Sperm competition and the dynamics of X chromosome drive in finite and structured populations

Jesse E. Taylor[1] & John Jaenike[2]

[1] *Department of Ecology and Evolutionary Biology, University of Arizona, Tucson, AZ 85721, USA (e-mail: jtaylor@math.arizona.edu)*

[2] *Department of Biology, University of Rochester, Rochester, NY 14627, USA (e-mail: joja@mail.rochester.edu)*

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Of the several deleterious consequences that sex chromosome meiotic drive can have for a population, extinction is the most severe. Several studies of this phenomenon have suggested that males carrying a driving X chromosome may be disadvantaged during sperm competition. Deterministic modeling indicates that sperm competition can maintain a balanced polymorphism of driving and non-driving X chromosomes, but that if the frequency of the driving chromosomes exceeds some threshold value, then these chromosomes will spread to fixation and the population will go extinct. In this article we present the results of individual-based simulations of a stochastic model of X chromosome drive in finite and structured populations. We show that in large populations the balanced polymorphism can be maintained for hundreds of thousands of generations, but that reductions in population size and certain forms of population structure promote fixation of the driving chromosome.

Introduction

By biasing sex ratios both within families and populations, alleles which distort the segregation ratios of sex chromosomes can lead to evolutionary conflicts involving genes, individuals, populations, and even species (Leigh 1977, Crow 1991, Hurst *et al.* 1996). Although the driving allele enjoys a substantial transmission advantage, the selection that produces this advantage operates among the gametes of a single individual and may permit the driving allele to accumulate linked mutations which are deleterious to the organism. If, as the allele spreads through the population, it biases the population sex ratio away from the Fisherian optimum, individuals for which the driving allele produces biased familial sex ratios will also suffer an indirect loss of fitness due to diminished reproductive opportunities for their offspring. These effects on individual fitness may be short-lived, however. Should the driving chromosome sweep to fixation, then at least for obligately sexual species, the extreme skewing of the population sex ratio that accompanies the spread of this chromosome can result in extinction of the population (Gershenson 1928, Hamilton 1967, Lyttle 1977). In principle, driving sex chromosomes could even be responsible for the extinction of a species, leading to selection between lineages which

differ either in their propensity to evolve driving alleles on the sex chromosomes or in their capacity to suppress the full expression of these alleles when they do arise (Carvalho & Vaz 1999).

Because of the impact that unchecked sex chromosome meiotic drive can have on populations, the persistence of driving sex chromosomes in populations of plants, mammals, flies, and possibly a butterfly has elicited many studies aimed at understanding the evolutionary and ecological attributes which prevent fixation of the driving allele (Jaenike 2001). This phenomenon may also have applications to human health. Some of the species of Diptera in which driving sex-linked alleles have been found are primary vectors of important human pathogens, e.g., *Aedes* mosquitoes and Tsetse flies (Rawlings & Maudlin 1984, Wood & Newton 1991). It has been suggested that driving chromosomes could be used to extirpate populations of the vector organisms in areas with dense human populations and thereby reduce human disease burden (OwusuDaaku *et al.* 1997).

Most species in which driving sex chromosomes have been found are polymorphic for two types of X chromosome, denoted X^{SR} (Sex-ratio) and X^{ST} (Standard). While males which carry an X^{ST} chromosome sire offspring with normal sex ratios, SR males sire primarily or exclusively female offspring because of a failure to produce functional Y-bearing sperm (Policansky & Ellison 1970, Cazemajor *et al.* 2000, Wilkinson & Sanchez 2001). In some species, females carrying an X^{SR} chromosome have reduced fitness, possibly because of the presence of deleterious alleles within SR-specific haplotypes (Wallace 1948, Edwards 1961, Curtsinger & Feldman 1980), but newly arisen SR alleles probably act primarily on male spermatogenesis with little or no pleiotropic effect on female fitness. Although a more diverse set of mechanisms opposing sex ratio meiotic drive may eventually be recruited, we suggest that the mechanisms initially preventing rapid fixation of a driving X chromosome introduced into a population will act, like the SR allele itself, on male reproductive biology.

In his studies of X chromosome drive in *Drosophila pseudoobscura*, Wu (1983a) observed that SR males are at a disadvantage in sperm competition with ST males and that this disad-

vantage increases with the number of matings per male. Empirical studies of several other species have shown that reduced sperm or pollen production and accelerated rates of sperm or pollen depletion with multiple mating are general properties of X^{SR} in these systems (Hickey & Craig 1966, James 1992, Jaenike 1996, Taylor *et al.* 1999, Wilkinson & Fry 2001). If the male mating rate increases as the population sex ratio becomes skewed towards females, then the fitness of the SR allele will be frequency dependent and sperm competition might maintain a balanced polymorphism at the locus responsible for drive. On the other hand, because the severity of sperm competition depends not only on the number of times that individual males mate, but also on the number of different males mated by individual females, extreme skews in the population sex ratio towards females will actually mitigate against sperm competition and may enable the driving allele to spread to fixation.

