
The maintenance of sexual reproduction in a structured population

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We present the results of a computer simulation model in which a sexual population produces an asexual mutant. We estimate the probability that the new asexual lineage will go extinct. We find that whenever the asexual lineage does not go extinct the sexual population is out-competed, and only asexual individuals remain after a sufficiently long period of time has elapsed. We call this type of outcome an asexual takeover. Our results suggest that, given repeated mutations to asexuality, asexual takeover is likely in an unstructured environment. However, if the environment is subdivided into demes that are connected by migration, then asexual takeover becomes less likely. The probability of asexual takeover declines towards zero as the number of demes increases and as the rate of migration decreases. The reason for this is that asexuality leads to a greater loss of fitness due to mutation and genetic drift, in comparison to what occurs under sexual reproduction. Population subdivision slows the spread of asexual lineages, which allows more time for the genetic degeneration caused by asexuality to take place.

Keywords: evolution of sex; asexual reproduction; theory; population genetics; structured populations; genetic drift

1. INTRODUCTION

Understanding sexual reproduction has been a long-standing problem for evolutionary biology (Maynard Smith 1978; Kondrashov 1993; Hurst & Peck 1996). One class of explanations for the evolution of sex relies on the idea that, as a result of genetic drift, deleterious mutations will rise to a high frequency more readily in asexual populations than in sexual populations. The possible importance of genetic drift as a source of advantage for sexual reproduction was recognized by Muller in the 1960s (Muller 1964). The process identified by Muller has come to be known as 'Muller's Ratchet', and a series of models has been explored in studies of the dynamics of this process (Muller 1964; Wagner & Gabriel 1990; Charlesworth *et al.* 1993; Lynch *et al.* 1993).

While theoretical studies of Muller's Ratchet have produced interesting results, they have also suffered from certain limitations. For example, these models have generally assumed that all mutations are deleterious. In a finite population, this assumption is unrealistic, as it leads to a situation where mean fitness declines forever, or until species extinction. This is true regardless of whether the population is sexual or asexual (Lynch *et al.* 1993, 1995; Peck *et al.* 1997). Fortunately, this difficulty can be addressed by using models of mutation similar to one described by Fisher (Fisher 1930; Burch & Chao 1999). Fisher's model allows for beneficial mutations. According to Fisher, beneficial mutations never occur to optimal genotypes, but they become increasingly more likely as a genotype becomes more and more suboptimal.

At least two studies have employed Fisherian mutation models in a study of asexual populations that undergo selection upon multiple loci. One of these was carried out by Wagner & Gabriel (1990), the other is the work of Peck *et al.* (1997). Both of these studies found that, with a Fisherian model of mutation, genetic deterioration does not continue without limit, and mean fitness approaches a stationary distribution. This means that, in the long run, there is no overall trend in changes in mean fitness, although it may rise or fall from one generation to the next. Peck and colleagues also studied sexual populations, and they focused on the fitness of sexual and asexual populations once a stationary distribution had been achieved. They found that, under a wide variety of circumstances, sexual populations were much fitter than asexual populations.

Models inspired by Muller's ideas about sex and genetic drift suffer from a second drawback. In general, researchers have concentrated on the long-term effects of the mode of reproduction on mean fitness. Calculations of this sort may help us to predict the outcome of evolution when sexual and asexual populations meet after long periods of isolation. However, the evidence suggests that most multicellular asexual populations are descended from sexual populations (Maynard Smith 1978; Bell 1982). If this is so, then it seems likely that asexual lineages are often in direct competition with ecologically similar sexual populations for some time after the asexual lineages arise.

