

## The influence of local extinctions on the probability of fixation of chromosomal rearrangements

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### Abstract

We investigated the influence of local extinctions in a subdivided population on the probability of fixation of an initially rare allele, for different migration rates. The selective regimes considered were strict underdominance, meiotic drive, and underdominance associated with meiotic drive.

We show that local extinctions can increase the probability of fixation of initially rare alleles in underdominant loci for relatively high migration rates, even when both homozygotes have the same fitness. This increase is due to drift during founder events. On the contrary, local extinctions decrease the probability of fixation of alleles favoured by meiotic drive. For a locus where both meiotic drive and underdominance act, the effect of local extinctions depends on the relative strength of the two selective regimes and the initial frequency of the rare allele. For parameter values such that the rare allele is initially selected against, local extinctions decrease the probability of fixation for low migration rates while they cause an increase for moderate migration rates. When the parameter values are such that the rare allele should always be favoured by selection, local extinctions always decrease the probability of fixation. In this latter case, we show the existence of an optimal migration rate which maximizes the probability of fixation.

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## Introduction

Many closely related species (or even races of the same species) may differ by a small number of chromosomal inversions or translocations. Such chromosomal differences have been reported to lead to a negative heterotic effect, thereby rendering the character underdominant. This has been observed for example for Robertsonian fusions in mice (Gropp et al., 1982) and chromosomal rearrangements in bats (Baker and Bickham, 1980). Underdominance is a situation in which the heterozygotes have a fitness inferior to that of the two homozygotes; there exists an unstable equilibrium point, such that when an allele (from a population genetics point of view we can regard a haploid karyotype as an allele) is below its equilibrium frequency it is selected against, while when it is above this frequency it is selected for. When the equilibrium frequency of a given allele is low, a greater range of allelic frequencies leads to its final fixation (Hedrick, 1981). Hence, any evolutionary force tending to reduce the equilibrium frequency of an allele in an underdominant system, will facilitate its eventual fixation (see Appendix 1 for the case of a single panmictic population). The fixation of many underdominant chromosomal variants is surprising, since such variants must occur at a very low frequency when they first appear.

In this paper computer simulations are used to study the effect of local extinctions and of recolonization on the probability of fixation of rare mutants in a subdivided population. The selective forces considered are strict underdominance (i.e. both homozygotes have the same fitness) and meiotic drive. The pattern of recolonization that we use is more realistic than that which is usually assumed by population genetics models, in that the probability of recolonization depends on the migration rate and that populations do not recover immediately after an extinction event but grow gradually towards carrying capacity. We show that local extinctions and recolonization increase the probability of fixation of a rare mutant even in the case of strict underdominance, a result not predicted by previous models (Lande 1979, 1985, and Slatkin, 1981). Furthermore we show that when meiotic drive and underdominance act at the same time, extinctions can either increase or decrease the probability of fixation, depending on whether the mutant is initially selected for or against. Under some conditions, and because of local extinctions, the probability of fixation may become a non-monotonic function of the migration rate.

## Theoretical background

### *1. Underdominant mutants*

Several population genetics models have attempted to explain how underdominant chromosomal rearrangements become fixed (Bengtsson and Bodmer, 1976; Lande, 1979 and 1985; Hedrick, 1981; and Slatkin, 1981). These models have shown that the factors which could favour the ultimate fixation of an initially rare mutant can be categorised as either (1) deterministic or (2) stochastic.

(1) Two deterministic factors may favour fixation, namely an advantage of the homozygote for the newly arisen allele and meiotic drive. Examples of meiotic drive are given by Zimmering et al. (1970) who defined it as any alteration of the normal process of transmission with the consequence that a heterozygote for two genetic alternatives produces an effective gametic pool with an excess of one type. Hedrick (1981) showed that the advantage of the new homozygote needs to be very high, and probably unrealistically high, to sufficiently lower the equilibrium frequency of the new allele in order to overcome its initial disadvantage. This is particularly true when the population size is finite (i.e. when drift may overcome the effects of a weak selection). A small amount of meiotic drive on the other hand can substantially modify the equilibrium frequency of such an allele (Hedrick, 1981). The important point is that meiotic drive, like underdominance, only affects heterozygotes. However, to explain the fixation of initially rare alleles of an underdominant system by such a mechanism, one has to assume that the mechanism leading to the segregation distortion arises at the same time as the new allele does, or at least soon after.

(2) The stochastic factors are also dominated by two processes: genetic drift and local extinctions. Genetic drift can increase the frequency of the recently arisen allele, such that by chance it rises above its unstable equilibrium frequency, and thus will be selected for. All population genetics models show that population subdivision, by decreasing the effective local deme size and therefore increasing the impact of genetic drift relative to that of selection, may lead to the fixation of initially rare alleles at an underdominant locus.

When migration is very limited (the "low migration limit", defined by  $Nm \ll 1/4$ , where  $N$  is the effective deme size and  $m$  the migration rate) the fixation of one allele in a single deme takes place much faster than the time scale associated with migration (Slatkin 1981; Lande, 1985). Therefore one can consider that at a given instant all demes are fixed for one allele or the other. Slatkin (1981) showed that in the low migration limit, the probability of spread of a given allele through the whole population once it is fixed in a single deme will only depend on the relative fitnesses of the two homozygotes. In particular, when both homozygotes have exactly the same fitness, the probability that a given allele will spread through the population once it is fixed in a single deme, is equal to the reciprocal of the number of demes. This result holds even when local extinctions occur (Lande, 1985). Recently, in a continuous population model, Barton and Rouhani (1991) have shown that the probability of fixation of a rare mutant can be significant even with high migration, provided that the local neighborhood size is small, and that the homozygote mutant has a substantial selective advantage over the standard homozygote.

