Genet. Res., Camb. (1997), **69**, *pp.* 49–60 *With 7 text-figures*

Consequences of gene flow in spatially structured populations

KATRINA A. LYTHGOE
Institute of Cell, Animal and Population Biology, King's Buildings, University of Edinburgh, West Mains Road, Edinburgh EH9 3JT, UK

(*Received 19 August 1996 and in revised form 6 December 1996*)

Summary

A simple model of migration between two populations, each in a balance between mutation and stabilizing selection on a polygenic trait, is explored. Below a critical migration rate, genetic differences between the two populations can be maintained, even if the populations are selected towards the same phenotypic optimum. Gene flow then maintains genetic variance within each population. For this process to account for heritable variation, there must be some mechanism that causes divergence. The possibility that fluctuating selection could lead to the initial differentiation of the populations is explored.

1. Introduction

There are many questions as to the genetic basis of divergence and speciation that still remain unsolved. How readily can populations adapt to local conditions despite gene flow? Can reproductive isolation evolve within an interconnected network of populations? Can gene flow between divergent subpopulations maintain genetic variation? Though these questions have received much attention (for example, Felsenstein, 1976; Endler, 1977; Barton & Turelli, 1989), almost all theoretical discussion has been based on models of single genes (exceptions include Lande, 1976, 1980; Slatkin, 1978).

A key difficulty in extending the theory to quantitative traits based on many genes is that, even assuming additive inheritance, the outcome depends in a non-trivial way on the genetic basis of such traits. This has become clear from the debate over the amount of genetic variation that theoretical models can explain. Genetic variation is essential for the process of adaptation, and high levels of quantitative genetic variation are found in natural populations (Mousseau & Roff, 1987; Houle, 1991). However, the reduced fitness of extreme phenotypes and the long periods of evolutionary stasis observed in most species provide strong support for the existence of stabilizing selection, which on its own will act to eliminate genetic variability within populations (Lande, 1976; Maynard Smith, 1983; Turelli, 1984; Barton & Turelli, 1989).

One possible mechanism which might explain the abundant quantitative genetic variation found in nature is recurrent mutation (Kimura, 1965). Various population genetic models have been developed that describe this 'mutation/selection balance', such as the 'Gaussian' (Lande, 1976) and the 'House of Cards' (Turelli, 1984) continuum-of-alleles models, and various discrete allele models (Wright, 1935*a*, *b*; Latter, 1960; Bulmer, 1972; Barton, 1986). In the Gaussian model mutations at each locus have a continuous range of effects drawn from a normal distribution, and if the effects are much smaller than the standing variance at a single locus the distributions of allelic effects will be approximately Gaussian. In contrast, the House of Cards model assumes that new mutations have effects much larger than the standing genetic variance so that most of the variance is contributed by rare alleles.

Discrete allele models were introduced by Wright (1935*a*, *b*). Wright showed that for an additive quantitative genetic trait under stabilizing selection in a diploid organism, where each of the loci segregate for two alleles of equal and additive effect, a whole series of stable equilibria exist (Wright, 1935*a*, *b*) in the absence of mutation. For example, if selection favours a state in which 50 loci are close to fixation for a '+' allele, and 50 are close to fixation for a '−' allele, any of the 10^{29} optimal gene combinations will be a local equilibrium. With mutation at a low rate this multitude of equilibria remain stable and genetic variation is maintained at each locus (Latter, 1960; Bulmer, 1972). Moreover, there are also stable equilibria where the mean of the population differs from the optimum (Barton, 1986). Thus, in the example above, for particular levels of mutation and

https://doi.org/10.1017/S0016672397002644 Published online by Cambridge University Press

selection some populations may have stable equilibria such that only 47 of the loci are close to fixation for the '+' allele, and the mean is slightly below the optimum. These can be considered different 'classes' of equilibria or genotype. The stable equilibria can be thought of as peaks on Wright's 'adaptive landscape' (Wright, 1932), where mean fitness (height of the peak) is measured against the frequency of the '+' allele at each of the 100 loci; this adaptive landscape will have 101 dimensions. If loci have equal effects, all peaks in which the mean phenotype of the population is equal to the optimum phenotype will have the same height. We refer to these as optimal peaks.

In Barton's 1986 model, the genetic variance is given by the House of Cards approximation when the mean is near the optimum, but it increases towards a value of the same order as that given by the 'Gaussian' approximation when the mean deviates from the optimum. Although these models clearly show that mutation can counter the unifying effects of stabilizing selection, the mutation rates that would be required to explain all the genetic variation observed in natural populations are unrealistically high, especially if there is pleiotropy (Turelli, 1984). Other factors are thus also required to explain these high levels of quantitative variation, of which fluctuating selection is one possibility. Compared with constant selection, fluctuating selection can increase the genetic variance within a single population by several orders of magnitude (Kondrashov & Yampolsky, 1996) due to allele frequencies continually moving towards new equilibria. At any one time, most of the variation will be due to one, or only a few, of the loci, which are in the process of shifting. Spatial polymorphism may also help to explain the high levels of quantitative genetic variation found in natural populations (Goldstein & Holsinger, 1992; Phillips, 1996). However, migration must not be too high, since otherwise the whole population will become uniform. Only below some critical level of migration will local adaptation be possible (Karlin & McGregor, 1972; Slatkin, 1973; Nagylaki, 1975; Endler, 1977; Phillips, 1996).

Although spatial polymorphism may be maintained in the presence of migration, it is not clear how populations might come to have different genetic structures. The various populations that make up a species may diverge, either because selection varies from place to place, or because even under uniform selection different gene combinations evolve due to the effects of random genetic drift. However, the extent to which such divergence can occur in the presence of gene flow is unclear. Such questions are fundamental if we are to understand the processes of reproductive isolation and speciation (Coyne, 1992).

This paper analyses a simple model of polygenic variation, extended from that of Barton (1986), in which stabilizing selection acts on an additive quantitative trait in each of two demes in the presence of mutation and gene flow. This model will be used to investigate the effects of gene flow on the genetic structure of the two populations under stabilizing selection to the same or different optima, and address questions such as whether population differences, and possibly eventual reproductive isolation, can arise in the presence of gene flow. This simple optimum model is unrealistic in that it assumes equal allelic effects on a single character under stabilizing selection. However, it provides a useful starting point for a more general understanding of spatial variation in quantitative traits.

I will first describe Barton's (1986) model of mutation/selection and then extend this to include the effects of migration between two demes. The key assumption throughout is one of linkage equilibria. This is reasonable if selection and migration are much slower than recombination. In the first part of the analysis we assume that the mean phenotypes of both demes are close to their respective optima. This is similar to the model of migration/selection balance developed by Phillips (1996), in which migrants move from a fixed into a polymorphic population. The model presented here differs from Phillips's since mutation is included in the model, and the populations exchange migrants as opposed to one of the populations being held fixed. The more general case, which is not investigated by Phillips, in which one of the demes occupies a suboptimal peak on the adaptive landscape, is then considered. Supporting Phillips's results, we find that if migration rates are low then genetic differentiation can be maintained between the two demes, and genetic variation within these demes can be two or three orders of magnitude higher than if there were no genetic differentiation. Once migration exceeds a critical level, migration swamps selection, and the two demes become genetically homogeneous and migration can no longer maintain genetic variation. Finally I consider how populations might diverge in the first place in the presence of gene flow, and consequently whether under the assumptions of this model differentiation and eventually reproductive isolation could evolve in the presence of gene flow.

2. The model

The analysis assumes weak selection, such that change is approximately continuous in time, and the population is in linkage equilibrium; the latter is a reasonable assumption if recombination is much faster than selection and migration. The notation is summarized in Table 1.