In this paper, we describe a mathematical model of a population of outcrossing plants. We assume that the plants are hermaphroditic, with each adult producing both pollen and seeds. We assume further that this

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population suffers the expected twofold cost of sex (Maynard Smith 1978). Thus half of their reproductive resources goes into the production of pollen, instead of seeds. We then consider the evolutionary outcomes when this population is invaded by a single asexual individual. This asexual individual may have arisen as a consequence of a single-locus genetic change, or as a result of a larger change, such as a polyploidization event. Alternatively, the asexual individual may appear as a result of a rare long-range dispersal event. In any case, we assume that the asexuals produce no pollen, and thus escape the twofold cost of sex. This means that, all else being equal, asexual individuals will produce about twice as many seeds as sexual individuals.

Will asexuals take over the environment as a result of their twofold advantage? If asexuality arrives initially in a single individual, then, despite its advantage, it may be lost as a result of stochastic forces. Even if asexuals increase to substantial numbers, they may eventually go extinct because, as Muller pointed out, genetic drift is expected to be more debilitating to asexuals than it is to sexuals, and so asexuals may not succeed in the long term. In addition, if deleterious mutations control fitness in a 'synergistic' fashion, so that deleterious mutations are most damaging in genomes that already have many deleterious mutations, then asexuals may decline in fitness, even if genetic drift alone is insufficient to do the job (Kondrashov 1988). Using our model, we study all of these possibilities. Our central finding is that a crucial determinant of the outcome of evolution is the degree to which the environment is subdivided.

2. THE MODEL

The model of mutation and selection we have studied is based on the ideas of Fisher (1930). This avoids the problems that are associated with the traditional Muller's Ratchet models described above. The model also reflects current data concerning the rate and characteristics of fitness-affecting mutations (see, for example, work by Barton 1995; Keightley 1994; Mackay *et al.* 1992; Ohta 1992). For the sake of brevity, we confine ourselves somewhat in our choice of parameter values for the simulation studies. We begin by describing the model as it operates in a single homogeneous population. A more complete exploration of how the model behaves in a homogeneous population is presented elsewhere (Peck *et al.* 1997).

We consider a population of diploid plants that are both outcrossing and hermaphroditic. This population is subject to fertility selection. Each individual is assumed to produce a large number of ovules. The exact number of ovules produced is proportional to w , a variable determined by the individual's genotype (where $0 < w \leq 1$). The number of pollen grains produced by an individual is also proportional to w . Each ovule is fertilized by a pollen grain that is selected at random from among all the pollen grains produced in the population. All of the ovules then mature and become seeds. Standard Mendelian segregation and recombination without interference are involved in the production of both ovules and pollen.

After reproduction, N seeds are selected at random, and these grow to reproductive maturity. Thus, N is the size of the adult population. In light of these assumptions,

it should be clear that, in any given generation, each adult's fitness is proportional to its value of w .

We assume that there are 500 loci within the genome that are capable of sustaining fitness-affecting mutations. This is likely to be an underestimate for any eukaryote, but handling much larger numbers of loci is impractical because of computational constraints. The 500 loci are spread evenly among ten chromosomes, so that there are 50 loci per chromosome. The rate of recombination is $r = 0.016$ between adjacent loci, and thus chromosomes are about 80 centimorgans in length, which is a typical value for sexual plants and animals.

Because the population is diploid, each locus occurs twice within the genome. Number the occurrences of each locus as 1 and 2, in arbitrary order. Assume that the state of each of an individual's 1000 alleles occurring at the loci can be represented by a real number x , where $-\infty < x < \infty$. Assume further that the optimum state for each allele is achieved when $x = 0$. Let $d_{i,j,k}$ represent the absolute value of the deviation from the optimum state of the allele at the j th occurrence of the i th locus in the k th adult for a particular generation (i.e. $d_{i,j,k} = |x|$). Let Z_k represent the sum of these deviations for the k th adult. That is:

$$Z_k = \sum_{i=1}^{500} [d_{i,1,k} + d_{i,2,k}]. \quad (1)$$

Let w_k represent the value of w for the k th adult during a particular generation (where $1 \leq k \leq N$). The value of w_k is assumed to depend on Z_k as follows:

$$w_k = \exp(-Z_k^E), \quad (2)$$

where $E \geq 1$. Thus, the fitness of an individual is an increasing function of the quality of each of the individual's alleles. The value of E determines the degree of synergistic epistasis. With $E = 1$, the model is multiplicative, and when $E > 1$ synergistic epistasis is in operation. For the results presented here, we either assumed $E = 1$, or in the case of synergistic epistasis, we assumed $E = 8$. We refer to the case of $E = 1$ and $E = 8$ as the multiplicative model and the epistatic model, respectively.