Because it was unclear from these verbal arguments whether sperm competition would stabilize or destabilize a polymorphism for X chromosome drive in a species in which SR males fare poorly at sperm competition, Taylor and Jaenike (2002) studied a mathematical model of the dynamics of a driving X chromosome under this scenario. They showed that a balanced polymorphism at the driving locus could be maintained by sperm competition alone, but that existence of a stable internal equilibrium implies existence of a second stable fixed point corresponding to fixation of the driving X chromosome. There is, consequently, an unstable internal equilibrium frequency above which the SR allele will spread to fixation. The long-term fate of a population may then depend on stochastic events, especially those occurring in small populations, that perturb the X^{SR} frequency above the unstable equilibrium frequency.

In the ideal population assumed by the Taylor and Jaenike (2002) model (infinite population size, panmixis), introduction of a single copy of the driving X triggers a deterministic convergence to the balanced polymorphism from which the population never deviates. Because real populations are finite, both the population sex ratio and the frequency of the SR allele will fluctuate between generations, so neither convergence to nor persistence of the balanced polymorphism is

certain. In particular, a population which starts at the stable internal equilibrium may subsequently drift into the domain of attraction of the coexisting stable fixed point and thus fix X^{SR} and go extinct. To the extent that geographical structure locally enhances the magnitude of these fluctuations, structured populations may be particularly susceptible to extinction.

We use this article to present the results of a study of the dynamics of a driving X chromosome in a finite population. Although explicit calculations seem to be intractable, it is possible to simulate such populations directly and to use these simulations to empirically estimate quantities of interest. Here we show that the qualitative predictions of the deterministic model are well matched by the simulated dynamics of populations of sufficiently large size and that the SR/ST polymorphism can persist for hundreds of thousands of generations. We also show that geographical structure can dramatically impact the persistence of this polymorphism, either depressing or extending the mean time during which both alleles are segregating.

Model formulation

The stochastic finite population models were constructed to emulate the deterministic model described in Taylor and Jaenike (2002). The notation used in these models is presented in Table 1. Generations are non-overlapping and divided into two steps: a bout of mating followed by reproduction and population regulation. Because of the complicated manner in which selection acts on the SR/ST locus during sperm competition, efficient simulations based on coalescent processes are not possible and it is instead necessary to keep track of the genotypes of individual males and females at the time of mating.

We first describe the mating step. Let k_f and k_m be the maximal number of times, respectively, that an individual female or individual male is able to mate. Then, assuming that there are N_f females and N_m males in the population, the maximal number of matings by all females and all males, respectively, are $N_f \times k_f$ and $N_m \times k_m$. The actual number of matings is just the smaller of these two numbers and we situationally define the two sexes to be the limiting sex and the limited sex depending on which corresponds to the smaller and which to the larger of the two numbers. Each member of the limiting sex mates the maximal number of times, but the number of matings per individual varies among members of the limited sex and some fraction of this sex may mate fewer than the maximal number of times. There are many schemes by which matings could

Table 1. Notation used in the stochastic models.

Term	Description
$\alpha(k) = a^k$	Sperm competition parameter. Measures the relative number of sperm transferred by an SR male as a function of the number of prior matings, k.
d	Number of discrete patches into which a population is divided
f	Proportion of females in the population
k	Number of prior matings by a male
k_f	Maximum number of times an individual female can mate
k_m	Maximum number of times an individual male can mate
m	Migration rate, the probability that an individual disperses from its natal patch
N	Total population size
N_f	Number of females in the population
N_m	Number of males in the population
n_1	Number of ST males with which a female has mated
n_2	Number of SR males with which a female has mated
p_f	Frequency of SR among females
p_m	Frequency of SR among males
p_{inv}	Probability of invasion of a driving chromosome
T_p	Persistence time, in generations, of the SR/ST polymorphism

be distributed among these individuals, but, in keeping with the deterministic model (Taylor & Jaenike 2002), we adopted that scheme which minimizes the variance of the number of matings per individual of the limited sex (by definition, this variance is zero for members of the limiting sex). For example, suppose that $N_f \times k_f < N_m \times k_m$ so that females are limiting for males, and let $j = [N_f \times k_f / N_m]$ be the greatest integer less than $N_f \times k_f / N_m$ and let $n = N_f \times k_f - N_m \times j$. Then, under this scheme, $N_m - n$ of the males are allotted j matings and the remaining n males are allotted $j + 1$ matings. Assignment of males to these two classes is done independently of their genotypes.