(i) *Mutation/selection balance*

I begin by briefly describing Barton's notation. Consider a single character z', which is determined by the sum of the effects of n loci. Each gene can be in one of two states: 0 (the '−' allele) or 1 (the '+' allele). In this, the diploid case, the state of the gene at locus

https://doi.org/10.1017/S0016672397002644 Published online by Cambridge University Press

Table 1. *Summary of the notation*

z'	Phenotype of an individual
s	Strength of stabilizing selection
α	The effect of each allele (assumed equal across all loci)
δ_X	Deviation of the mean from the optimum in deme X
μ	Mutation rate
γ	Scaled mutation, $\gamma = \mu/s\alpha^2$
$\hat{\lambda}$	Migration rate
λ	Scaled migration, $\lambda = 2\hat{\lambda}/s\alpha^2$
t	Time measured in generations
T	Scaled time, $T = ts\alpha^2/2$
p_{Xi}	Frequency of the '+' allele at locus i in deme X ($q_{Xi} = 1-p_{Xi}$)
z_0	Optimum phenotype
z_X; z_{Tot}	Mean phenotype in deme X; mean phenotype of total population
V_X; V_{Tot}	Genetic variance of deme X; genetic variance of total population
n	Number of loci
c	Number of clashing loci
m_X	Number of loci close to loss for the '+' allele in deme X

i from the maternal chromosome is denoted l_i, and from the paternal chromosome l_i^*. Thus, if we ignore any epistatic effects, z' is defined as:

$$z' = \alpha\sum_i (l_i + l_i^* - 1), \tag{1}$$

where α is the effect of each allele, assumed equal across loci. The character is assumed to be completely heritable, and the fitness of an individual with phenotype z' is assumed to follow a Gaussian curve centred on some optimum, z_0, with variance $1/s$, where s is the strength of stabilizing selection, which is assumed to be weak. Environmental variance is neglected, but this could be included by rescaling the parameters.

By rescaling time relative to $s\alpha^2/2$ such that $T = ts\alpha^2/2$, where t denotes time measured in generations, the equation for the effects of selection is:

$$\mathrm{d}p_i/\mathrm{d}T = p_i q_i[(p_i - q_i) - 2\delta] \tag{2a}$$

(Equation 4 in Barton, 1986). Here, p_i and q_i are the frequencies of the two alleles '+' and '−' at the ith locus, and δ is the deviation of the mean phenotype, z, from the optimum, z_0, relative to the effect of a single gene, α:

$$\delta = (z - z_0)/\alpha = 2\sum_i (p_i - 1/2) - z_0/\alpha. \tag{2b}$$

This rescaling greatly simplifies the analysis, but is possible only if selection is weak. The first term in (2a) represents selection acting against the genetic variance, and the second term represents selection on the mean towards the optimum phenotype.

If we now introduce recurrent mutation at an equal rate μ in each direction, (2) becomes:

$$\mathrm{d}p_i/\mathrm{d}T = p_i q_i[(p_i - q_i) - 2\delta] - 2\gamma(p_i - q_i). \tag{3}$$

Here γ is a measure of the rate of mutation, relative to the selection pressure on a single locus: $\gamma = \mu/s\alpha^2$.

(ii) *Mutation/selection balance with migration between two demes*

Suppose now that we have two demes, A and B, which have both independently reached equilibrium to the same or differing optima, as described by setting (3) to zero. Now assume that migration occurs at an equal rate, $\hat{\lambda}$, between these two demes. Migration will restore linkage disequilibrium every generation, and moreover the number of linkage disequilibrium coefficients will increase with the square of the number of loci involved in the system. Consequently migration will have to be very low if the combined effects of selection and migration are to be much less than the effects of recombination, which is necessary for the assumption of linkage equilibrium. In the following analysis we will find that differences between the two populations can only be maintained at these very low migration rates, making this assumption of linkage equilibrium reasonable. Now (3) can be extended to each of the two demes. The subscript A denotes results for deme A, and similarly for deme B:

$$\mathrm{d}p_{Ai}/\mathrm{d}T = p_{Ai}q_{Ai}[(p_{Ai} - q_{Ai}) - 2\delta_A] - 2\gamma(p_{Ai} - q_{Ai}) + \lambda(p_{Bi} - p_{Ai}), \tag{4a}$$

$$\mathrm{d}p_{Bi}/\mathrm{d}T = p_{Bi}q_{Bi}[(p_{Bi} - q_{Bi}) - 2\delta_B] - 2\gamma(p_{Bi} - q_{Bi}) + \lambda(p_{Ai} - p_{Bi}), \tag{4b}$$

where λ is a measure of the rate of migration, relative to the selection pressure on a single locus such that $\hat{\lambda}/s\alpha^2$. At equilibrium we have a pair of simultaneous equations, each of third order as in the one-deme case, resulting in a ninth-order polynomial giving nine solutions for p_{Ai} and p_{Bi}. That is, at equilibrium, the '+' allele at each of the loci controlling the quantitative trait could be at one of nine possible frequencies.

The means and the variances of the quantitative trait z' are:

$$z_x = 2\alpha\sum_i (p_{xi} - 1/2), \tag{5a}$$

$$V_x = 2\alpha^2\sum_i (p_{xi}q_{xi}), \tag{6a}$$

where X denotes the deme A or B. For the population as a whole the mean, z_{Tot}, and the variance, V_{Tot}, are given by:

$$z_{Tot} = \frac{z_A + z_B}{2}, \tag{5b}$$

$$V_{Tot} = \frac{V_A + V_B}{2} + \tfrac{1}{4}(z_A - z_B)^2. \tag{6b}$$

Thus the genetic variance for the population as a whole depends on both the variance within the two demes, and the difference between the means in the two populations.

https://doi.org/10.1017/S0016672397002644 Published online by Cambridge University Press

3. Results

(i) *No deviation from the optimum phenotype*

I first consider the case where the mean phenotype matches the optimum in each deme, described by (4a) and (4b) with $\delta_A, \delta_B = 0$. Note that the optima may or may not be the same across the demes. Although this is a very special case, it lends itself to analysis and will give a good guide to the full problem. The situation may arise if the mean can evolve to match the optimum in each deme, although in reality this is very unlikely to occur. In the absence of migration, two isolated demes could evolve to match the optimum in each of their habitats, especially in the absence of epistasis and pleiotropy. However, once migration between the two demes is allowed the populations will be pulled away from their optima due to the migration pressure, and consequently the mean phenotype will no longer match the optimum in each deme. For the mean to match the optimum in the respective demes, in the presence of migration, a situation must be imagined in which the migration itself pulls the demes from sub-optimal mean phenotypes to optimal ones.

Not all the nine equilibria will be feasible and stable (see Appendix for a description of the multilocus linear stability analysis). For this system, at most five of the equilibria are stable (Table 2). The first of the solutions ($p_A = p_B = 1/2$) is stable only when mutation is so high that all effects of selection are effectively swamped, resulting in the '+' and '−' alleles reaching intermediate frequencies in both the demes. Consequently, for the purpose of this analysis, it will be assumed that this solution is unstable. Of the remaining eight solutions, four can be stable: the solutions where $p_A = p_B = (1 \pm \sqrt{1-8\gamma})/2$ are feasible and are stable whenever $\gamma < 1/8$. These are called 'non-clashing' solutions since the '+' allele is either close to loss in both the demes, or close to fixation in both the demes. The solutions where $p_A = q_B =$

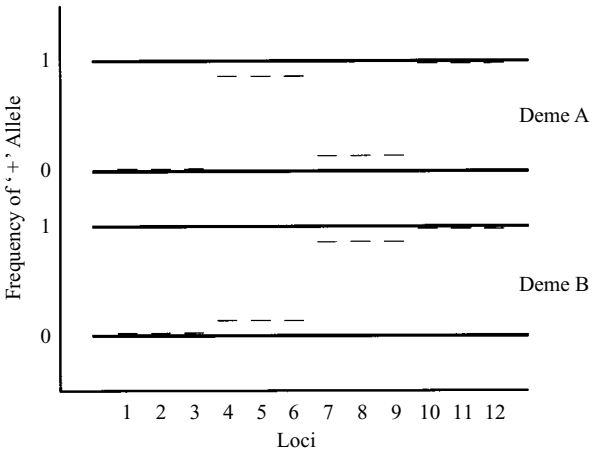

Fig. 1. A sketch showing allele frequencies in a 12-locus system. The dashes show the frequency of the '+' allele in the two demes at each of the loci numbered 1 to 12. Loci 1, 2 and 3 are close to loss for the '+' allele in both the demes, and loci 9, 10 and 11 are close to fixation for the '+' allele in both the demes. These loci are 'non clashing'. Loci 4, 5, 6 and loci 7, 8, 9 are 'clashing' since, for each of these loci, in one of the demes the '+' allele is close to fixation, whereas in the other it is close to loss.