## 2. Local extinctions and recolonization

Wright (1941) was the first to consider local extinctions in his shifting balance model, arguing that they may further reduce the average effective deme size, thus

enhancing the fixation of major chromosomal rearrangements over a wide area. Lewis (1962) suggested that periodic extinctions and recolonizations played a dominant role in the establishment of genetic deviants and evolutionary novelties. More recently the effects of local extinctions have been formalised in population genetics models (Slatkin, 1977; Maruyama and Kimura, 1980; Lande, 1985; Lande and Barrowclough, 1987; Ewens et al., 1987; Wade and McCauley, 1988; Whitlock and McCauley, 1990). Local deme extinctions have three main effects. They reduce the total population size since they decrease the number of extant populations. Recolonization can either enhance gene flow or increase the differentiation of local demes, depending on the interaction between the number of colonists relative to that of the migrants and the probability of common origin of the colonists (Wade and McCauley, 1988; Whitlock and McCauley, 1990). Finally, if recolonization is accomplished by a limited number of individuals, genetic drift will be very important during the period following foundation.

The recolonization rate has two components. The first is the probability that a site at which extinction has occurred will be recolonized, and the second is the number of recolonizers relative to the number of migrants. Most models consider that the number of recolonizers is equal to that of migrants, therefore enhancing the gene flow between local demes (Slatkin, 1987), and that the probability of recolonization after a local extinction is equal to one, so that the number of demes is constant.

Probabilities of fixation of an advantageous mutation at an underdominant locus (assuming that the homozygote for the mutation has a higher fitness than the standard homozygote), when local extinctions occur have been calculated by Lande (1985). He considers two distinct situations, soft and hard selection. Under soft selection, all demes send the same number of emigrants, while in the hard selection model the number of emigrants is proportional to the mean fitness of each deme (the migration rate which is considered lies within the low migration limit). His results show that hard selection increases the probability of fixation of such mutants, while frequent local extinctions and recolonizations accelerate their spread. Lande also showed that the spread over the whole population of a mutant fixed in one deme will only depend on the relative fitnesses of the two homozygotes.

In this paper we extend existing results, through computer simulations, for migration rates higher than those used in the previous analytical models. We investigate the variation of the probability of fixation of an initially rare allele as a function of population subdivision, and how this pattern is altered by local extinctions. The model assumes a soft selection. In our model the number of colonizers is equal to the number of immigrants, while recolonization is not immediate after extinction as in Lande's (1985) model but depends on the migration rate. Following recolonization a deme grows up to carrying capacity gradually, and not immediately like in all population genetics models. The selective forces taken into account are strict underdominance (meaning that both homozygotes have the same fitness) and meiotic drive. We did not consider the case where the mutant homozygote has a selective advantage over the standard one, because as Hedrick (1981) has shown, such an advantage should be very large in order to significantly

alter the unstable equilibrium frequency, and such advantages have never been reported. On the contrary, very small amounts of meiotic drive, such that they are undetectable in practice, can have a dramatic effect on the probability of fixation (Hedrick, 1981, Results section).

### **The model**

We consider a one locus, two alleles model in which a population is subdivided into a square grid of 25 demes on a two-dimensional torus. Each deme has a carrying capacity  $K$ , meaning that no deme could have more than  $K$  individuals after the reproductive period. The net fecundity is the same for all individuals of a particular genotype and constant through time. When one of the two alleles is fixed in the whole population the simulation is stopped and a new one is started.

#### *Migration*

Each deme may only send adult emigrants to its four neighbouring demes (i.e. a stepping-stone model) with a probability corresponding to the migration rate (which is constant for a particular simulation and identical for all individuals).

#### *Extinctions – recolonizations*

Each deme has a certain probability of going extinct, corresponding to the extinction rate. The recolonization rate is determined by the mean and the variance of the number of immigrants in each site (before establishment), and it thus depends on the migration rate (as well as on other parameters such as the local extinction rate, carrying-capacity and fecundity). Following extinction, a deme may be recolonized in the next generation or stay vacant, depending on the migration-recolonization rate. Migration being a stochastic process, the number of non-vacant demes is not constant, and it is even possible that the whole population goes extinct. In this respect our model differs from Lande's (1985) model in which recolonization is immediate after a local extinction and therefore the number of demes is constant. In fact, we have not examined cases where the migration rate is inferior to the extinction rate, because in such cases the whole population is driven to extinction. Following recolonization, a deme grows gradually back to carrying capacity. The speed of this process is determined by the individual fecundity. Regulation of the deme size by density takes place only when the deme reaches carrying capacity.

#### *Selection – reproduction*

Selection takes place during the reproductive stage. Three situations were simulated: underdominance, meiotic drive, and underdominance with meiotic drive.

