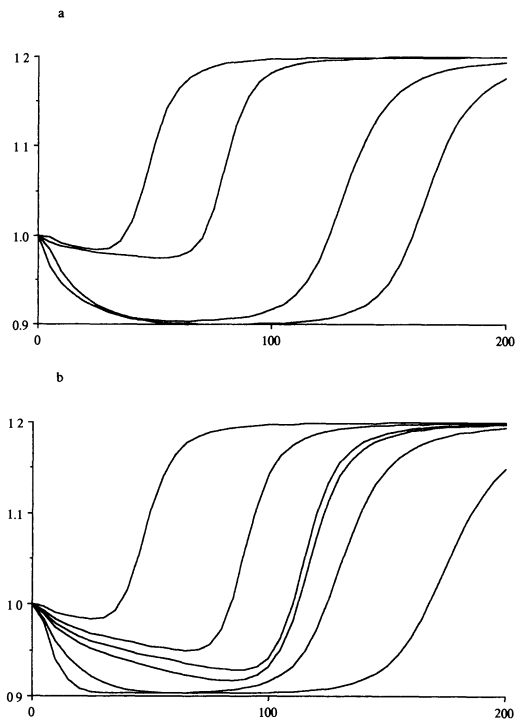

FIG. 2. Graphs of mean fitness against time, for $n = 2$ loci (left-hand pair), and $n = 10$ loci (right-hand pair). In each pair, the left-hand curve gives results from exact simulations, and the right-hand curve gives the approximation of Equation 2b, which assumes linkage equilibrium. $k = 2$, $s = 0.1$, $m = 0.005$; adults migrate after selection. b. Simulation results for $n =$ 2–20 loci; parameters are as above. Reading clockwise from the left-hand axis ($\overline{W} = 1$), $n = 2, 3, 4, 5, 10, 20$ loci. Note the hiatus between 4 and 10 loci. This graph is an extension of Figure 3 in Crow et al. (1990).

tions of more than a few loci are not feasible, because there will be a prohibitive number of genotypes: Crow et al. (1990) simulated only up to nine loci. However, where the genes are unlinked, and where all have equivalent effects on fitness, individuals need only be distinguished according to the number of alleles corresponding to the new and old peaks. Thus, with n loci, one can simply record the proportions carrying 0, 1, . . . , n alleles from the donor population, rather than following the 2^n haploid genotypes. Details are given in the Appendix.

Figure 2a shows the change in mean fitness over time. Parameters were chosen to match Figure 3 of Crow et al. (1990), and lead to fixation of the new combination of genes. The analytic approximation (Eq. 2b), which ignores linkage disequilibrium, overestimates the delay before the new genotype is established; this is presumably because associations are built up by selection favoring the new combination, and increase its frequency. However, the early stages of the process are almost identical, and as is shown below, the critical migration rate required to establish the new combination depends rather little on linkage disequilibria. Figure 2b shows exact results for 2–20 loci. Between 5 and 10 loci, the pattern changes very little; it may be this that led Crow et al. (1990) to believe the threshold to be insensitive to the number of loci. However, as the number of loci increases further, the time to fixation increases substantially, as predicted by Crow et al. (1990), in their model of an infinite number of loci.

The process falls into three stages. First, migration introduces alleles at low frequency, and overwhelms selection: analytic results show that the greatest opposing force is at around $p = 1/(2n)$. Once this is overcome, alleles accumulate steadily; neither of the two advantageous combinations are produced at appreciable frequency, and so mean fitness is close to $1 - s$ for a long period. When the new allele reaches high frequency, the fitter phenotype appears, and the process is completed with the aid of selection. Crow et al. (1990 p. 245) gave essentially this interpretation, arguing that incoming genes can be established relatively easily, because migration soon contaminates the recipient population, reducing its mean fitness, and so decreasing the selection against introgression. The crucial point is that this process is independent of any selective advantage accruing to the new combination: migration can establish sets of genes even if they are uniformly deleterious.

Figure 3a shows how the critical migration rate depends on the number of loci. When the analytic values are calculated numerically, using Equation 2c (upper curve), agreement with simulations is good, even though selection is fairly strong ($s = 0.1$). Agreement improves as the number of loci increases; the curve converges to the crude prediction, $m^* = s/2en$ (middle curve). Figure 3b shows the dependence of m* on selection strength, for $n = 5$ loci. Agreement with the prediction made by ignoring linkage disequilibria ($m^* = s/2en$) is reasonable when selection is less than about $s = 20\%$. This prediction is independent of k, the advantage of the new combination; the threshold needed to establish a deleterious set of alleles ($k = -1$) converges to that for $k = 2$ as selection becomes weak.