We assume that mutations occur during gamete formation. A mutation is assumed to change the value associated with an allele by an amount y , such that the mutated value of the allele is given by $x = y + x^*$, where x^* is the value of x that would have been associated with the allele if no mutation had occurred (i.e. x^* is the parental value of x for the allele in question).

The distribution of y used in the simulation studies is a 'reflected gamma' distribution. This distribution has been used to model mutations of genes that control quantitative characters (Hill & Rabash 1986; Keightley & Hill 1987). In generating the reflected gamma distribution, we follow Keightley and Hill's example, and use a gamma distribution with shape parameter of one-half (Keightley & Hill 1987). This ensures that a considerable proportion of mutations will have a very small effect, while others will have a substantial effect. This sort of distribution is in line with most current data on the effects of mutations (Mukai *et al.* 1972;

Mackay *et al.* 1992; Ohta 1992; Keightley 1994). The probability density function ($f(y)$) for the reflected gamma distribution used in this paper is given by:

$$f(y) = \frac{a^{0.5} e^{-\alpha|y|} |y|^{-0.5}}{2\Gamma(0.5)}, \quad (3)$$

where $\Gamma(0.5)$ is a gamma function with parameter 0.5. Note that the expected value of y is zero. For the multiplicative model, we set $\alpha = 24.253$. This ensures that mutations to near-perfect alleles will decrease fitness by about 2%, and that the coefficient of variation in fitness is about 18%. These figures are in line with most current data (Mukai *et al.* 1972; Crow 1979; Charlesworth 1987). (However, not all of the data are in agreement.) In the case of the epistatic model, the effects of mutations (and hence, variation in fitness) depend upon the Z_k values, and thus upon N and the mode of reproduction. For this model, we chose $\alpha = 100.000$, which ensures that the coefficient of variation in fitness is between 14% and 31% in sexual populations where $50 \leq N \leq 1000$.

The probability of mutation is assumed to equal 0.002 per allele. This means that, on average, each zygote will contain two new mutations. However, under the probability density function given by equation (3), many of these mutations will have extremely small effects and will be virtually undetectable (Peck *et al.* 1997).

Under the above-specified set of assumptions governing mutation, reproduction and selection, only deleterious mutations are possible when an allele is in its optimal state. On the other hand, beneficial mutations (i.e. mutations that reduce the selection coefficient against an allele) become more likely as an allele becomes less perfect (i.e. as $|x|$ becomes large). Indeed, as $|x|$ tends towards infinity, the probability that any new mutation will be beneficial tends towards 0.5. These characteristics are in line with Fisher's ideas about the nature of mutation (Fisher 1930).

We assume that asexual populations produce no pollen, and that their seeds contain exact copies of their genotypes, except for new mutations. Mutations occur at the same rate and in the same manner as in sexual populations. We also assume that, as a consequence of the resources saved by not producing pollen, an asexual with a particular value of w will produce twice as many seeds as a sexual individual with the same value of w .

3. RESULTS

(a) Evolution in a homogeneous environment

We used computer simulations to study the model. Each simulation began with a perfect population (all x values equal to zero) and ran for 50 000 generations, which was always sufficient to achieve an apparent stationary distribution for all parameters measured. We then ran for an additional 50 000 generations, during which time the arithmetic mean fitness was calculated each generation. The data presented in figure 1 is the geometric mean of these 50 000 mean fitness values. (Using an arithmetic rather than a geometric mean would produce no substantial change in the data, but the geometric mean is more appropriate for predicting evolutionary outcomes (Peck *et al.* 1997).)