When the locus is underdominant (where the heterozygote fitness disadvantage is equal to  $s$ ) there is an unstable equilibrium as stated above. Meiotic drive corresponds to the situation where one heterozygote carrying two alleles  $A$  and  $B$  would transmit the allele  $B$  with a frequency  $d$  and the allele  $A$  with a frequency  $1 - d$ . We can define the meiotic drive coefficient  $D$  as that which satisfies the equation  $d = 1/2*(1 + 2D)$ , so that when  $B$  is transmitted at a frequency  $d = 0.51$  the meiotic drive coefficient  $D$  is equal to 0.01. When meiotic drive in favour of  $B$  acts alone the system behaves as if the homozygotes for  $B$  had a greater fitness than the homozygotes for  $A$ . In this model we assume that meiotic drive affects both sexes, while in most described cases meiotic drive acts on only one sex (Charlesworth, 1988). However, this would not qualitatively alter the results (Lieberman and Feldman, 1982).

Migration, extinction and reproduction are random processes.

#### *Parameter values*

We have run simulations for three values for each parameter (heterozygote disadvantage ( $s$ ), meiotic drive ( $D$ ) and extinction rate ( $e$ )). Their values are shown in Table 1. The combination of the values of  $s$  and  $D$  leads to two qualitatively different situations. If there is only underdominance (i.e.  $s > 0$  and  $D = 0$ ) or if underdominance is much stronger than meiotic drive (i.e.  $s = 0.10$ ,  $D = 0.01$  or  $0.03$ ), an unstable equilibrium exists and the initial frequency of the rare allele is below this equilibrium value. Thus under these circumstances selection is initially acting against the rare allele. On the contrary, when meiotic drive is stronger than underdominance, either the rare allele is always favoured by selection (i.e.  $s = 0.02$   $D = 0.03$ , in which case no intermediate equilibrium frequency exists), or its initial frequency is larger than the equilibrium frequency (i.e.  $s = 0.02$   $D = 0.01$ ) and therefore it is selected for.

#### *Initial conditions*

All simulations were run from the same starting point: each deme had an initial deme size of 10. This size also corresponds to the carrying capacity of each deme

**Table 1.** Values of parameters  $s$  (heterozygote disadvantage) and  $D$  (meiotic drive coefficient) and the corresponding unstable equilibrium frequencies (the initial frequency of the rare allele ( $B$ ) is 0.05)

$s$	$d$	eq. freq.
0.02	0	0.5
0.10	0	0.5
0.10	0.01	0.41
0.10	0.03	0.23
0.02	0.01	0.01
0.02	0.03	$B$ fixed

*K.* In all cases homozygotes for both alleles had the same net fecundity (an expectation of 5 offspring per parent): selection only concerned heterozygotes. Given that the carrying capacity that we used is low compared to individual fecundity, all demes have approximately the same size, so that our model corresponds to soft selection (Lande, 1985). The initial frequency of the rare allele (*B*) was 5% in each deme and thus in the whole population, with one heterozygote per deme. This situation may seem unrealistic since any newly arisen mutation exists in very few specimens (if not only in one). But our purpose was not to obtain exact values of the probability of fixation but rather to elucidate the influence of population subdivision and local extinctions on the pattern of fixation. Hence the results we obtain should not be regarded as absolute values, but as general patterns. This hypothesis has been tested for several parameter values, by running simulations with the new rearrangement present in a single copy in a single deme. We show (results section) that the two processes are qualitatively equivalent.

We first ran simulations without local extinctions in order to verify whether our results agreed with those of the previous authors (i.e. Lande, 1979, Slatkin, 1981) and then considered local extinctions.

The model was written in Turbo-Pascal 4.0, and run on AT microcomputers. For each data set a Duncan's multiple range test was performed on the probability of fixation of the initially rare allele.