Two-Way Migration

Crow et al. showed that the new peak can still spread, even when two demes exchange migrants in both directions. For example, their Figure 9 plots the critical migration rate in the forward direction (i.e., from new peak to old; m_+) as a function of selection, for various fixed rates of migration in the reverse direction (m_-). They assume three loci, and $k = 2$. When selection is much stronger than the reverse migration rate, the critical forward rate is hardly affected. When selection is weak (i.e., the left-hand intercept of their figure), the new peak is fixed if $m_+/(m_- + m_+) > 0.2$ if the new peak consists of dominant alleles, and if $m_+/(m_- + m_+) > 0.6$ if the new peak consists of recessives. This can be understood by seeing that when selection is weaker than migration ($s \ll m$), the two demes quickly converge to $p = m_+/(m_- + m_+)$. The outcome then depends on whether this mixed population lies within the domain of attraction of the new or old peak. The boundary between the two domains lies at the minimum of mean fitness; differentiating Equation 3 shows that when the new peak consists of dominant alleles, the threshold is at:

$$p^* = 1 - \frac{1}{\sqrt{1 + (k + 1)^{-1/(n-1)}}}$$

(dominant) (5a)

Where the new peak consists of recessive alleles:

$$p^* = \frac{1}{\sqrt{1 + (k + 1)^{+1/(n-1)}}}$$

(recessives) (5b)

With three loci and $k = 2$, these thresholds are at $p = 0.204$, and $p = 0.605$, respectively. This agrees with Crow et al.'s results for weak selection.

When the number of loci is large, the thresholds for dominant and recessive alleles tend to $1 - 1/\sqrt{2} \approx 0.2929$ and $1/\sqrt{2} \approx 0.7071$, respectively. These values are independent of the advantage of the new peak, k, showing that dominant alleles tend to spread, even when they produce a lower adaptive peak. A similar phenomenon is found in continuous populations: tension zones tend to move in favor of dominant alleles (Mallet, 1985; Johnson et al., 1990). In general, peaks with large domains of attraction will spread: these may often give higher fitness, but as this example demonstrates, they need not. Thus, the third phase of Wright's "shifting balance" is only weakly adaptive, in that the success of new adaptive peaks does not depend solely, or even mainly, on whether they increase individual or group fitness.

When a new combination of genes is first established, it is likely to be surrounded by the original genotype. It is then much more likely to be swamped than when demes only interact in pairs. For example, if a deme exchanges migrants at an equal rate with four neighbors, the whole set will converge to $p = 0.2$: it is unlikely that this will lie above the threshold needed to carry the mixed population to the new peak. If the population is spread continuously over two dimensions, the new combination can only spread if the tension zone that separates it from the original form tends to move in its favor, and if it covers a large enough area to begin with. Even then, it may be trapped by minor barriers to gene flow (Barton and Hewitt, 1989).