Given the procedure for determining the number of matings allotted to individual males and females, there is still some flexibility in how pairings may be sampled. Because the severity of sperm competition depends not only on how many times individuals mate but also on how many different male partners mate with individual females, the choice of these pairings will influence the dynamics of SR alleles. In the scheme implemented in this model, we require that before any individual is allotted their $k + 1$'st mating, all members of the same sex have mated k times. This rule tends to increase the number of different partners with which individuals mate and thus enhances sperm competition.

Each mating is accompanied by a transfer of sperm from male to female. We assume that each ST male transmits a large number of sperm with X^{ST}-bearing sperm and Y-bearing sperm present in equal proportions and that the number of sperm transferred is independent of the number of times that the male has already mated. In contrast, SR males transmit only X^{SR}-bearing sperm and the number of sperm transmitted is a declining function, $\alpha(k)$, of the number of prior matings, k, by that male. For both ST and SR males we assume that the number of sperm transmitted per mating is so large that we can treat these numbers as continuous variables and characterize each mated female by the proportion of X^{ST}, X^{SR} and Y bearing sperm transmitted to her. Specifically, if n_1 of a female's matings were with ST males and n_2 of these matings were with SR males, and if the i'th of these latter matings was with a SR male who had already mated

k_i times, then the proportions of X^{ST}, X^{SR} and Y-bearing sperm transmitted to this female are n_1/K, $1 - 2n_1/K$, and n_1/K, where K is defined by the equation:

$$K = 2n_1 + \sum_{i=1}^{n_2} \alpha(k_i) \qquad (1)$$

Reproduction and population regulation were merged in a manner reminiscent of the discrete time Wright-Fisher process. Having completed the mating step, we can choose an individual's genotype by first choosing the individual's mother uniformly from the pool of mated females and then choosing the maternal and paternal sex chromosomes based on the mother's genotype and on the composition of the sperm stored by this female. We assume that drive does not operate in females — empirically, meiotic drive systems are limited to one sex (Lyttle 1991) — so that heterozygous females are equally likely to pass on standard and driving X chromosomes. We also assume that selection on paternal sex chromosomes due to either meiotic drive or sperm competition is limited to transmission of sperm from males to females, so that the likelihood that an individual inherits a paternal sex chromosome of a given type is equal to the proportion of sperm of that type in the mother's sperm pool. Implicit in this procedure is the additional assumption that sperm of all types which are represented by non-zero proportions are present in sufficient number to justify sampling with replacement. Given a final adult population size of N, this sampling process is repeated N times, with independent and identically distributed samples. If these N individuals are all of the same sex, then the population goes extinct in the next time step and the process is stopped.

To study the effects of population structure on sex chromosome drive we incorporated the above process into a linear stepping stone model. Mating and population regulation occur independently in each patch and are followed by migration of surviving offspring between nearest neighbor patches. We define the migration rate, m, to be the probability that an individual moves from its natal patch to a neighboring patch. Migration is independent of genotype and independent between individuals, so that

the total number of migrants out of an occupied patch of size N is binomially distributed with mean $N \times m$. Migrants from boundary patches always move inwards, but migrants from internal patches move to either neighboring patch with equal probabilities. Migration rates for individuals born in internal patches were capped at 2/3 which corresponds to either remaining within the natal patch or moving to one of the two neighboring patches with equal probability; similarly, migration rates for individuals born in boundary patches were capped at 1/2.

In the stepping stone model, individual patches may suffer temporary extinction and then be subsequently recolonized by migrants from neighboring patches. We assume that individuals disperse before they mate and so at least one male and one female immigrant in the same time step are required for such a recolonization event to occur. If all immigrants into an empty patch are of the same sex, these produce no offspring and the patch suffers another extinction event. The process is stopped only if all patches are simultaneously empty.

Code implementing both the panmictic and stepping stone models was written in C and is available from the authors upon request.

Results

Simulations in the panmictic setting were carried out under several formulations of the sperm competition disadvantage function $\alpha(k)$, with various population sizes ranging up to 10 000, and with different values of the maximal female and male mating rates, k_f and k_m. Even in large populations, some combinations of k_f and k_m appear to be unable to sustain the SR/ST polymorphism irrespective of the disadvantage function. However, when k_m is taken to be sufficiently large relative to k_f, e.g., $k_m = 20$ with $k_f = 2$ or 3, long-term persistence of this polymorphism is observed with both linear and exponential disadvantage functions. Because both formulations of α produced qualitatively similar results, we report numerical values only for exponential disadvantage functions: $\alpha(k) = a^k$. For conciseness we refer to the parameter a simply as the competition parameter. Observe that with $a = 1$
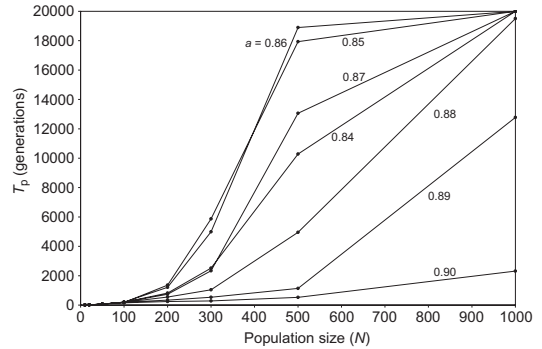

Fig. 1. The mean persistence time of the polymorphism, T_p, plotted against population size for the panmictic model. Runs were terminated after 20 000 generations if the polymorphism persisted that long. $a \in [0.84, 0.90]$, $k_f = 3$, $k_m = 20$.

there is no disadvantage other than that due to the death of Y-bearing sperm (assumed to be half of the sperm produced by a male) and that the disadvantage becomes both increasingly severe and increasingly sensitive to male mating rate as a decreases.