Table 2. *The solutions to (4a, b), and the criteria for their existence and stability, in the case where* $\delta_A = \delta_B = 0$

	$p_A q_A$	p_A	p_B	Conditions for existence of solution	Conditions for stability of solution
$p_A = p_B$	$1/4$	$1/2$	$1/2$	Always	$\gamma > 1/8$
$p_A = p_B$	2γ	$\frac{1-\sqrt{1-8\gamma}}{2}$	$\frac{1-\sqrt{1-8\gamma}}{2}$	$\gamma < 1/8$	$\gamma < 1/8$
$p_A = p_B$	2γ	$\frac{1+\sqrt{1-8\gamma}}{2}$	$\frac{1+\sqrt{1-8\gamma}}{2}$	$\gamma < 1/8$	$\gamma < 1/8$
$p_A = q_B$	$2\gamma+\lambda$	$\frac{1-\sqrt{1-8\gamma-4\lambda}}{2}$	$\frac{1+\sqrt{1-8\gamma-4\lambda}}{2}$	$\gamma < 1/8-\lambda/2$	$\gamma < 1/8-3\lambda/4$
$p_A = q_B$	$2\gamma+\lambda$	$\frac{1+\sqrt{1-8\gamma-4\lambda}}{2}$	$\frac{1-\sqrt{1-8\gamma-4\lambda}}{2}$	$\gamma < 1/8-\lambda/2$	$\gamma < 1/8-3\lambda/4$
	$(x+y)/8$	$\frac{2+\sqrt{2(x+y)}}{4}$	$\frac{2-\sqrt{2(x-y)}}{4}$	$\gamma < 1/8-3\lambda/4$	Never
	$(x+y)/8$	$\frac{2-\sqrt{2(x-y)}}{4}$	$\frac{2+\sqrt{2(x+y)}}{4}$	$\gamma < 1/8-3\lambda/4$	Never
	$(x+y)/8$	$\frac{2-\sqrt{2(x+y)}}{4}$	$\frac{2+\sqrt{2(x-y)}}{4}$	$\gamma < 1/8-3\lambda/4$	Never
	$(x+y)/8$	$\frac{2+\sqrt{2(x-y)}}{4}$	$\frac{2-\sqrt{2(x+y)}}{4}$	$\gamma < 1/8-3\lambda/4$	Never

Where $x = 1+8\gamma+2\lambda$, and $y = \sqrt{1-16\gamma+64\gamma^2-4\lambda+32\gamma\lambda-12\lambda^2}$.

https://doi.org/10.1017/S0016672397002644 Published online by Cambridge University Press

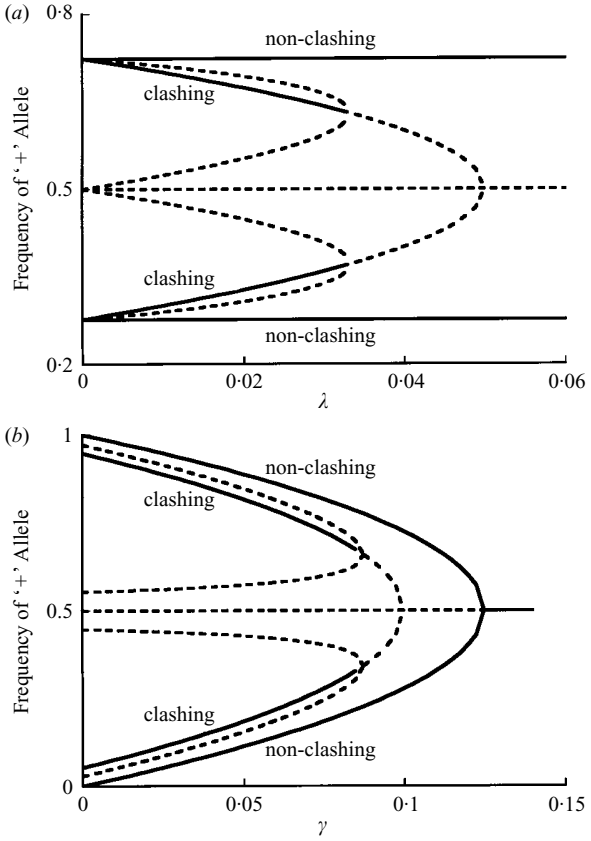

Fig. 2. Solutions to (4a, b), where $\delta_A = \delta_B = 0$, $s = 1$ and $\alpha = 0{\cdot}1$. The continuous lines represent the stable solutions, and the dashed lines the unstable solutions. The solutions form a series of pitch-fork bifurcations. (*a*) For γ held fixed at 0·1 (corresponding to a mutation rate of 0·001), the frequency of the '+' allele at non clashing loci remains constant as λ increases, but at clashing loci the frequency approaches 0·5. Once λ reaches 0·033 (migration rate = 0·000167) the solution at clashing loci becomes unstable. The maximum value of λ for which a solution exists is 0·050 (migration rate = 0·000250). The non-clashing solutions always exist and are always stable. (*b*) For λ held fixed at 0·05, the frequency of the '+' allele at clashing and non-clashing loci approaches 0·5 as γ increases. Once γ-reaches 0·0875 (mutation rate = 0·000875) the solution at clashing loci becomes unstable, and the maximum value of γ for which a clashing solution exists is 0·100 (mutation rate = 0·001). The non-clashing solutions both become unstable and cease to exist when $\gamma = 0{\cdot}125$ (mutation rate = 0·00125).

$(1 \pm \sqrt{1-8\gamma-4\lambda})/2$ are feasible and stable whenever $\gamma < 1/8 - 3\lambda/4$. These are called 'clashing' solutions since the '+' allele is close to loss in one of the demes and close to fixation in the other (Fig. 1).

The multilocus stability analysis shows a remarkably simple result: the stability of the system does not depend on the state of all the loci. If there are any clashing loci the system will be stable if $-1+8\gamma+6\lambda$ is negative, and if there are no clashing loci the solution will be stable if $-1+8\gamma$ is negative.

Fig. 2 shows how the gene frequencies change for varying levels of migration and selection. If the mutation rate is kept constant ($\gamma = 0{\cdot}1$), then, as migration is increased (Fig. 2*a*), the frequency of the '+' allele at non-clashing loci remains constant, whereas at clashing loci the allele frequencies gradually become more intermediate, since at these clashing loci migration will tend to reduce the discrepancy in allele frequencies between the two demes. When λ exceeds 0·0333, the solutions at clashing loci become unstable, and when λ exceeds 0·05 the solutions at clashing loci become imaginary. If migration is now held constant ($\lambda = 0{\cdot}05$), the clashing and non-clashing allele frequencies become more and more intermediate as mutation increases (Fig. 2*b*). Once γ exceeds 0·0875 the clashing solutions become unstable, and they no longer exist when γ exceeds 0·100. The non-clashing solutions both become unstable and imaginary when $\gamma = 0{\cdot}125$. Thus as migration and/or mutation increase, it becomes less likely that we will see divergence between two populations.