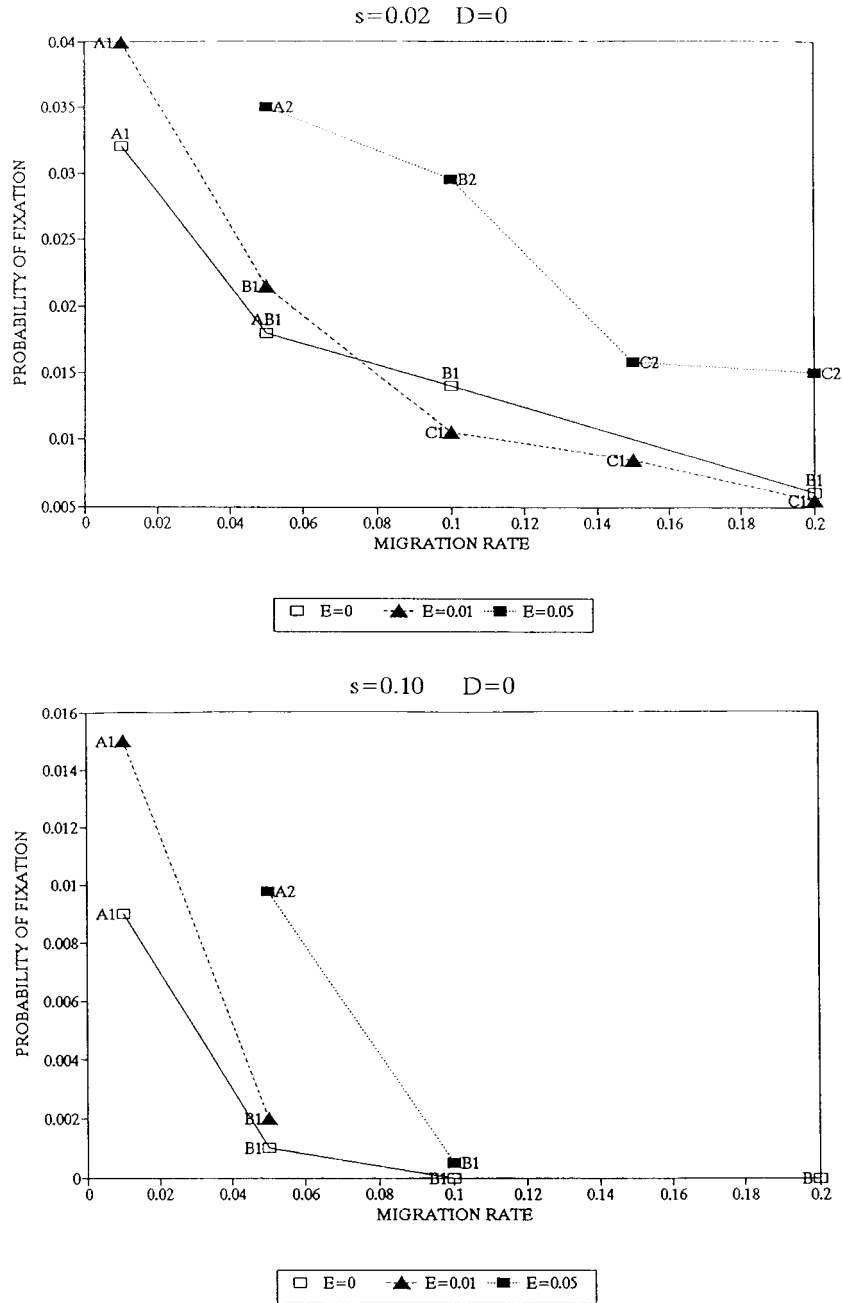
## Results and discussion

One feature which must be kept in mind is that for very low values of *m* all the demes become rapidly fixed for one allele and then exchange migrants in the homozygous state. So for low values of *m*, the time to fixation of a given allele in a single deme is much shorter than the time scale associated with the migration process (Slatkin, 1981). This will be particularly important when local extinctions occur.

### 1. Underdominance

First consider the cases without extinctions (Fig. 1). The probability of fixation of the initially rare allele *B* decreases as the heterozygote disadvantage increases (compare values from Figs. 1a and 1b), and for a given value of *s* it is a monotonically decreasing function of the migration rate, as predicted by Lande (1979) and Slatkin (1981). When the interdeme migration rate is low, the deme effective size is also small and local heterozygosity declines. Only in such cases can drift overcome selection, and the rare allele become fixed.

Local extinctions increase the probability of fixation for moderate values of *m* (Fig. 1). Indeed, for such values of the migration rate the number of colonizers is relatively small, so that genetic drift is important during the foundation of the population. It could also be that the increase of the probability of fixation is not



**Fig. 1.** Probability of fixation as a function of the migration rate for a strictly underdominant locus (a.  $s = 0.02$ , b.  $s = 0.10$ ), with and without extinctions. Letters compare values obtained for a given extinction rate as the migration rate increases. Two values with the same letter do not differ significantly. Numbers compare values obtained for a given migration rate as the extinction rate increases (Duncan test,  $\alpha = 0.05$ ).

**Table 2.** Probabilities of fixation with 16 demes and no extinctions compared to those obtained for 25 demes and  $e = 0.05$  (4000 replicates per parameter set), for  $m = 0.05$ 

$s$	$e$	$n$	$u$
0.02	0	16	0.026
0.02	0.05	25	0.035
0.10	0	16	0.001
0.10	0.05	25	0.010

due to the stochasticity added in the process by the founder events, but simply to the fact that with local extinctions there are fewer extant populations, and therefore the size of the whole population is reduced. To test this assumption we performed simulations with 16 demes for  $m = 0.05$  for both values of  $s$  (with 25 demes,  $m = 0.05$  and  $e = 0.05$  the mean number of demes is 23.75). In both cases (Table 2) the probability of fixation with 25 demes and local extinctions was significantly higher than the probability of fixation with 16 demes and no extinctions, thus demonstrating that the main cause of the increase in the probability of fixation is drift during the founder events and not the decrease of the total population size.

We also studied the effect of considering the rare allele to be initially present in all demes. We ran some simulations with only one heterozygote present in a single deme. The results (Table 3) qualitatively agree with those when one heterozygote is initially introduced in each deme: the probability of fixation decreases monotonically with the migration rate, and local extinctions significantly increase the probability of fixation for a given migration rate. In fact, even though initially each deme contains an heterozygote, the mutant allele, in general, quickly disappears from most populations, so that our initial conditions were in fact much closer to the usual initial conditions than they might appear to be.