In Fig. 1 we plot the mean persistence time of the polymorphism (T_p) as a function of the panmictic population size N and the SR sperm disadvantage. The simulations used to obtain these estimates were initiated with frequencies of X^{SR} among males and females of 0.50 and with a 1-to-1 population sex ratio, and were terminated after 20 000 generations if the polymorphism persisted that long. T_p was estimated by the empirical mean over 100 independent trials of the number of generations for which the population continues to segregate both driving and non-driving X chromosomes. Populations moved rapidly from these initial conditions into the vicinity of the balanced polymorphism, and accordingly the statistic T_p reported here is a measure of the persistence of the polymorphism given that a driving chromosome has successfully invaded the population. (One could also define a mean persistence time for when the driving chromosome is introduced as a single copy, but since the fate of most such populations will be to rapidly lose the driving chromosome through genetic drift, even when meiotic drive is strong and sperm competition is weak, this statistic would depend on both the invasion probability for the driving chromosome, p_{inv}, and
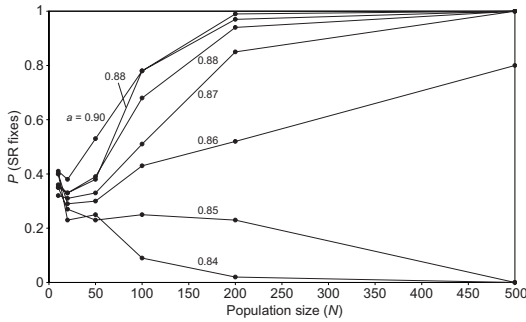
Fig. 2. Fixation probabilities of the SR allele conditional on a fixation event within 20 000 generations. Mating and sperm competition parameters as in Fig. 1.

Fig. 3. Equilibrium values of the frequency of SR allele among females, p_f, and the proportion of the population which is female, f, for a panmictic population of 1000 individuals. The error bars indicate the mean standard deviations of these state variables about the equilibria. The threshold value of p_f was estimated using the fixation curves depicted in Fig. 4. Mating and sperm competition parameters are as in Fig. 1.

the persistence of the polymorphism conditional on a successful invasion, and will be of order $p_{inv} \times T_p$. Since we report invasion probabilities below, we report T_p separately here.)

Because of the upper bound on the number of generations per trial, which was necessitated by the length of the simulations, this estimate is negatively biased and for some parameter values is a substantial underestimate of the true mean. To obtain a crude estimate of T_p for some parameter values for which the upper bound of 20 000 was saturated, sets of 10 independent trials were conducted with a population size of 1000, with $k_f = 3$, $k_m = 20$ and a ranging from 0.84 to 0.89, and with the maximum length of each trial increased to one million generations. For values of a between 0.84 and 0.87, the mean persistence time of the polymorphism was in excess of 800 000 generations and most trials lasted the full one million generations. For larger values of a, the polymorphism is more vulnerable to fixation of the driving allele and T_p is smaller: 203 228 generations and 23 656 generations, respectively, when $a = 0.88$ and $a = 0.89$.

Figure 2 displays the probability of fixation of the SR allele conditional on a fixation event, using the same simulations that produced the estimates shown in Fig. 1. The estimate was taken as the proportion of runs in which the SR allele was fixed out of all runs in which either the SR or ST allele was fixed within the 20 000 generations allowed for each simulation. No estimates of the fixation probability are shown for populations of size 1000 because for many values of the competition parameter all 100 trials persisted for the full 20 000 generations.
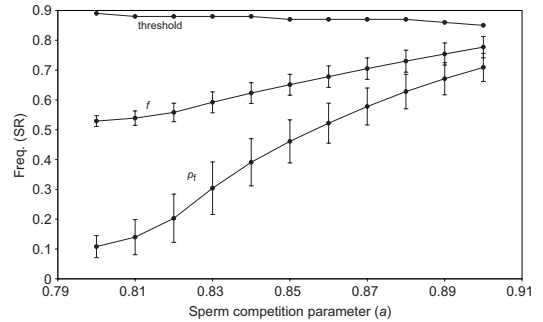
Because the only absorbing states of the finite population processes correspond to fixation of the SR or ST alleles, polymorphic equilibria are not well defined for these models. However, in those cases in which a polymorphism persists for many generations, we can use the mean values assumed by the state variables (the male and female frequencies of the SR allele, p_m and p_f, and the proportion of the population which is female, f) averaged over multiple generations and independent trials to describe the typical state of a polymorphic population. In Fig. 3, we plot these means for p_f and f for populations of size 1000. Means of p_f and p_m differed by less than 0.01, so the curve for p_m is effectively superimposed on that for p_f. Means were computed only for populations which remained polymorphic for at least 200 generations and the first and last 100 generations were excluded from these estimates in order to discount initial and final transients.