So, if two demes within a population independently adapt optimally to the selection pressures in their respective environments, differences can be maintained between the two populations if $-1+8\gamma+6\lambda$ is negative, that is if $\hat{\lambda} < (s\alpha^2/12) - (2\mu/3)$ (the criterion for stability). Migration must therefore be very low in relation to selection if migration is not going to swamp selection and the two demes are to remain distinct. If, for example, $s\alpha^2 = 0{\cdot}01$ and $\mu = 0{\cdot}0001$, then $\hat{\lambda}$ must be less than 0·00077. This value of migration is very low, amounting to fewer than 8 migrants per 10 000 individuals per generation in each population. This small value implies a very large barrier to migration, which may be very uncommon in nature. This criterion for the maintenance of polymorphism differs from Phillips's (1996) critical migration rate. He does not consider mutation, and since he deals with unidirectional migration there are only three possible equilibria. Only one of these equilibria can be stable, and it is stable wherever it exists. Thus Phillips's criterion for the maintenance of polymorphism is $\hat{\lambda} < (s\alpha^2/16)$. This differs from the criterion for the existence of clashing loci in the model presented here ($\hat{\lambda} < (s\alpha^2/8)$, for $\mu = 0$) by a factor of 2 since here gene flow occurs in both directions. Consequently, for low mutation rates, the conditions for the maintenance of polymorphism are less restrictive than in Phillips's model. In effect, when the mean equals the optimum, the critical migration rate calculated under unidirectional migration gives a lower bound to the rate, whereas the assumption here of balanced migration rates provides an upper bound. If migration rates are unbalanced between the two populations, as will be the most likely scenario in natural populations, the actual critical migration rate will fall somewhere between the two bounds.

If the deviation of the mean from the optimum in the two demes is negligible, the genetic variance within the two demes can be found analytically:

$$V_A = V_B = 2\alpha^2(2n\gamma + c\lambda) = \frac{4}{s}(n\mu + c\hat{\lambda}), \qquad (7)$$

https://doi.org/10.1017/S0016672397002644 Published online by Cambridge University Press

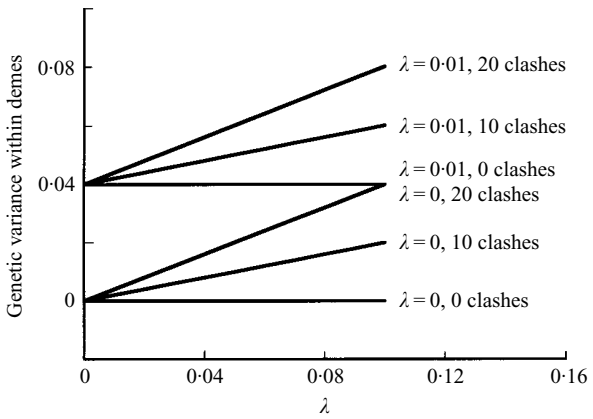

Fig. 3. The genetic variance within demes, for increasing migration ($\lambda = 2\hat{\lambda}/s\alpha^2$), where δ_A, $\delta_B = 0$, and consequently $V_g = 4/s(\mu n + \hat{\lambda}c)$. Genetic variance increases with the mutation rate at all the loci, and with the migration rate at each of the clashing loci.

where n is the total number of loci, and c is the number of clashing loci. Thus, the genetic variance within the demes is dependent on the mutation rate at all the loci, and on the migration rate between clashing loci. Interestingly (7) is the sum of the two, although the equations are non-linear. The first term corresponds to the variation in a system of mutation/selection balance (Latter, 1960; Bulmer, 1972; Turelli, 1984), and the second term to a system in migration/selection balance (Phillips, 1996).

Fig. 3 shows how the genetic variance within each deme increases with increasing migration, mutation and number of clashing loci. For example, for $\gamma =$ 0·01, increasing the number of clashes from 0 to 20 doubles the quantitative genetic variance within the two demes.

The minimum genetic variance for each deme can be estimated, given the difference in the optima between the two demes at equilibrium. The increase in genetic variance due to linkage disequilibrium caused by incoming migrants for a quantitative trait can be expressed as $(\Delta z)^2\hat{\lambda}(1-\hat{\lambda})/r$, where r is recombination fraction and $\Delta z = z_A - z_B$ (Barton & Gale, 1993). The minimum number of clashes will be $\Delta z/2\alpha$. At low migration rates, such as for the value 0·00077 calculated above, the minimum genetic variance, V_g, expected in each of the demes will therefore be:

$$V_g = \frac{4n\mu}{s} + \frac{2\Delta z\hat{\lambda}}{s\alpha} + \frac{(\Delta z)^2\hat{\lambda}}{r}, \tag{8}$$

where the first term represents the increase in the genetic variance attributable to mutation, the second term the increase due to clashing loci, and the last term is the increase in the variance created by linkage disequilibrium due to incoming migrants. We can see from (8) that the ratio between the amount of genetic variance generated from linkage disequilibrium from incoming migrants and that generated by increased heterozygosity is $s\alpha\Delta z$ (if r is taken to be 1/2). We can express this in terms of dimensionless quantities by defining $L = (s\Delta z^2/2)$ as the difference in fitness between a native individual at the optimum for its own deme, and an immigrant at the mean value of the other deme. Then, the ratio becomes $2L(\alpha/\Delta z)$. Thus, if the typical fitness difference between immigrants and natives is small ($L \ll 1$), and if several loci have diverged ($\alpha \ll \Delta z$), then increased heterozygosity will generate much more genetic variance than will linkage disequilibrium. For example, if we take $s = 1$, $\alpha = 0{\cdot}1$ and $\Delta z = 1$, then L will equal 1/2 and the ratio of the amount of genetic variance generated from linkage disequilibrium to that created by increased heterozygosity will be only 0·1. Heterozygosity will therefore account for 10 times more genetic variance than will linkage disequilibrium produced from incoming migrants. The Bulmer effect, where negative linkage disequilibrium is produced due to stabilizing selection, will reduce the genetic variance by $s(V_s)^2/r$ each generation, where V_s is the standing genetic variance (Bulmer, 1985). However, since sV_s is small and $r =$ 1/2, the reduced genetic variance resulting from the Bulmer effect will be small. Thus for the range of

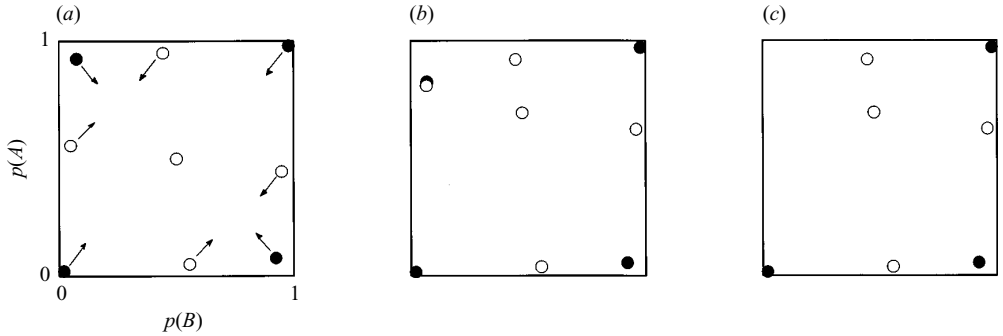

Fig. 4. The nine dots show the solutions to (4a, b). The filled circles represent the stable solutions, open circles the unstable solutions. In all cases $\gamma = 0{\cdot}01$, $\lambda = 0{\cdot}05$ and $\delta_B = 0$. (*a*) Solutions where $\delta_A = 0$. The arrows show how the solutions move on the plane if γ or λ are increased (the non-clashing solutions do not move if λ is increased). (*b*) Solutions where $\delta_A = 0{\cdot}149$. Two of the solutions in this case have almost converged. (*c*) $\delta_A = 0{\cdot}150$. Two of the solutions have formed a conjugate pair with imaginary parts, and are therefore no longer shown on the plane.

https://doi.org/10.1017/S0016672397002644 Published online by Cambridge University Press

migration rates expected to maintain differences between populations, the effects of linkage disequilibrium on the genetic variance are small.