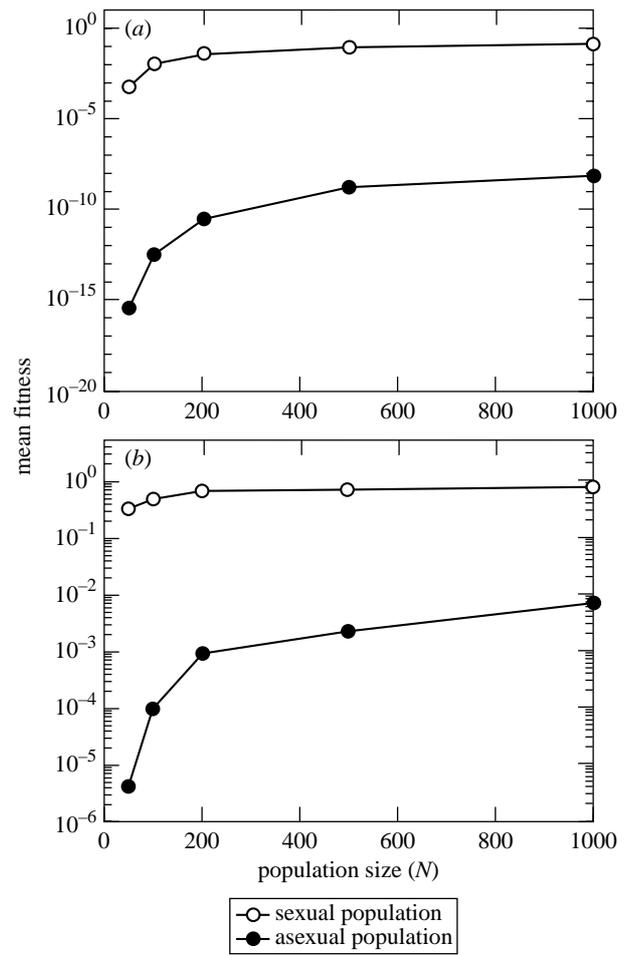


Figure 1. Mean fitness as a function of population size (N) in an unstructured environment. (a) Gives the data for the multiplicative model ($E = 1$), while (b) is for the epistatic model ($E = 8$). Mean fitness is simply the mean of the values denoted by w_k in equation (2). Mean fitness is proportional to mean fertility. Note that the w_k values do not incorporate the 'cost of sex'. The highest value of mean fitness shown (for a sexual population with $N = 1000$) is 0.115 in (a) and 0.739 in (b). Data shown are for $N = 50$, $N = 100$, $N = 200$, $N = 500$ and $N = 1000$.

Figure 1a shows that, under the multiplicative model, equilibrium mean fitness tends to increase with population size (N). This makes sense, given that genetic drift becomes weaker as population size increases. The figure also shows that mean fitness depends on whether the population reproduces sexually or asexually. As one might expect from the results of traditional Muller's Ratchet models, asexuality seems to lead to much lower levels of fitness than those experienced by sexual populations. All of the fitness values shown in figure 1a are much less than 1.0, and this means that the populations are well below their maximum possible levels of fertility (i.e. they are characterized by high genetic load). On the other hand, the data from the epistatic model (figure 1b) show that low levels of load occur in relatively large sexual populations, and this means that the epistatic model may be more realistic. Otherwise, the data from the epistatic model are similar to those for the multiplicative model, showing that both small populations and asexual reproduction lead to low levels of fitness.