**Table 3.** Probabilities of fixation with a single heterozygote for the mutant allele, present in only one deme (100,000 replicates per parameter set), for several  $s$ ,  $m$  and  $e$  values

$s$	$m$	$e$	$u$
0.02	0.05	0	0.00053
0.02	0.10	0	0.00031
0.02	0.20	0	0.00010
0.02	0.05	0.05	0.00140
0.02	0.10	0.05	0.00083
0.02	0.20	0.05	0.00044
0.10	0.05	0	0
0.10	0.05	0.05	0.00030

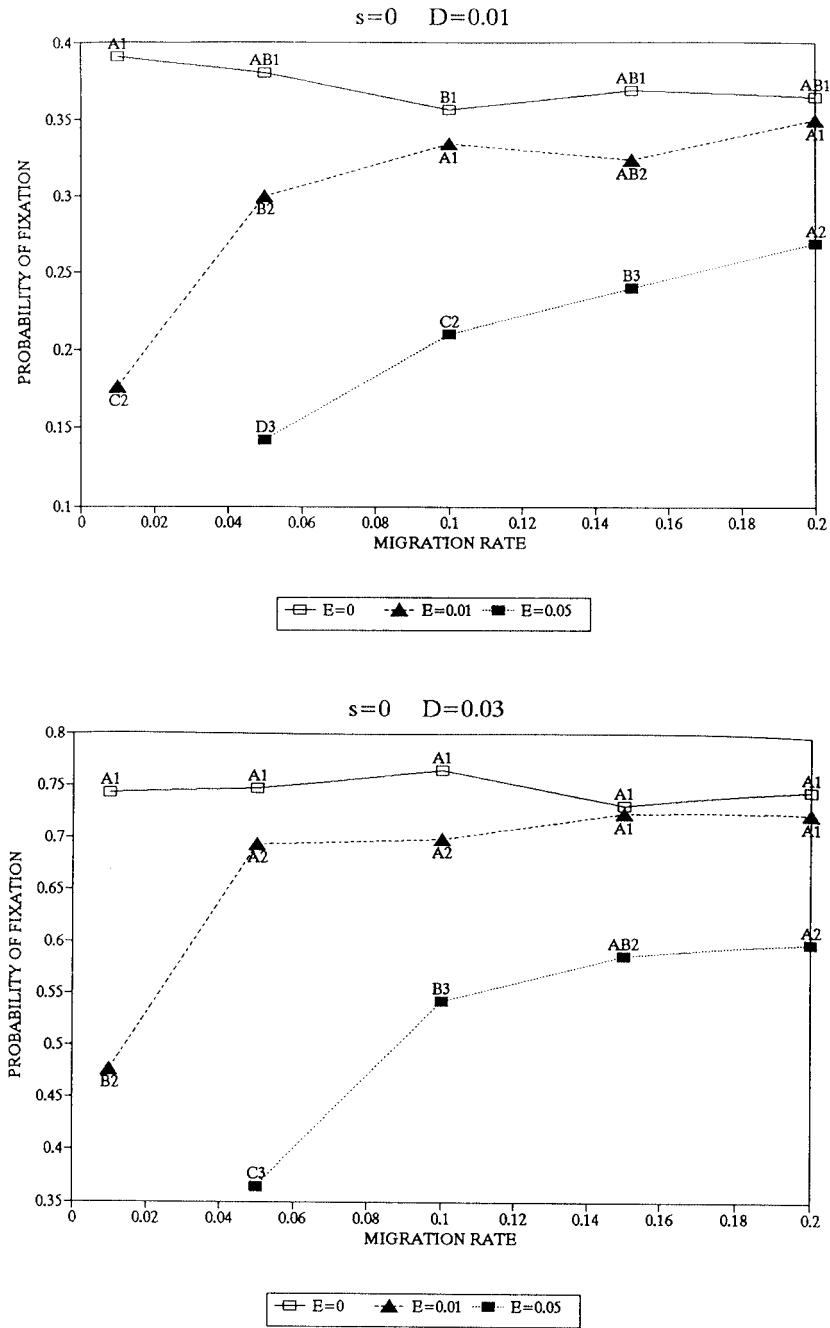


Fig. 2. Probability of fixation as a function of the migration rate with meiotic drive alone (a.  $D = 0.01$ , b.  $D = 0.03$ ), with and without extinctions. Letters and numbers have the same meaning as in Fig. 1.

## 2. *Meiotic drive*

With meiotic drive alone the probability of fixation of allele  $B$  is the same for all values of  $m$  and higher than it would be in a neutral system (Fig. 2). In fact it can be shown that when meiotic drive acts alone, the rate of change in gene frequency over time is of the same form as that of a codominant locus (Hedrick, 1981), and for a codominant locus we know that population subdivision does not alter the probability of fixation (Maruyama, 1983). Local extinctions however alter this pattern, through genetic drift during population foundations.

With local extinctions the probability of fixation monotonically increases as a function of  $m$  (Fig. 2), since the number of colonizers also increases (and therefore the influence of drift decreases).

## 3. *Underdominance and meiotic drive*

In this case we have two qualitatively different situations depending on the parameter values. In the first situation ( $s = 0.10$ ) an unstable equilibrium always exists and the initial frequency of the rare allele is below this equilibrium value (Table 1). Therefore in this situation selection acts against the rare allele. In the second situation ( $s = 0.02$ ) either the unstable equilibrium does not exist and the rare allele should always be deterministically driven to fixation ( $D = 0.03$ ), or the unstable equilibrium exists ( $D = 0.01$ ) but the initial frequency of the rare allele is larger than the equilibrium value so that the rare allele is also selected for from the initial stage.