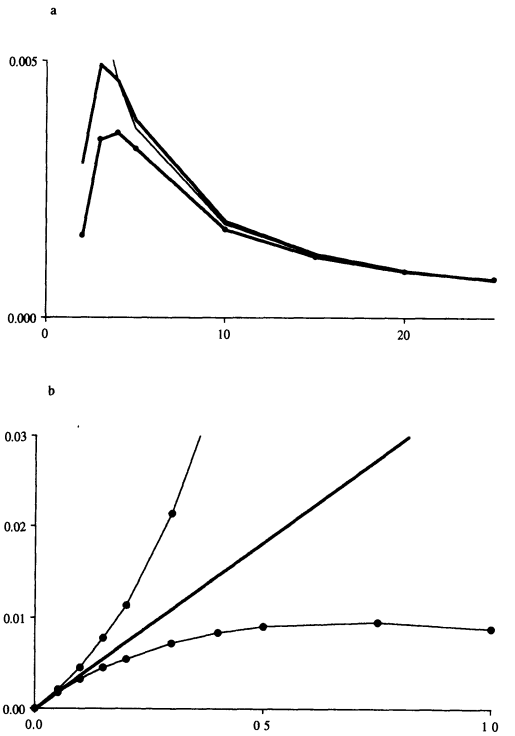

FIG. 3a. The critical migration rate as a function of the number of loci. The lower heavy curve gives simulation results; the upper heavy curve gives the analytic approximation, which assumes linkage equilibrium (from Eq. 2c). The light curve at top left is the crude approximation, $m^* = s/2en$. ($s = 0.1$, $k = 2$). b. The critical migration rate as a function of selection pressure; $n = 5$ loci. The straight line gives the crude prediction ($m^* = s/2en$). The lower curve gives simulation results for $k = 2$, while the upper curve gives results where the new peak has no advantage ($k = -1$).

DISCUSSION

Crow et al.'s model of exchange between two demes shows that the success of a new adaptive peak depends primarily on the rate at which it is propagated by emigration: this corresponds to the sensitivity of tension zones to differences in density and dispersal in a two-dimensional population. Following Wright, Crow et al. argue that populations that have reached a higher adaptive peak will be fitter, and hence will send out more migrants, ensuring the spread of the new peak. Crow et al. suggest that when mean fitness rises above a threshold, excess individuals emigrate. This ensures an extremely strong dependence of gene flow on fitness, and justifies their use of one-way migration, out of the fitter deme. Though conceivable, such a relationship is difficult to justify in an explicit model of population regulation. Suppose that the absolute fitness is a function of both numbers and genotype; the population will equilibrate at a size which increases with mean genotypic fitness (the latter being defined in terms of fitnesses measured at a standard population density; Barton, 1986). The change in population size caused by changes in gene frequency will be of the same order as the selection coefficient, and so will feed back only a negligible second order effect on the gene frequencies (Barton and Hewitt, 1989; Barton and Clark, 1990). This argument assumes that numbers of migrants are proportional to population size. The actual relation will depend on obscure details of reproduction and behavior. However, it is difficult to see that differences in genotype that have only a small effect on relative fitness could have a large effect on population size or migration rate.

The most important implication of this analysis may be that a little introgression can readily destroy adaptations that depend on many genes. This conclusion is at first sight contradicted by Bulmer's (1980 pp. 181–183) results on stabilizing selection on a polygenic trait. He modeled migration between two demes, in which selection favors different values of a polygenic trait, and found that migration reduces the difference in means by a factor that is independent of the number of loci.

In contrast, Crow et al.'s model shows that migration will always overwhelm selection if it is spread over enough genes.

Two possible explanations come to mind. Bulmer treats the genetic variance as being fixed, while Crow et al. fix the fitness of hybrids, relative to the original form, at $(1 - s)$. The equivalent assumption for an additive trait is to fix the total range of the character (the difference between $++++$ and $----$). Then, as the number of loci increases, the additive genetic variance decreases, and so does the response to selection. One can also argue that in Crow et al.'s model, migrants come from a population that is at or near fixation for + alleles at all loci; hence, migration increases allele frequency by $\approx m$, whereas selection reduces it only by $\approx s/n$. In Bulmer's model, the difference in allele frequency between the demes decreases with n: hence, the effect of migration is weaker, and it does not overwhelm selection. Thus, one must distinguish the case of an additive polygenic trait with more-or-less constant genetic variance, from the case where a particular combination of genes is favored over its complement. If such particular gene combinations are required, then gene flow may limit the ability of a species to adapt to conditions found only in small regions, or at the edge of their range.

The striking results of Crow et al. (1990) are not due to selection in favor of a novel combination of genes, but rather, reflect the power of gene flow over selection: the outcome is decided while the incoming alleles are at low frequency, when the new well-adapted combination of genes has yet to appear. Their results do not depend on linkage disequilibria, because unless selection is very strong, recombination quickly breaks up favorable combinations. The interpretation set out here suggests that while migration can spread a new combination of genes through a population, the success or failure of the new adaptive peak depends more on the quirks of population structure and dominance relations than on its effect on individual or group fitness. Thus, while populations may well diversify through a "shifting balance," it is difficult to see that this process leads to significant adaptation.