Also shown in Fig. 3 are estimates of the 'threshold' value of p_f for fixation of the SR allele. The threshold values of the state variables were defined operationally by calculating the proportion of independent trials with initial state variables equal to p_f, p_m, and f which fix the SR allele in fewer than 50 generations. The initial male and female frequencies of X^{SR} were taken to be equal and the initial value of f was set equal to $1/(2 - p_f)$ in keeping with the expected value of f in an infinite population with these frequencies of SR
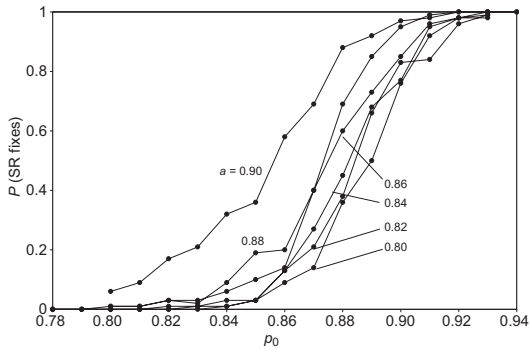
Fig. 4. The probability of fixation of the SR allele in fewer than 100 generations in a panmictic population of 1000 individuals. p_0 was the initial frequency of the SR allele among males and females and the initial population sex ratio f/m was determined by setting $f = 1/(2 - p_0)$. Mating and sperm competition parameters are as in Fig. 1.

Fig. 5. The probability of persistence of the SR/ST polymorphism for 500 generations when a single SR-bearing X chromosome is introduced among the males. Mating parameters were as in Fig. 1.

(Taylor & Jaenike 2002). Figure 4 shows these plots for a range of initial values of p_f and for different values of the SR disadvantage parameter in populations of size 1000. In all cases, the curves are S-shaped with a middle region in which the probability of rapid fixation of X^{SR} increases steeply as a function of the initial frequency of X^{SR}. The threshold value of p_f was defined to be the midpoint of the interval on the p_f axis over which this slope was greatest. Although our requirement that a rapid fixation occur in fewer than 50 generations is arbitrary, for all values of $a < 0.9$, fixation either occurred this rapidly or else the polymorphism persisted for at least 200 generations and typically for many more. With $a = 0.9$, some fixations of X^{SR} occurred within 50 to 200 generations, but the distribution of times to fixation of X^{SR} was still bimodal with most fixations of X^{SR} either requiring fewer than 50 generations or more than 200 generations.

Invasion probabilities for the SR allele resulting in a sustained polymorphism were estimated by conducting simulations in which the initial population was fixed for X^{ST} except for a single SR allele introduced among the males. The initial population-level sex ratio was 1:1. The invasion probability was estimated as the proportion of trials for which polymorphism was sustained for 500 generations and 1000 independent trials were conducted for population sizes of 100, 1000, and 10 000. These are shown in Fig. 5.
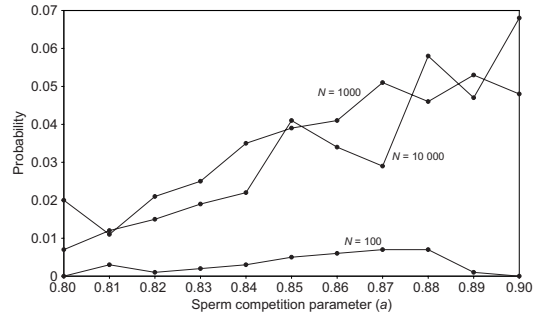
Estimates of the mean persistence time were obtained for populations with a linear stepping stone structure using the same procedures applied to the panmictic model. Note that polymorphism was defined in terms of the global population and that individual patches could be fixed for either allele. Because fixation of X^{SR} results in local extinction, global polymorphism does imply the existence of at least one patch which is itself polymorphic for the SR/ST alleles. The total population size N was taken to be either 500 or 1000 and simulations with $d = 1, 2, 5, 10, 20,$ and 50 patches, each of size N/d, were run. Figure 6 shows the relationship between the mean persistence time and the migration rate for $a = 0.50$ and $a = 0.45$ when $N = 1000$; additional simulations were run for $a = 0.90$ and $a = 0.85$ with qualitatively similar results and these are not shown.