### 3.1. *Rare allele initially selected against*

In all cases the probability of fixation is a monotonically decreasing function of  $m$  (Fig. 3). Recall that the probability of fixation when meiotic drive is acting alone is not altered by population subdivision, while it is altered when the locus is underdominant. Thus the probability of fixation is increased by meiotic drive for all  $m$  values compared to the case with underdominance alone (section 1.1), while it decreases as  $m$  increases due to the effect of subdivision on an underdominant locus. Local extinctions have qualitatively different effects, depending on the migration rate (Fig. 3). As already stated in section 1.1, when  $m$  is very small the effect of underdominance is relatively reduced. Thus, for small  $m$  values, the main factor acting on the probability of fixation is meiotic drive; as we have seen in section 1.2 in this case local extinctions decrease the probability of fixation. As  $m$  increases the influence of underdominance increases such that for larger  $m$  values local extinctions increase the probability of fixation.

### 3.2. *Rare allele initially selected for*

Without extinctions the probability of fixation is a monotonically decreasing function of  $m$ , for the same reasons as in the previous section (Fig. 4). Local extinctions decrease the probability of fixation for a given migration rate (this effect

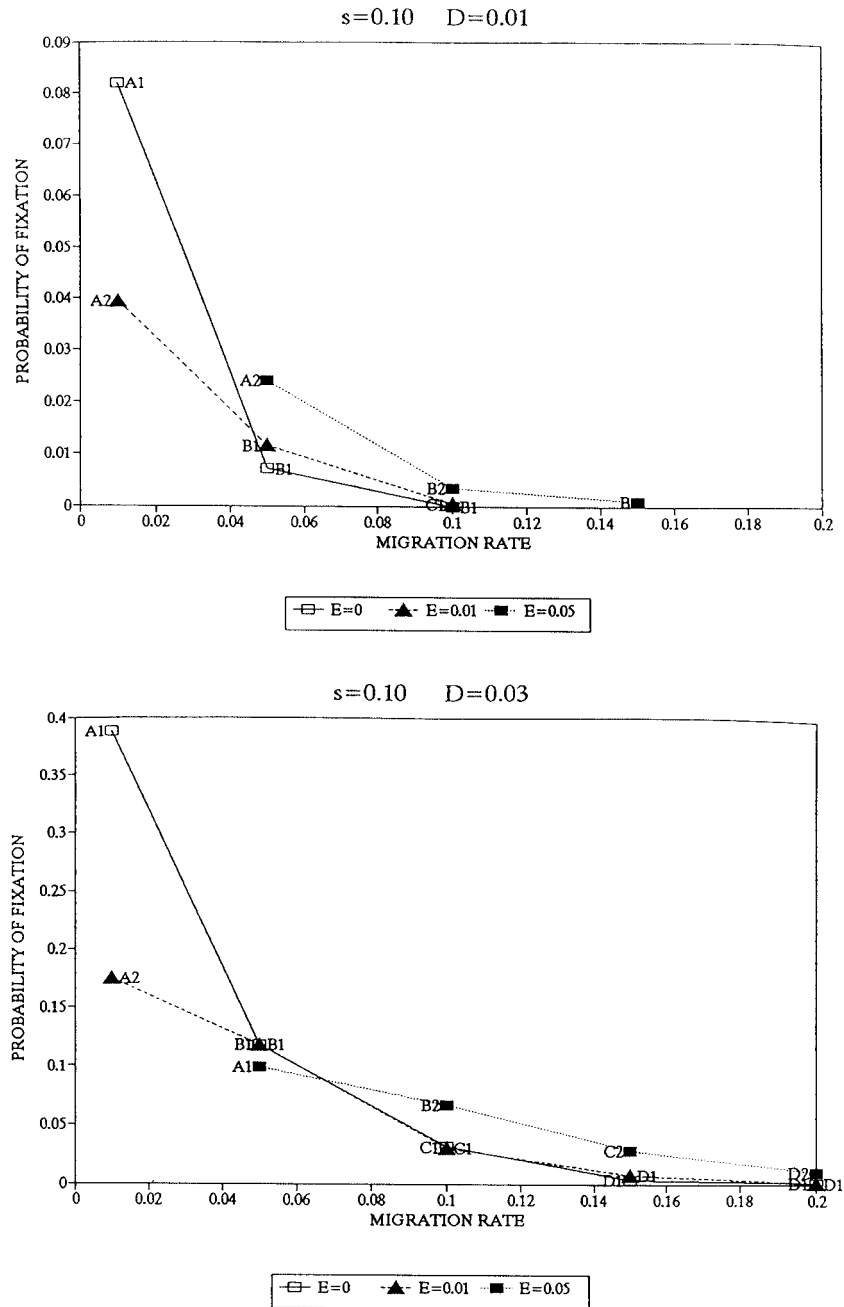
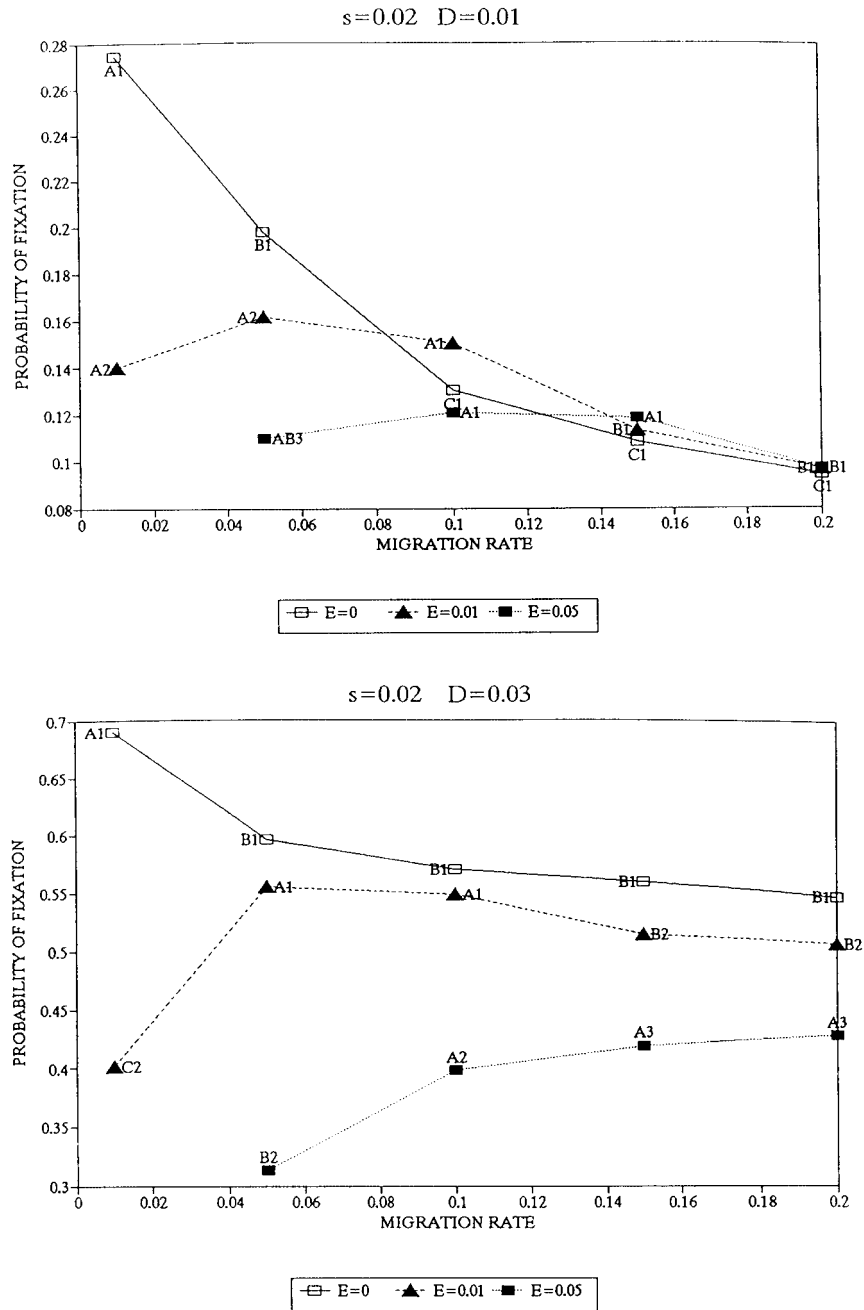