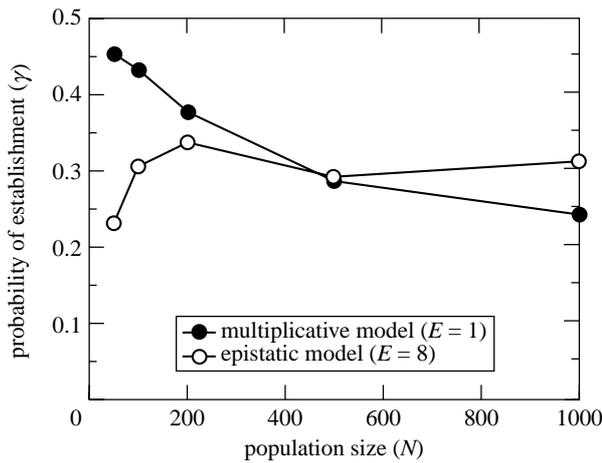


Figure 2. Estimates of γ (the probability of establishment of *asex*) in an unstructured environment. Establishment of *asex* occurs when all individuals in the population possess the *asex* allele, and thus reproduce asexually. The filled circles give the data for the multiplicative model, while the open circles give the data for the epistatic model. Data shown are for $N = 50$, $N = 100$, $N = 200$, $N = 500$ and $N = 1000$.

Despite the foregoing observations, it is not obvious that a sexual species will be safe from takeover by mutations that lead to asexual reproduction. While asexuality can lead to a long-term decline in fitness, the initial advantages of asexuality may determine the course of evolution. For example, say that asexuality results from a dominant mutant allele, which we shall call *asex*. Suppose that, when *asex* occurs in an adult, it causes that adult to produce no pollen, and to produce diploid seeds by asexual means. Let us assume further that, as expected from theory, elimination of pollen production doubles seed production (Fisher 1930; Charlesworth & Charlesworth 1981). Thus, a sexual adult with a genome characterized by a particular value of ζ will produce half as many seeds as an asexual with the same value of ζ (where ζ is as defined by equation (1)). This generates a twofold intrinsic advantage to asexual reproduction (Maynard Smith 1978). However, the data in figure 1 suggest that any initial advantage might eventually be reversed because of the genetic decay associated with asexual reproduction.

After a new mutation arises, it either vanishes from the population or it becomes ‘established’, which means that it cannot be lost as a result of genetic drift alone. In the case of a sexual population, establishment of a mutation occurs when it becomes fixed. In the case of *asex*, establishment means that every individual bears *asex* in heterozygous form. Once *asex* is established, the population is completely asexual (because *asex* is dominant).

Say that *asex* arises by mutation in a newborn juvenile, and that this juvenile survives to become an adult. What is the probability that *asex* will be established? This question was addressed by means of a further series of computer simulation studies, which are summarized in figure 2. We denote the probability of establishment of *asex* by γ . To estimate γ for a particular set of parameters, we begin by generating a sexual population that is approximately at a stationary distribution by starting with a perfect population, and then running for 50 000 generations. We call the resulting population the base