Discussion

The simulations discussed in this paper demonstrate that a polymorphism for driving and non-driving X chromosomes can be sustained by sperm competition for hundreds of thousands of generations in both panmictic and structured finite populations. They also confirm that fixation of the driving X chromosome is locally attracting and that, in small populations, fluctuations in the frequency of the SR allele due to genetic drift can perturb a population at equilibrium into the domain of attraction of this second fixed point
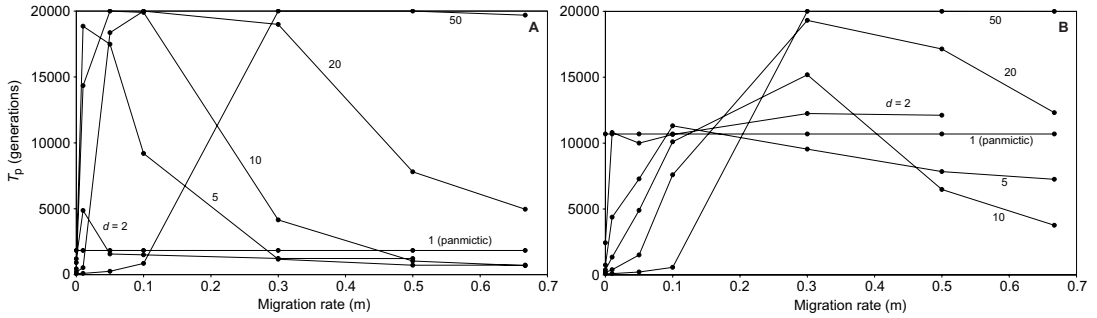
Fig. 6. The mean persistence time of the polymorphism, T_p, plotted against migration rate for the stepping stone model. Total population size was 1000, distributed among $d = 1, 2, 5, 10, 20, 50$ patches. (**A**) $a = 0.50$; (**B**) $a = 0.45$, $k_f = 2$, $k_n = 20$.

and result in the extinction of the population. Because the magnitude of these fluctuations is inversely correlated with population size, large populations are more likely to sustain a balanced polymorphism for long periods of time than are small populations. As can be seen in Fig. 1, the mean persistence time for the polymorphism increases faster than linearly with the population size and, for large populations, the balanced polymorphism is maintained for many more generations than is a neutral polymorphism for which the mean persistence time is proportional to the effective population size (Kimura & Crow 1970).

Interestingly, fixation of X^{SR} is not the inevitable fate of a population polymorphic for the driving chromosome. Depending on the strength of the sperm competition disadvantage of the SR allele and the size of the population, genetic drift may be more likely to lead to loss of the driving chromosome than to its fixation (Fig. 2). This behavior is contrary to what is suggested by the deterministic model, in which existence of a balanced polymorphism implies that the fixed point corresponding to fixation of X^{SR} is locally stable and that the fixed point corresponding to fixation of X^{ST} is locally unstable. One might infer from these local stability properties that any balanced polymorphism will ultimately be resolved by convergence of the process to the stable absorbing state. However, the likelihoods of trajectories from the balanced polymorphism to either of the absorbing states depend not only on the local behavior of the process about each absorbing state but also on the behavior of the process in regions intervening between the sev-

eral equilibria. In Fig. 3 we see that the separation between the equilibrium value of p_f and the threshold value of that state variable increases substantially as the SR disadvantage becomes increasingly severe, principally because the equilibrium value of p_f decreases towards zero. When this separation is large, the likelihood of drifting from the balanced polymorphism to the threshold value is less than the likelihood of drifting to zero. How the polymorphism is resolved becomes increasingly skewed as the population size increases. In small populations, fixation of either allele can occur with appreciable probability. In large populations, however, only one of the two absorbing states is likely to be reached from the balanced polymorphism. If the internal equilibrium frequency of X^{SR} is close to the threshold value, then the probability of extinction due to fixation of the driving allele actually increases with population size (Fig. 2). This observation is consistent with the predictions of large deviations theory for a stochastically perturbed dynamical system with multiple stable equilibria: as the magnitude of the noise decreases to zero, for each equilibrium there is a single most probable trajectory connecting that equilibrium to some other stable equilibrium such that most noise-induced transitions proceed along this trajectory (Freidlin & Wentzell 1998). When the internal equilibrium frequency of X^{SR} is close to the threshold, this most probable trajectory leads from the balanced polymorphism to the boundary fixed point corresponding to fixation of the driving allele.