Fig. 3. Probability of fixation as a function of the migration rate with meiotic drive and underdominance. In these cases the rare allele is initially selected against (a.  $s = 0.10$   $D = 0.01$ , b.  $s = 0.10$   $D = 0.03$ ), with and without extinctions. Letters and numbers have the same meaning as in Fig. 1.



**Fig. 4.** Probability of fixation as a function of the migration rate with meiotic drive and underdominance. In these cases the rare allele is initially selected for (a.  $s = 0.02$   $D = 0.01$ , b.  $s = 0.02$   $D = 0.03$ ), with and without extinctions. Letters and numbers have the same meaning as in Fig. 1.

is increased as the rare allele is more favoured by selection). For a given set of parameters the probability of fixation is no longer a monotonic function of  $m$ , but rather an optimal migration rate exists (Fig. 4). Recall that in this situation meiotic drive is more influential than underdominance since the rare allele is selected for. For small values of  $m$ , as seen in the previous section, meiotic drive is almost acting alone and local extinctions cause a large decrease of the probability of fixation. As  $m$  increases the negative effect of extinctions on meiotic drive becomes moderate to negligible while the beneficial effect on underdominance is still present. For even larger values of  $m$ , extinctions no longer have any effect on meiotic drive while the negative effects of increasing  $m$  on underdominance become more influential, and therefore the probability of fixation decreases again. The optimal migration rate shifts towards larger values as the extinction rate and selection for the rare allele increase.

## Conclusion

Local extinctions increase gene flow, create founder events and reduce the number of occupied sites. Our results show that the effect of founder events is the most important factor acting on the probability of fixation. The comparison of the probabilities of fixation of rare mutations with and without extinctions shows that the effect of local extinctions depends on the selective forces involved. Local extinctions facilitate the fixation of initially rare mutants when these mutants are selected against, whereas they impede fixation of rare mutants which are selected for.

When both underdominance and meiotic drive are acting on the evolution of the locus, local extinctions lead to non trivial dynamics. We can distinguish two situations. In the first situation, the initially rare allele is at a frequency below the unstable equilibrium frequency (and therefore selected against at the initial stage). In this case, local extinctions decrease the probability of fixation for low migration rates, while they increase the probability of fixation for larger values of  $m$ . In the second situation, the rare allele is initially favoured by selection either because its initial frequency is higher than the unstable equilibrium, or because the selective forces are such that the only possible deterministic equilibrium is fixation. Under these circumstances local extinctions decrease the probability of fixation. Interestingly, the probability of fixation is no longer a monotonic function of the migration rate; instead an optimal migration rate exists. The optimum is at the point where the negative effect of extinctions on meiotic drive is dampened while the positive effect on underdominance is still appreciable. This optimum value shifts towards larger values as selection becomes stronger and the extinction rate is larger.