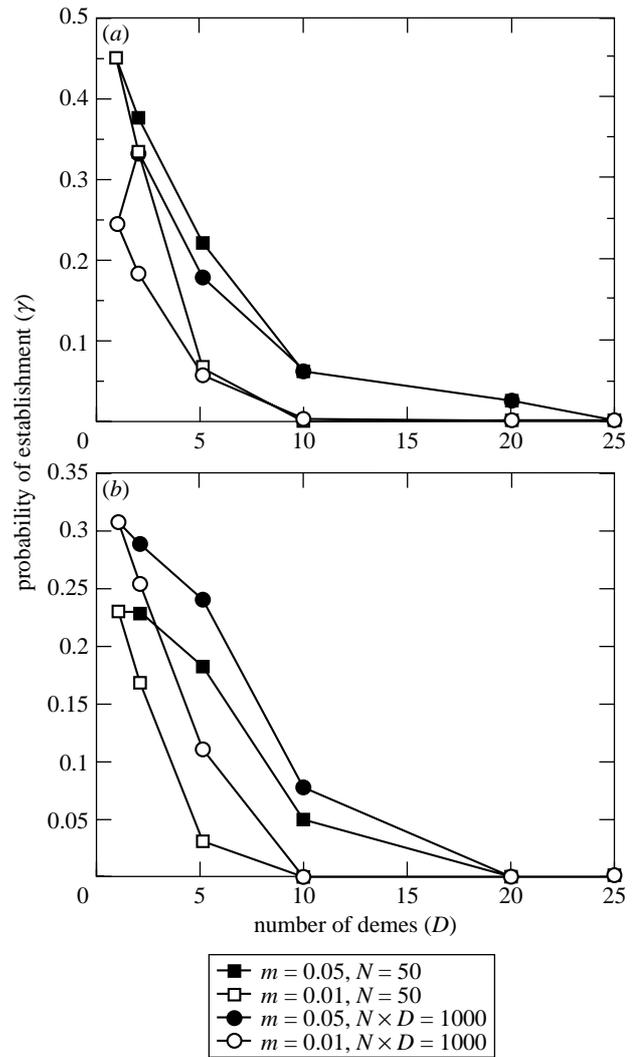


Figure 3. Estimates of γ as a function of D . (a) Gives the data for the multiplicative model ($E = 1$), while (b) is for the epistatic model ($E = 8$). Filled symbols give the data for $m = 0.05$, while open symbols are for $m = 0.01$. Two sets of simulations were run. In one (represented by squares) deme size was held constant at $N = 50$. Thus, the number of adults in the metapopulation is $50 \times D$. In the other set of simulations (represented by circles) metapopulation size was held constant at 1000. Thus, the number of adults per deme was $1000/D$. In (a), some data points lie nearly on top of one another, and this makes them difficult to distinguish. We therefore list here the data for $m = 0.05$, $N \times D = 1000$. In order of increasing D values (from $D = 1$, $D = 2$, $D = 5$, $D = 10$, $D = 25$) the data are: 0.246, 0.331, 0.179, 0.062, 0.027, 0.000. For $m = 0.01$ and $N \times D = 1000$ the data are: 0.246, 0.184, 0.059, 0.003, 0.000, 0.000.

population. We then select an adult at random from among all the adults in the population. This adult is assumed to have a copy of *asex*, and thus she and all her descendants reproduce by asexual means only. We continue the trial until *asex* either becomes extinct or becomes established in the population. For the next trial we return to the sexual base population and allow it to evolve for five generations to create a new base population. We then choose a new adult at random to become asexual. This continues for 1000 trials. Statistical tests showed that the outcome of each trial was independent