In light of the observation that for some parameter values the polymorphism is most

likely to be resolved by loss of the SR allele, we need to ask how likely it is that a balanced polymorphism will be established in a population into which a single driving chromosome by mutation or migration. The deterministic model predicts that any perturbation off of zero is followed by convergence to the stable internal equilibrium, but it is possible that the rate of growth from zero is so slow that in a finite population genetic drift dominates this growth and the SR allele is more likely to be lost than to reach equilibrium. As shown in Fig. 5, for all values of the competition parameter, a single SR allele is always more likely to be lost than to establish a polymorphism that persists for 500 generations in populations of size up to 10 000. Persistence is extremely unlikely in populations of size 100 (which is not surprising in light of the mean persistence times shown in Fig. 1), but in populations of size 1000 or 10 000, the probability of persistence is at least 0.01, but never greater than 0.1. Although these values are not very large, they are not so small as to make the establishment of a balanced polymorphism implausible when the competitive disadvantage is of sufficient strength to allow an already established polymorphism to persist. Furthermore, recurrent mutation or migration of SR alleles into a population will increase the likelihood that a species will eventually become polymorphic at the driving locus. Even in the absence of competitive disadvantage ($a = 1$), the probability of fixation of the SR allele is only 0.137 if $N = 1000$ and 0.121 if $N = 10\,000$. We also observe that the persistence probabilities do not differ greatly between populations of size 1000 and of size 10 000. Although genetic drift is weaker in larger populations, the initial frequency of the SR allele is proportionately smaller and these two opposing factors compensate each other in this range of population sizes.

The dynamics of X chromosome drive in a structured population are complicated by the fact that the local fixations of SR that tend to occur in single patches supporting small populations can either promote or impede the global fixation of this allele. The intricacy of the situation can be attributed to the fact that a rise in the frequency of X^{SR} above the threshold usually results in a local extinction and a precipitous drop in X^{SR} frequency. Whether these local events stabilize or destabilize the global dynamics depends on how many SR-bearing individuals disperse out of populations undergoing fixation of X^{SR} before extinction occurs and on how rapidly extinct patches are recolonized.

Our simulations of a linear stepping stone model reveal two related trends. On the one hand, the mean persistence time is a unimodal function of the migration rate (Fig. 6). On the other hand, the probability that the polymorphism is resolved by fixation of SR increases monotonically with this rate. When the migration rate is very small, individual populations tend to independently fix or lose the SR allele and the fate of the metapopulation depends on whether X^{ST} is fixed in any of the patches. If some patches do fix this allele, then migrants from these patches eventually recolonize the rest of the metapopulation and X^{ST} is fixed globally. If the metapopulation is divided into many patches, global fixation of X^{SR} (followed by global extinction) is very unlikely with small migration rates, even when the competitive disadvantage of SR males is small, because X^{ST} is likely to be fixed by drift in at least one of these patches. Furthermore, because fixation or loss of the SR allele occurs rapidly in small populations, the mean persistence time of the polymorphism is small.

As the migration rate increases from zero, patches in which both alleles are segregating are able to export some SR alleles before extinction or fixation of X^{ST}. Since empty patches can be recolonized by both alleles, the mean persistence time and the likelihood of global extinction increase. This situation is reminiscent of Wallace's verbal model for the persistence of a driving sex chromosome in a metapopulation (Wallace 1968). When the competitive disadvantage of SR males is such that a panmictic population is likely to fix the driving chromosome, structure coupled with moderate migration can extend the mean persistence time by a factor of ten or greater (Fig. 6A). Although the linear population is still prone to extinction, the frequent extinctions of local populations fixing X^{SR} augment the selection against this allele due to sperm competition, thus enhancing the stability of the polymorphism. When loss of the SR allele is more likely in panmictic populations, structure can still extend the mean persistence time but does so to a

lesser degree than in the previous case and for a narrower range of migration rates (Fig. 6B).

As the migration rate saturates, so that most individuals disperse out of their natal patch, the likelihood of global extinction continues to increase, but the mean persistence time now decreases. Drift within individual patches sometimes drives the frequency of the SR allele above the threshold value, but most SR-bearing individuals born in these patches disperse to neighboring populations before local extinction occurs. Because increases in X^{SR} frequency skew the sex ratio towards females and because females carry two X chromosomes and males only one, there is an asymmetric movement of SR-bearing X chromosomes and of females between populations. Consequently, transient increases in X^{SR} frequency in individual patches proceed to fixation more slowly and are able to destabilize neighboring populations. It is possible that extinction events propagate in a wave-like fashion among the patches until they either hit the boundary or collide with another wave moving in the opposite direction. This picture is consistent with our observation that in very long island chains ($d = 50$) the mean persistence time generally increases with the migration rate up to its saturation point. Even with high migration rates, there is some positive probability that a local population will fix X^{SR} and go extinct without destabilizing a neighboring population. Waves of instability may propagate for some distance, but are more likely to produce a cluster of local extinctions that reduce the global frequency of X^{SR} than they are to drive all patches to extinction.