For strictly underdominant mutations, we find that for intermediate migration rates, local extinctions can facilitate the ultimate fixation of such mutations, as Wright (1941) predicted. This is due to founder events at the recolonization stage. For lower values of  $m$ , the species could not be maintained in the landscape, while for higher values there is a large number of recolonizers and therefore the founder effects are much less influential.

The fact that for intermediate migration rates local extinctions may alter the probability of fixation of a mutation at a strictly underdominant locus, is qualitatively different from the result reached by Lande (1985) at the low migration limit. At the low migration limit, the extinction-recolonization events are too rare to have an appreciable effect on the probability of fixation. At realistically high migration rates however, relatively frequent recolonization events increase the probability of spread of the rare mutant, relative to the case without extinctions-recolonizations. Hence our model shows that local extinctions can facilitate the fixation of new variants in underdominant systems for migration rates which seem more realistic than the ones considered by analytical models (Lande, 1985).

This pattern seems compatible for instance with the fixation of chromosomal rearrangements. One good example of such mutations are Robertsonian fusions in mice (*Mus musculus domesticus*). These rearrangements are fixed either on islands (Scriven and Brooker, 1990, Britton-Davidian, 1983, Lehmann and Radbruch, 1977) or in places where mice are commensal, whereas they seem to be absent in localities where mice live in continuous external populations (Auffray et al., 1986). In both situations where rearrangements are fixed, we can legitimately assume that the populations of mice are quite subdivided, and that they experience local extinctions (because of insular conditions in the first case (Simberloff, 1974), and because of human action in the second).

What should be stressed however, is that even though the probability of fixation of a rare allele is not negligible for small selection coefficients (e.g. 0.02), it becomes rapidly very weak as  $s$  increases (Table 3). This indicates that in natural conditions the fixation of new chromosomal variants is possible only in those cases where underdominance is very weak, or absent. In mice, Gropp et al. (1982) measured the number of aneuploid gametes produced by heterozygous mice for one Robertsonian fusion. They found that males presented a rate of non-disjunction from 4 to 28% depending on the fusion involved, while the rate varied from 33 to 61% in females. These experiments were conducted on laboratory strains in which the fusions had been incorporated. Interestingly, Winking (1986) repeated the same kind of experiment but on wild animals. He found that the rate of non-disjunction varied from 0 to 4% for males. When he reintroduced the fusions in laboratory strains he found the same results as Gropp et al. (1982), thus demonstrating the importance of the genetic background. Nevertheless these results show that if there is any underdominance it is very weak. Nachman and Myers (1989) have shown that chromosomal rearrangements in the South American marsh rat *Holochilus brasiliensis* are not accompanied by strongly reduced heterozygote fitness (if it exists, selection against heterozygotes should be less than 0.10). Coyne et al. (1991) have also shown that a naturally occurring pericentric inversion in *Drosophila melanogaster* is not associated with strong underdominant effects on fitness (if any, underdominance must be below 0.6%). These data indicate that, if any underdominance is related to fixed chromosomal rearrangements, it is very weak. This is compatible with the possibility of fixation of chromosomal rearrangements, under the joint effect of low migration and genetic drift. In these conditions, even low (and undetectable) amounts of meiotic drive

could be very influential, although it is true that drift is likely to be the most important factor (Coyne, 1989).

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## Appendix 1

Consider one locus with two alleles ( $A$  and  $B$ ), in a panmictic population of infinite size. Let  $q$  be the frequency of  $B$  and  $p$  the frequency of  $A$  at generation  $t$ . Relative fitnesses are 1 for both homozygotes and  $1 - s$  for heterozygotes. Suppose that the heterozygote produces  $d$  gametes of type  $B$  and  $1 - d$  gametes of type  $A$  (if  $d = 0.5$  there is no meiotic drive). We treat here the case where meiotic drive affects both sexes to a similar degree. The case where meiotic drive affects only one sex is treated by Hedrick (1981).

The frequency of  $B$  in generation  $t + 1$  is thus:

$$q' = \frac{q^2 + 2d(1-s)q(1-q)}{1 - 2sq(1-q)}$$

and

$$\delta q = q(1-q) \frac{2sq - \{1 - 2d(1-s)\}}{1 - 2sq(1-q)}$$

At equilibrium  $q = 0$ , and

$$q_c = \frac{1 - 2d(1-s)}{2s}$$

When  $q > q_c$ ,  $\delta q$  is positive, while when  $q < q_c$ ,  $\delta q$  is negative, hence the equilibrium is unstable.

This equilibrium does not exist under either of the two following conditions:

a) When  $q \approx 0$ ,  $q' = 2 \cdot d \cdot (1-s) \cdot q$  and therefore  $q' > q$  if  $2 \cdot d \cdot (1-s) > 1$ . If this condition is met  $B$  is always fixed.

b) Similarly, when  $q \approx 1$ ,  $q' < q$  if  $2 \cdot (1-s) \cdot (1-d) > 1$ . In this case  $B$  can never be fixed.