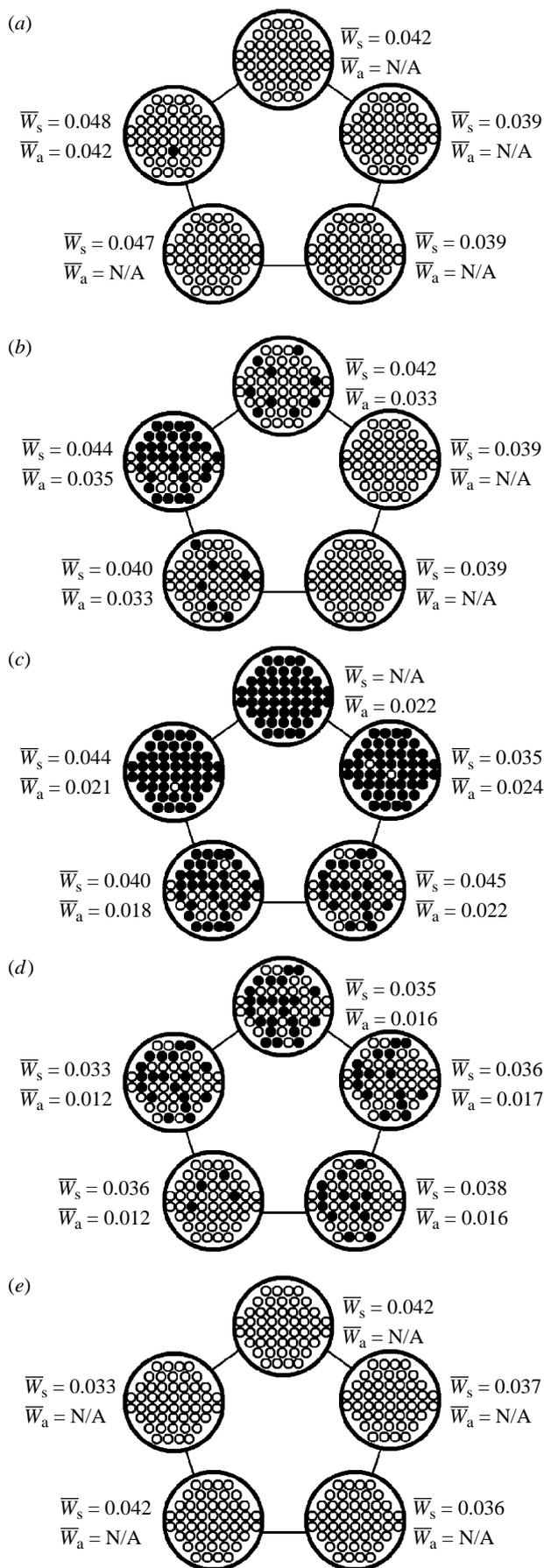


Figure 4. The results from a single computer-simulation trial with $D = 5$ and $m = 0.05$. The large circles represent demes, and the straight lines connect adjacent demes. The small

(or nearly independent) of the outcome on the preceding trial. The estimate of γ is the proportion of trials for which *asex* was established.

Figure 2 shows that, for the multiplicative model, the probability of establishment of *asex* (γ) declines as N increases (at least for the parameter values used). Under the epistatic model, the relationship between N and γ is more complex. For both models, the value of γ was in excess of 0.230 in all cases studied. Note that, if *asex* were a completely neutral allele, then its chance of establishment would be $1/(2N)$. Thus, asexuality apparently confers a very substantial advantage.

(b) Evolution in a subdivided environment

The results presented so far suggest that *asex* has a substantial chance of establishment in an unstructured environment. However, what will happen if the population is subdivided? To address this question, we modified the model by assuming that the population is subdivided into D discrete demes, which are arranged in a circle (where $D \geq 1$). Adult sexual individuals mate within their own demes according to the assumptions specified above. After reproduction, juveniles migrate to adjacent demes with probability m (except when $D = 1$). Emigrants move to each of the demes adjacent to theirs with probability 0.5. After migration, N juveniles are selected at random on each site, and these grow to reproductive maturity (adulthood). The rest die. We ran 1000 trials for each set of parameter values used (except in the case of $N = 40$, $D = 25$, $m = 0.01$ and $E = 1$, for which we ran 3000 trials).

Figure 3 shows the effect on γ of increasing the value of D (the number of demes). In the cases studied, γ can be reduced to a very low level by increasing D . Indeed, when $D = 25$, we never found a case where *asex* became established (in either the epistatic model or the multiplicative model). Figure 3 also shows that the value of m affects the rate at which γ falls as D increases (although data are shown here for only two values of m).