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Corresponding Editor: B. Charlesworth

Appendix I

If all loci are unlinked, and are exchangeable in their effects on fitness, the population can be described by $X(i)$, the proportion of gametes having i alleles from the donor population; $i = 0 \ldots n$. After random combination of gametes, and selection, the proportion of diploid genotypes is $X(i)X(j)W(i, j)\overline{W}$. After completion of one generation by migration and gamete production, the distribution of gametes is:

$$X'(k) = (1 - m)\sum_{i=0}^{n}\sum_{j=0}^{n} X(i)X(j)\frac{W(i, j)}{\overline{W}}P(i, j; k) \quad \text{(A1)}$$

If $k = n$, a term m is added, representing the influx of the new gene combination.

$P(i, j; k)$ is the proportion of gametes carrying k "+" alleles that are produced by diploids carrying i and j "+" alleles. Calculation of P is complicated, because many different diploid genotypes can give the same i, j (for example, $\frac{--++}{++--}, \frac{--++}{--++}, \ldots$). Genotypes that are more heterozygous will produce offspring with a higher variance of k. Suppose that the diploid contains m loci homozygous for "+"; it will therefore be heterozygous at $(i + j - 2m)$ loci. Its offspring will inherit m "+" alleles from the m loci homozygous for "+," and will also inherit between 0 and $(i + j - 2m)$ "+" alleles from the heterozygous loci. It remains to calculate the distribution of m, for genotypes in the class (i, j). Suppose that $j \leq i$; the opposite case can be treated in the same way. The chance that m loci are homozygous for "+" is the chance that m of the j "+" alleles on one chromosome are homologous to the set of i "+" alleles on the other chromosome. Because this corresponds to sampling without replacement, m follows a hypergeometric distribution. Combining this with the binomial distribution of k, given m, and summing over m, gives:

$$P(i, j; k) = \sum_{m=0}^{\min(j,k,i+j-k)} \frac{\binom{i}{m}\binom{n-i}{j-m}}{\binom{n}{j}} \cdot \binom{i+j-2m}{k-m}\left(\frac{1}{2}\right)^{i+j-2m} \quad \text{(A2)}$$

Here, $j \leq i$, and $\max(0, i + j - n) < k < \min(i + j, n)$.

Calculation of the fitness, $W(i, j)$, is complicated by dominance: $W(i, j)$ is an average over all possible permutations of i and j across loci. $W(0, 0) = 1$; otherwise, $W(i, j) = 1 - s + (k + 1)sY(i, j)$, where Y is the chance that all n sites are hit by at least 1 of (i/n) and (j/n)—i.e., that all sites carry at least one dominant allele:

$$Y(i, j) = \frac{i!j!(i + j - n)!}{n!} \quad \text{(A3)}$$

The calculations were speeded by setting up tables of $W(i, j)$ and $P(i, j; k)$ beforehand. Most of the results were produced by a program written in Pascal; as a check on rounding errors, some calculations were repeated using a Mathematica notebook (Wolfram, 1988), with increased precision. There were no discrepancies.

The threshold migration rate was found by a binary search. The migration rate started at the theoretical prediction, $1/(2en)$. Two values, m_+ and m_-, were then chosen around this value, such that the new combination was fixed for the upper value, but not the lower. $m_0 = (m_+ + m_-)/2$, was then tried; if the new combination was fixed, m_+ was replaced by m_0; otherwise m_0 replaced m_-. This continued until $(m_+ - m_-) < (m_- + m_+)/40$, guaranteeing an estimate within 5% of the true value. The criterion for ending a run was that allele frequency had changed by less than $10^{-4}(m_+ - m_-)$ for 10 consecutive generations: this allows for the slower evolution of the system when m and s are low. The new combination was deemed to have fixed if the final allele frequency was above 0.9. These criteria are similar to those used by Crow et al. (1990), but give more accurate results for large numbers of loci and low migration rates. Numerical values of the critical migration rate, which were kindly supplied by Crow et al., agree with the simulations described here, to within the margin of error of the search algorithms.

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GRAPHICAL ANALYSIS OF MATING SYSTEM EVOLUTION IN PLANTS

TETSUKAZU YAHARA
Department of Biology, University of Tokyo, Komaba, Tokyo 153, JAPAN

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Mixed mating systems or intermediate levels of selfing have been reported for a few plant species, particularly those in which populations exhibit a broad range of outcrossing rates (reviewed by Schemske and Lande, 1985*a* and Barrett and Eckert, 1990; see also Holtsford and Ellstrand, 1989; Waller and Knight, 1989; Barrett and Husband, 1990; Morishima and Barbier, 1990). It remains uncertain, however, whether the variation