Note also that (8) represents the increased genetic variance within the two demes due to selection for different optima in the two demes. The genetic variance will increase further if there is also cryptic genetic divergence between the two demes, resulting in more than the minimum number of clashes. In this case the genetic variance due to both migration and linkage disequilibrium will increase.

(ii) *Deviation from the optimum*

So far I have only considered the case where the mean equals the optimum in each of the demes. In general, however, the mean will deviate from the optimum. Migration may, for example, pull the mean away from the optimum in the two demes if the genetic structure of the demes differs. In many cases this deviation will be very small if the demes are at optimal adaptive peaks, but if one or both of the demes are at sub-optimal peaks then the discrepancy is likely to be larger (Barton, 1986). It may be that even in this case the deviation will be small enough that the preceding analysis provides a good approximation, but this can not be assumed. Barton (1986) showed that in the one-deme case, δ will always be less than $1/2$. Although this deviation is small, it could nevertheless have a substantial effect on the genetic variance.

For δ_A and δ_B not equal to zero, (4a) and (4b) can no longer be solved analytically, but solutions can be found numerically, given the number of loci and clashes and given the optima in the two demes. In the following analysis, the equations were solved numerically using the secant method, and stability determined from the eigenvalues of the matrix S (Appendix).

Suppose that the deviation of the mean from the optimum in deme B (δ_B) is zero, but in deme A it varies. Note again that the optima in the two demes may or may not be the same; it is the deviation of the mean from the optimum that is important. Fig. 4 shows the nine possible solutions, and their stability, for each locus for increasing δ_A. If $\delta_A = \delta_B = 0$, clashing solutions become unstable when any of the neighbouring unstable solutions become imaginary. In all other cases, the four solutions that can be stable will be stable if they exist. For the subsequent analysis we have assumed that the other five solutions are always unstable, which, considering the outcomes of the numerical iterations of the equations, I think is a reasonable assumption. Wright (1935*b*) has shown that in some circumstances intermediate allele frequencies can be stable, but only if just one of the loci is at this intermediate state. Moreover, this requires low mutation rates such that $(n+1)^2\gamma < 1$ (Barton, 1986).

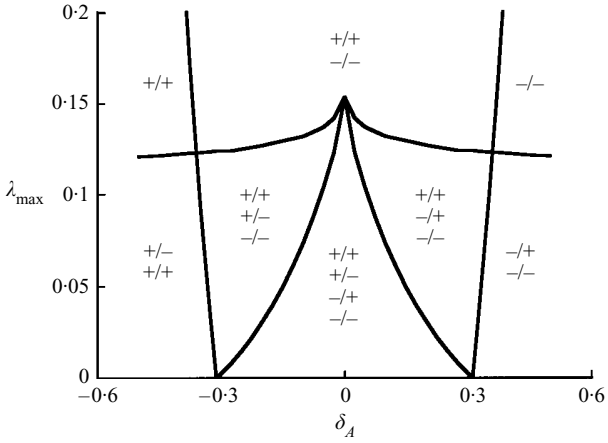

Fig. 5. The areas of the graph show which solutions can be stable as δ_A deviates from zero and as migration increases, where $\delta_B = 0$ and $\gamma = 0{\cdot}01$ (corresponding to a mutation rate of 0·0001, if $s = 1$ and $\alpha = 0{\cdot}1$). $+/-$ represents the solution where deme A is close to fixation for the '+' allele, and deme B is close to loss for this allele.

Fig. 5 shows the range of values of migration for which the four possibly stable solutions exist given a value of δ_A (δ_B is fixed at zero). We can see that, as the mean phenotype of deme A deviates from the optimum phenotype, the maximum migration rate at which differences can be maintained between the populations decreases.

If we have a system in which both $+/-$ (the '+' allele is close to fixation in deme A, and close to loss in deme B) and $-/+$ clashes exist, we can define λ_{max} as the maximum level of migration, above which the system can no longer exist because one or other of the clashing solutions becomes imaginary. This is analogous to the critical migration rate defined above. Fig. 6*a* shows how λ_{max} varies as the optimum phenotype of deme A changes, and as the number of loci close to loss for the '+' allele in deme A, m_A, differ, for $\gamma = 0{\cdot}01$. We see that the migration rate between the two demes dictates the possible values of m_A, and hence the number of peaks on the adaptive landscape for deme A. If the optimum for deme A is equal to zero, for example, then the higher the migration rate the less m_A can deviate from 50, and consequently fewer combinations of genes, or classes of genotypes, are possible in deme A. If λ remains less than 0·1533 (corresponding to an actual migration rate of 0·00077), divergence between the two demes can be maintained, but once λ exceeds this the only stable system is one in which there are no clashes, leaving us with a single monomorphic population. Consequently the variance within the two demes would also decrease.

Fig. 6*b* shows the maximum genetic variances within deme A, obtained by setting migration to λ_{max}. Comparing the numerical calculation of genetic variance, and the value that an analytical approximation would give (that is, where the mean equals the optimum in both the demes, and hence where δ_A and

https://doi.org/10.1017/S0016672397002644 Published online by Cambridge University Press

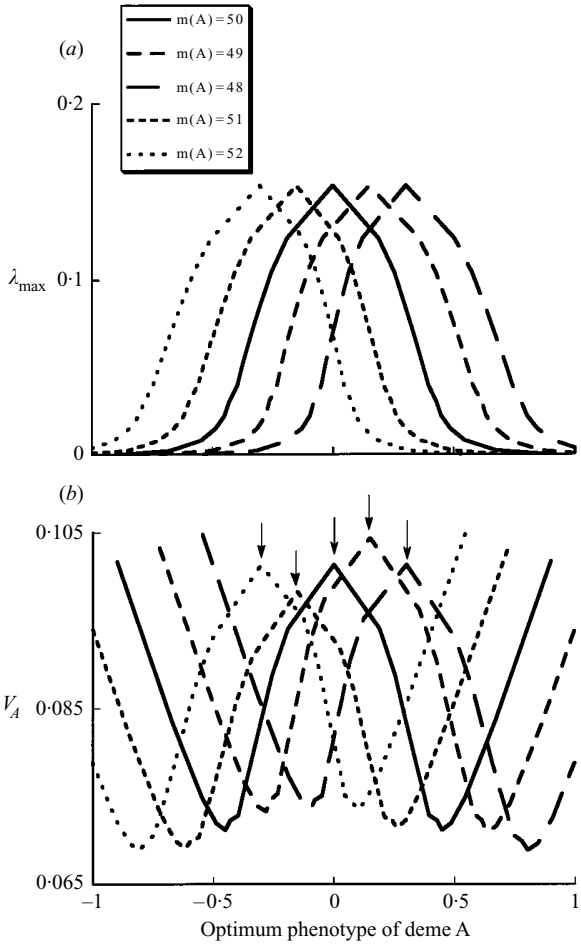

Fig 6. (*a*) The maximum migration, λ, at which the system can exist and be stable as the optimum phenotype of deme A varies, for $\gamma = 0{\cdot}01$ and optimum of deme B fixed at 0. m_B is fixed at 50, and consequently δ_B assumed to be negligible. The five lines represent varying values of m_A. For $m_A = 52$, 50 and 48 the number of clashes is 20, for $m_A = 49$ there are 21 clashes; and for $m_A = 51$ there are 19 clashes. (*b*) The corresponding genetic variances in deme A, the arrows indicating the genetic variance if δ_A and δ_B are assumed to equal zero. The asymmetry arises because of the varying number of clashes.