If the number of individuals in the metapopulation (i.e. the collection of all demes) is kept constant while D is increased, then the number of individuals in each deme will fall as D rises. This could produce some difficulty in interpreting the results. With this in mind, we carried out two sets of trials for each set of parameter values. In one, we kept the size of the metapopulation constant at 1000 individuals. In the other, we set $N = 50$ for all values of D (thus, in this case, the metapopulation contains $N \times D$ adults). Figure 3 shows that the same trends tend to occur regardless of whether the size of the metapopulation increases with D , or not. However, in one case (labelled as $m = 0.05$, $N \times D = 1000$ in figure 3a) increasing D initially

Figure 4. (Cont.) open circles represent sexual adults, and the small filled circles represent asexual adults. (a) Generation 1; (b) generation 10; (c) generation 35; (d) generation 60; (e) generation 74. The \bar{W}_s and \bar{W}_a values are indicators, respectively, of fitness for the sexual and asexual adults in each deme. These statistics give the mean values of w_i for the sexual and asexual adults (see equation (2)). The \bar{W}_s and \bar{W}_a values do not incorporate the 'cost of sex'. Parameter values were set as in the multiplicative model.

causes an increase in γ . Presumably, this occurs because, when the number of individuals in the metapopulation is held constant, increasing D leads to a decrease in N .

Figure 4 provides a graphical representation of a single unsuccessful invasion of *asex*. The asexual lineage expands, but its relative fitness declines over time. Eventually, it becomes sufficiently unfit that it contracts again and goes extinct.

4. DISCUSSION

The results presented here suggest that if asexual lineages arise in an outcrossing population that lives in a single deme, and if the asexuals are able to escape from the 'twofold' cost of sex, then they will often displace the outcrossing population. However, if the population is subdivided into a substantial number of demes, then the spread of asexuality may be checked, and outcrossing populations may be able to persist over the long term, despite occasional challenges from asexual lineages.

The results also suggest that increasing the number of demes and/or decreasing migration rate between demes is likely to diminish the chances of takeover by asexuality. This is because these changes in parameter values slow down the spread of asexuality through the metapopulation. This provides more time for the genetic quality of the asexuals to decline (see figure 4). We expect that, for any choice of the other parameters, if we wish to depress γ (the probability of a successful asexual invasion) below some arbitrarily low level, it will always be possible to find a migration rate sufficiently small to allow this (so long as there is more than one deme in the metapopulation). Furthermore, we believe that, for any migration rate, γ can be reduced to an arbitrarily low level by increasing the number of demes.

We have assumed a very special type of population structure for the purposes of this study. The demes in our study are arranged in a circle, and each deme is connected by migration to only two other demes (when $D \geq 3$). This population structure is computationally convenient. However, we are confident that the trends we have observed will hold for a wide variety of different population structures. The crucial feature is that migration is a local process, so that most immigrants come from nearby demes.

Other things being equal, the results presented here suggest that asexual populations should tend to accumulate in homogeneous environments, while sexuals should be most successful in environments that are highly structured, with individuals living in separate demes that are connected by rare migration events. Unfortunately, 'other things' are unlikely to be equal. For example, it is common for environments to vary from place to place in a way that favours some genotypes in some areas and other genotypes elsewhere. In these circumstances, there is a complex interaction between population structure, migration, historical factors, and the accumulation of sexual and asexual populations (Peck *et al.* 1999). Differences in the length of the growing season from place to place can also affect the geographic distributions of sexual and asexual populations (Peck *et al.* 1998). Thus, while the processes described here may help us to under-

stand the maintenance of sexual reproduction, they may not be of much assistance in predicting where sexual and asexual populations are likely to occur.

In this study, we have considered two factors that can produce benefits to populations that engage in sex and outcrossing. These are genetic drift and synergistic epistasis. However, it is important to recognize that these are not the only processes that can produce an advantage for sexual reproduction (Kondrashov 1993). For example, it has been suggested that sex evolves because it helps defences against parasites (Hamilton *et al.* 1990), and because it aids in the incorporation of beneficial mutations (Fisher 1930; Pamilo *et al.* 1987; Peck 1993, 1994). Population subdivision may be able to provide the time needed for exclusion of asexual mutants by means of some of these alternative evolution-of-sex mechanisms.

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As this paper exceeds the maximum length normally permitted, the authors have agreed to contribute to production costs.