δ_B are assumed to be zero, as shown by the arrows), it can be seen that in most cases, where migration is at the critical rate, the analytical approximation would tend to overestimate the variance. If the mean is close to the optimum in both the demes, the analytical approximation is fairly close both for the maximum level of migration at which the system can be maintained and for the genetic variance within the populations.

(iii) *Divergence of populations*

Finally, I consider how clashes can be created between populations. They may simply result from random genetic drift (Wright, 1932; Barton, 1989; Barton & Rouhani, 1991; Goldstein and Holsinger, 1992), or alternatively could originate deterministically if selection is fluctuating in time or space. Suppose we begin with a single monomorphic population where the optimum phenotype is zero and where 50 of the 100 loci are close to fixation for the '+' allele. Next, suppose there is a change in optimum for one deme within this population (call this deme A), such that the optimum is now less than $-0{\cdot}483$, where $\lambda = 0{\cdot}1$. By calculating δ_A from (2b), we find δ_A will exceed 0·351 for this system, and thus from Fig. 5 we see that the solutions where both demes are close to fixation for the '+' allele are no longer feasible. However, if m_A changes to 51 (that is, if one of the loci close to fixation for the '+' allele in deme A changes such that it becomes close to loss for the '+' allele), we see from Fig. 6*a* that the equilibrium now exists and is stable. If the optimum phenotype changes further in this direction more switches become necessary (in practice, random genetic drift will play a role in determining which of the loci switch). If the optimum fluctuates back to zero or beyond, loci in deme A would switch from close to loss, to close to fixation, for the '+' allele. However, the loci which switch in this process will not necessarily be the ones that switched originally (although since the variance at clashing loci is greater this will tend to be the case). Hence, in the space of one environmental fluctuation we can envisage four clashing loci being created, and consequently the variance within the two demes increases from 0·040 to 0·048. If 20 clashes were created in such a process the genetic variance within the two demes would equal 0·080.

If the unscaled versions of (4a, b) are iterated for 20 loci, adding a Binomial expression for genetic drift with mean p and variance $pq/(2n)$ during each iteration of the calculation of the gene frequencies, then each of the loci settles down to either clashing or non-clashing solutions as expected. Moreover, the more clashing loci there are in the system, the greater the genetic variance when the system settles down close to equilibrium. However, if the optimum changes in one of the demes such that one of the loci must switch, the tendency of the system will be to reduce, and not increase, the number of clashes. This is because the genetic variance at clashing loci is greater than at non-clashing loci and so these loci respond quicker to changes in selection pressures. Thus, if there is constant migration during environmental fluctuations, clashes will continually be created or lost because the two demes are adapting to different optima, but there will not be a tendency for the number of clashes to escalate. Consequently, the highest genetic variance within the two demes is observed when the optima of the demes are most different. An accumulation of clashing loci could occur if fluctuations are accompanied by isolation (no migration) or by a large amount of genetic drift. The numerical iterations of the equations were checked by comparing the output with the expected analytical results and the amount of variance expected due to random drift.

https://doi.org/10.1017/S0016672397002644 Published online by Cambridge University Press

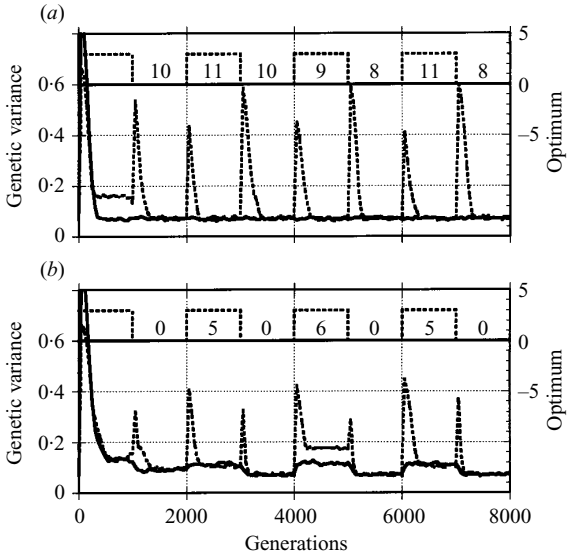

Fig. 7. The genetic variance within both the demes when (4a, b) are iterated for 8000 generations with 20 loci in the presence of random genetic drift (number of individuals in each population, N, is 5000) where $s = 1$, $\alpha = 0{\cdot}3$ and $\gamma = 0{\cdot}01$. The optimum of deme B remains constant at 0 (continuous line), while the optimum of deme A fluctuates between 0 and 3 every 1000 generations (dotted line). The numbers represent the number of clashing loci. (*a*) The two demes are isolated. The average genetic variance in deme A is 0·132, and for deme B is 0·072. (*b*) There is gene flow between the two demes such that $\lambda = 0{\cdot}05$. The average genetic variance in deme A is 0·127, and for deme B is 0·093.

Fig. 7 shows how the genetic variance within the two demes varies in time, as the optimum in one of the demes fluctuates. In both cases the random component added to the iterations describes the expected drift if the two demes each contain 5000 individuals, and the mutation rate, μ, equals 0·0009. In the first simulation (Fig. 7*a*) the two populations are isolated, whereas in the second simulation (Fig. 7*b*) the rate of migration, $\hat{\lambda}$, is 0·00225. In the case where there is no migration the genetic variance within the two demes remains close to that predicted by the analytical results ($V_A = V_B = 0{\cdot}0720$). The peaks in the genetic variance in deme A are a consequence of the switching of five of the loci each time the optimum phenotype of deme A changes from 0 to +3, or vice versa, since these loci temporarily find themselves at intermediate gene frequencies (Kondrashov & Yampolsky, 1996). At these switches V_B remains close to 0·0720, but V_A reaches up to 0·60. There is a high genetic variance in deme A for the first 1000 generations (V_A approximately 0·15) because one of the loci is at an intermediate gene frequency.

For the case where there is migration, we see that when the optimum in the two demes is the same (0 in both cases) the genetic variance is close to 0·0720, which is as expected since there are no clashing loci. However, when the optimum in deme A changes to +3, a few of the loci in deme A switch causing some of the loci to clash. The genetic variance within the demes consequently increases due to two processes. Firstly, as for the case where there is no migration, the switching of some of the loci temporarily increases the genetic variance within the deme where the switching is occurring, resulting in the peaks of genetic variance observed (V_A reaches up to 0·45). Secondly, some of the loci are clashing, and moreover the mean may deviate from the optimum in each of the demes, resulting in an increased genetic variance within the two demes at equilibrium (where there are five clashes V_A and V_B are both close to 0·11). Typically five clashes are created when the optimum in deme A changes from 0 to +3, which is close to what we would expect since the expected number of clashes when the mean equals the optimum in the two demes is $\Delta z/2\,\alpha$, which is five in this case. However, at generation 4000, six clashes were created. Consequently the differences in the means of the two demes are larger than when there are only five clashes, and each clash has a greater effect on the variance in this deme (V_A and V_B are approximately 0·18 and 0·12 respectively).

Taking the average genetic variance in each of the two demes for the two cases shown (the first 2000 generations are not included in this calculation since the system is still settling down) the addition of migration increases the mean genetic variance in deme B from 0·072 to 0·093. However, within deme A migration has the opposite effect and the mean genetic variance decreases from 0·132 to 0·127 since in the presence of migration the switching of loci from clashing to non-clashing happens faster than in its absence. If fluctuations were less frequent, the effects of switching on the variance would become less, and the mean genetic variance in deme A would then be greater in the presence rather than in the absence of migration.

4. Discussion

In this model of two demes, each in a mutation/selection balance, divergence between the populations can be maintained if migration is very low. For the assumptions made here on mutation and selection, migration must typically be less than 8 individuals migrating per 10000 individuals in each population per generation (from Table 2). When migration is even lower than this many possible classes of stable equilibria exist for each of the demes, but as migration increases the number of possible equilibria decreases. Once migration exceeds the threshold, divergence between the populations can no longer be maintained, leaving a single undifferentiated population. These migration rates are tiny, requiring a very strong barrier to gene flow which may be relevant to few natural populations. Moreover, the model is unrealistic for a number of reasons: pleiotropic effects

https://doi.org/10.1017/S0016672397002644 Published online by Cambridge University Press

have been ignored, and selection is assumed to be very weak. Where selection is strong, the effects of linkage disequilibrium can no longer be ignored, and the critical migration rate is likely to increase (Phillips, 1996).

If the optima in the two demes are the same, the process modelled here is a special case of the 'shifting balance' between drift, intrapopulation selection and interpopulation selection (Wright, 1932). The process is divided into three phases. In phase 1 genetic drift causes sub populations to cross adaptive valleys, and consequently occupy different regions of the adaptive landscape to one another. Phase 2 involves local selection taking populations to new optima, and during phase 3 adaptive peaks compete with each other so that fitter peaks spread through the whole species. This third phase is controversial for several reasons. For example, it is argued that analyses which model this last process (Crow *et al.*, 1990; Phillips, 1993) are in fact only demonstrating how migration swamps selection. This process is not adaptive because populations could move towards suboptimal peaks (Barton, 1992) . Here, however, we can see that if we have two subpopulations, one occupying an optimal peak on the adaptive landscape (deme B) and the other a suboptimal peak (deme A), then as migration increases symmetrically between the two populations the possible number of classes of equilibria for deme A decreases until eventually the only stable class is where deme A occupies one of the possible optimal adaptive peaks. If migration increases further the only stable equilibrium will be one in which the two populations occupy the same adaptive peak. Thus, as migration increases, it is the fitter peaks that spread through the whole species under the assumptions of this model. The consideration of only two demes may not be what Wright had in mind when he envisioned the shifting balance (Gavrilets, 1996), although it does provide a useful starting point for the analysis. If a fit deme were to be surrounded by unfit demes in a island type model, the fit deme would get swamped by the unfit migrants if migration is too high. At lower levels of migration the fit peak could still sweep through the population, although the critical migration rate will be higher (Gavrilets, 1996) .

We find also that divergence between demes within a population can greatly increase the quantitative genetic variance within these demes. Suppose, for example, that the strength of stabilizing selection, s, is 1, that the effect of each locus, α, is 0·1 and that migration between the two demes exceeds 0·005. If the two demes are undifferentiated such that there are no clashes, then in the absence of mutation there will be no genetic variance. If there are 20 clashes between the two demes, however, the genetic variance within each of these demes will increase to over 0·04 even if both populations occupy the optimal adaptive peaks and are subject to the same selection pressures. These clashes could be built up if the two populations are isolated, and then subject to differing selection regimes. Alternatively, if the selection pressures of the two demes are divergent, clashes could be built up even in the presence of gene flow, leading to possible reproductive isolation. For example, if the mean equals the optimum in the two demes, and for s and α as above, then if the difference in the means of the two populations is 2, there will be at least 10 clashing loci. This corresponds to the estimated minimum number of genes involved in producing large differences in quantitative traits between natural populations (Castle, 1921; Wright, 1952; Lande, 1981) . This estimate assumes that none of the loci act in opposition. That is, in the context of the model presented here, clashes are due to differing selection pressures and not cryptic genetic divergence. Moreover, for this number of clashes, the genetic variance attributable to migration is 5 times greater than that due to linkage disequilibrium (8), and as such the omission of linkage disequilibrium from the model should not greatly bias the results.

If the selection pressures are not divergent, but fluctuating, an escalating build-up of clashes is unlikely unless accompanied by peripheral isolation or high levels of genetic drift. Fluctuating selection does, however, increase the genetic variance within the two demes, since during the periods in which clashes occur the variance is increased. Moreover, when loci switch from near fixation for the '+' allele to near loss, or vice versa, the genetic variance increases dramatically during the switch. This is a similar observation to that found in single populations, where fluctuating selection can increase the genetic variance within a single population by several orders of magnitude, provided the fluctuations are in the right range of frequencies (Kondrashov & Yampolsky, 1996). Kondrashov & Yampolsky attribute the increase in variance to two factors. First, the population will often find itself at suboptimal equilibria leading to a higher genetic variance (Barton, 1986). The second, and far greater, effect comes when the population switches to a new equilibrium due to the changing optimum, since the actual process of substitution at a locus then greatly increases the variance. So, fluctuating selection in a system of two demes increases the genetic variance within each of the demes due to the intermediate gene frequencies of switching loci, and due to the existence of clashing loci in the presence of migration. As the frequency of fluctuation decreases, the latter will contribute more to the genetic variance than will the former.

This model shows that polymorphism can be maintained between two populations if levels of migration are sufficiently low, and that gene flow can then increase the genetic variance within the populations by several orders of magnitude. However, escalating divergence of the populations is unlikely in the presence of gene flow unless they experience persistently different selection pressures.

Appendix

Table A1. *Eigenvalues*

Condition for the existence of the eigenvalues	Eigenvalues	No. of repeats of the eigenvalues
Always	$-1+8\gamma+6\lambda$ $-1+8\gamma+4\lambda$	$(c-1)$ times
When $n-c=0$	$-1-8(n-1)\gamma-4(n-1)\lambda$ $-1-8(n-1)\gamma-4((n-1)-2)\lambda$	Once
When $n-c\geqslant 1$	$-1+8\gamma$ $-1+8\gamma-2\lambda$	$(n-c-1)$ times
When $c=0$	$-1-8(n-1)\gamma$ $-1-8(n-1)\gamma-2-\lambda$	Once
Always	$1/2[-2-8(n-2)\gamma-(4c-6)\lambda \pm \sqrt{[(2+8(n-2)\gamma+(4c-6)\lambda)^2-4(1+8(n-2)\gamma-64(n-1)\gamma^2+(4c-6)\lambda-16(2n-2-c)\gamma\lambda)]}]$ $1/2[-2-8(n-2)\gamma-(4c-2)\lambda \pm \sqrt{[(2+8(n-2)\gamma+(4c-2)\lambda)^2-4(1+8(n-2)\gamma-64(n-1)\gamma^2+(4c-2)\lambda-16(2n-1-c)\gamma\lambda+8(c-1)\lambda^2)]}]$	Once

n, number of loci; c, number of clashes.

In the model used here, a particular solution will be stable if the eigenvalues of the matrix:

$$s=\begin{pmatrix}(\partial\dot{p}_{Ai}/\partial p_{Aj}) & (\partial\dot{p}_{Ai}/\partial p_{Bj})\\ (\dot{p}_{Bi}/\partial p_{Aj}) & (\partial\dot{p}_{Bi}/\partial p_{Bj})\end{pmatrix},\ \text{are negative, where}$$

$$\frac{\partial\dot{p}_{Ai}}{\partial p_{Ai}}=2p_{Ai}q_{Ai}-4\gamma-\lambda-1-2\delta_A(q_{Ai}-p_{Ai}) \qquad \text{if } i=j$$

$$\frac{\partial\dot{p}_{Bi}}{\partial p_{Bi}}=2p_{Bi}q_{Bi}-4\gamma-\lambda-1-2\delta_B(q_{Bi}-p_{Bi}) \qquad \text{if } i=j$$

$$\frac{\partial\dot{p}_{Ai}}{\partial p_{Aj}}=-4p_{Ai}q_{Ai} \qquad \text{if } i\neq j$$

$$\frac{\partial\dot{p}_{Bi}}{\partial p_{Bj}}=-4p_{Bi}q_{Bi} \qquad \text{if } i\neq j$$

$$\frac{\partial\dot{p}_{Ai}}{\partial p_{Bi}}=\frac{\partial\dot{p}_{Bi}}{\partial p_{Ai}}=\lambda \qquad \text{if } i=j$$

$$\frac{\partial\dot{p}_{Ai}}{\partial p_{Bj}}=\frac{\partial\dot{p}_{Bi}}{\partial p_{Aj}}=0. \qquad \text{if } i\neq j$$

In the case where δ is assumed to be equal to zero, we have explicit expressions for the values pq in terms of λ and γ, and as a result the matrix, S, and its eigenvalues can be found analytically. For example, if we have three loci, where one of the loci is clashing, we have:

$$S=\begin{pmatrix}-1-\lambda & -8\gamma & -8\gamma & \lambda & 0 & 0\\ -8\gamma & -1-\lambda & -8\gamma & 0 & \lambda & 0\\ -8\gamma-4\lambda & -8\gamma-4\lambda & \lambda-1 & 0 & 0 & \lambda\\ \lambda & 0 & 0 & -1-\lambda & -8\gamma & -8\lambda\\ 0 & \lambda & 0 & -8\gamma & -1-\lambda & -8\lambda\\ 0 & 0 & \lambda & -8\gamma-4\lambda & -8\gamma-4\lambda & \lambda-1\end{pmatrix}.$$

If delta is equal to zero and the number of loci is greater than two, then eigenvalues are as in Table A1. Thus, when the deviation of the mean phenotype from the optimum phenotype is zero and when there are two or more clashing loci, the eigenvalue $-1+8\gamma+6\lambda$ always exists, independent of the number of loci. Moreover, by simple algebraic manipulation we find that if this eigenvalue is negative, then all the other eigenvalues are also negative. Hence, if $-1+8\gamma+6\lambda$ is negative, the system is stable. If there are no clashes, the system will be stable if $-1+8\gamma$ is negative.

For the case where delta is not necessarily equal to zero, the eigenvalues of the matrix need to be found numerically (e.g. using 'Mathematica': Wolfram, 1991).

Many thanks go to my supervisor Nick Barton. Thanks are also due to Ellen Baake and two anonymous referees for their helpful comments, and to BBSRC for financial support.

References

Barton, N. H. (1986). The maintenance of polygenic variation through a balance between mutation and stabilising selection. *Genetical Research* (*Cambridge*) **47**, 209–216.

Barton, N. H. (1989). The divergence of a polygenic system under stabilising selection, mutation and drift. *Genetical Research* (*Cambridge*) **54**, 59–77.

Barton, N. H. (1992). On the spread of new gene combinations in the third phase of Wright's shifting-balance. *Evolution* **46**, 551–557.

Barton, N. H. & Gale, K. S. (1993). Genetic analysis of hybrid zones. In *Hybrid Zones and the Evolutionary Process* (ed. R. G. Harrison), pp. 13–45. Oxford: Oxford University Press.

https://doi.org/10.1017/S0016672397002644 Published online by Cambridge University Press

Barton, N. H. & Rouhani, S. (1991). The probability of fixation of a new karyotype in a continuous population. *Evolution* **45**, 499–517.
Barton, N. H. & Turelli, M. (1989). Evolutionary quantitative genetics: how little do we know? *Annual Review of Genetics* **23**, 337–370.
Bulmer, M. G. (1972). The genetic variability of polygenic characters under optimizing selection, mutation and drift. *Genetical Research* (*Cambridge*) **19**, 17–25.
Bulmer, M. G. (1985). *The Mathematical Theory of Quantitative Genetics*. Oxford: Oxford University Press.
Castle, W. E. (1921). An improved method of estimating the number of genetic factors concerned in cases of blending inheritance. *Science* **54**, 223.
Coyne, A. C. (1992). Genetics and speciation. *Nature* **355**, 511–515.
Crow, J. F., Engels, W. R. & Denniston, C. (1990). Phase three of Wright's shifting-balance theory. *Evolution* **44**, 233–247.
Endler, J. A. (1977). *Geographic Variation*, *Speciation*, *and Clines*. Princeton, NJ: Princeton University Press.
Felsenstein, J. (1976). The theoretical population genetics of variable selection and migration. *Annual Review of Genetics* **10**, 253–280.
Gavrilets, S. (1996). On Phase Three of the shifting balance theory. *Evolution* **50**, 1034–1041.
Goldstein, D. B. & Holsinger, K. E. (1992). Maintenance of polygenic variation in spatially structured populations: roles for local mating and genetic redundancy. *Evolution* **46**, 412–429.
Houle, D. (1991). Genetic covariance of fitness correlates: what genetic correlations are made of and why it matters. *Evolution* **45**, 630–648.
Karlin, S. & McGregor, J. (1972). Application of method of small parameters to multi-niche population genetic models. *Theoretical Population Biology* **3**, 186–209.
Kimura, M. (1965). A stochastic model concerning the maintenance of genetic variability in quantitative characters. *Proceedings of the National Academy of Sciences*, *USA* **54**, 731–736.
Kondrashov, A. S. & Yampolsky, L. Y. (1996). High genetic variability under the balance between symmetric mutation and fluctuating stabilizing selection. *Genetical Research* (*Cambridge*) **68**, 157–164.
Lande, R. (1976). The maintenance of genetic variability by mutation in a polygenic character with linked loci. *Genetical Research* (*Cambridge*) **26**, 221–236.
Lande, R. (1980). Genetic variation and phenotypic evolution during allopatric speciation. *American Naturalist* **116**, 463–479.
Lande, R. (1981). The minimum number of genes contributing to quantitative variation between and within populations. *Genetics* **99**, 541–553.
Latter, B. D. H. (1960). Natural selection for an intermediate optimum. *Australian Journal of Biological Science* **13**, 30–35.
Maynard Smith, J. (1983). The genetics of stasis and punctuation. *Annual Review of Genetics* **17**, 11–25.
Mousseau, T. A. & Roff, D. A. (1987). Natural selection and the heritability of fitness components. *Heredity* **59**, 181–198.
Nagylaki, T. (1975). Conditions for the existence of clines. *Genetics* **80**, 595–615.
Phillips, P. C. (1993). Peak shifts and polymorphism during Phase Three of Wright's shifting balance process. *Evolution* **47**, 1733–1743.
Phillips, P. C. (1996). Maintenance of polygenic variation via a migration–selection balance under uniform selection. *Evolution* **50**, 1334–1339.
Slatkin, M. (1973). Gene flow and selection in a cline. *Genetics* **75**, 733–756.
Slatkin, M. (1978). Spatial patterns in the distribution of polygenic characters. *Journal of Theoretical Biology* **70**, 213–228.
Turelli, M. (1984). Heritable genetic variation via mutation–selection balance: Lerch's zeta meets the abdominal bristle. *Theoretical Population Biology* **25**, 138–193.
Wolfram, S. (1991). *Mathematica*. New York: Addison-Wesley.
Wright, S. (1932). The roles of mutation, inbreeding, crossbreeding and selection in evolution. In *Proceedings of the Sixth Annual Congress on Genetics*, vol. 1, pp. **1**, 356–366.
Wright, S. (1935*a*). The analysis of variance and the correlation between relatives with respect to deviations from an optimum. *Journal of Genetics* **30**, 243–256.
Wright, S. (1935*b*). Evolution in populations in approximate equilibrium. *Journal of Genetics* **30**, 257–266.
Wright, S. (1952). The genetics of quantitative variability. Agricultural Research Council, Quantitative Inheritance. London: Her Majesty's Stationary Office (1) 1952. Reprinted in *Yearbook of Physical Anthropology*, pp. 159–195.