Based on our simulations of finite and structured populations, we can draw several inferences about how sperm competition is likely to influence the dynamics of driving X chromosomes in real populations. In a large panmictic population with more than a few thousand individuals, sperm competition can maintain a driving allele for hundreds of thousands of generations. Substantial reductions in population size, such as may accompany environmental change or habitat destruction, will compromise this stability, and persistence of the driving allele and of the population will then depend on whether the disrupted population is panmictic or divided into smaller, isolated units. Extensive subdivision with little gene flow between patches is likely to result in global loss of the driving allele as well as in local extirpations, but the species will survive in patches in which the driving allele is lost through drift. Global fixation of X^{SR} followed by species extinction appears improbable unless the population is either small and panmictic, or else is subdivided into patches connected by extensive gene flow.

If the X chromosome polymorphism does persist for hundreds of thousands of generations, then the population-level sex ratio bias may be gradually eroded by mutations which interfere with transmission of the SR allele or which lower the fitness of carriers of this allele. Y-linked and autosomal suppressors of X chromosome drive have been found in some species and enable SR males to produce some functional Y-bearing sperm (Jaenike 2001). The sex ratios of broods sired by SR males that also carry suppressor mutations are less female biased than those sired by SR males lacking suppressors. Consequently, suppressor mutations may be favored both by the transmission advantage that they confer to non-X chromosomes (Thomson & Feldman 1975, Wu 1983b) and by selection for Fisherian sex ratios. SR alleles in some species are also associated with chromosomal inversions, which can accumulate deleterious recessive mutations and result in decreased fitness for SR-homozygous females (Wallace 1948, Curtsinger & Feldman 1980, Jaenike 1996). Because the inversion suppresses recombination, linkage between the SR allele and deleterious alleles at neighboring loci is stable, and deleterious mutations can use the transmission advantage of the SR allele to hitch-hike to high frequencies. These mutations do not alter brood sex ratios, but they do result in a less female-biased population sex ratio by depressing the equilibrium frequency of X^{SR}. Both of these mechanisms will oppose fixation of X^{SR} and may either extend or shorten the evolutionary lifespan of the polymorphism depending on whether X^{SR} is more likely to be fixed or lost in their absence. A formal model combining these several mechanisms has yet to be studied and their relative contributions to either resolving or maintaining the polymorphism probably depends on the details of the biology of the affected species.

What is attractive about sperm competition as a short- to medium-term stabilizer of X chromosome drive is that defects in spermatogenesis caused by the driving allele may directly impact the sperm competitive ability of SR males and so provide an immediate mechanism for preventing the fixation of the driving chromosome.

Of course, even if SR males do suffer a severe disadvantage when forced into sperm competition with ST males, this disadvantage will counter meiotic drive only if there is sufficient opportunity for sperm competition between the two types of males. How much opportunity there is for sperm competition depends in part on how matings are distributed and ordered among individuals. In the mating scheme implemented in these simulations, the distribution of matings was chosen in such a way as to maximize the number of matings per individual of the limited sex (subject to that limitation) and the ordering of matings was chosen in such a way as to inflate the number of distinct partners per individual. As noted above, these rules promote sperm competition between males. Many alternative schemes could be formulated in which there is greater variance in the number of matings per individual and greater temporal clustering in the matings of each individual. Such alterations will tend to reduce the number of partners per individual, thus limiting the opportunities for sperm competition and increasing the likelihood and rate of fixation of the driving allele. Haig and Bergstrom (1995) have suggested that meiotic drive may select for female mating behaviors which enhance sperm competition if drive is associated with diminished individual fitness and if ejaculates containing sperm bearing the segregation distorter are disadvantaged during sperm competition. In a species in which segregation distorters arise frequently at both autosomal and sex-linked loci, sperm competition that is initially selected for in accordance with Haig and Bergstrom's model to ameliorate the deleterious impact of drive on individual fitness may subsequently protect populations of that species from extinction caused by sex chromosome meiotic drive. Alternatively, if drive is limited to the sex chromosomes or is not typically associated with costs to individual fitness, then group selection in a structured population may enhance sperm competition as local populations with insufficient sperm competition are driven to extinction when invaded by driving sex chromosomes.

We have deliberately kept the population dynamics incorporated into our model simple, with populations that are either extinct or else regulated to a fixed size N that is independent of the population-level sex ratio and frequency of X^{SR}. A more realistic demography could alter the long-term fate of a driving allele. A possible consequence is that as the frequency of X^{SR} approaches 1, the population sex ratio will become so skewed that the number of mated females may be insufficient to maintain the population at its carrying capacity. Spread of the driving allele will result in genetic drift becoming increasingly important relative to meiotic drive and sperm competition. Because the population size declines at very high frequencies of X^{SR}, when sperm competition is relaxed and meiotic drive pushes X^{SR} towards fixation, the net effect of finite clutch sizes will be to increase the probability that X^{SR} is lost rather than fixed (compare Fig. 2). In contrast, unless small deviations in sex ratio result in significant declines in population size, we expect the mean persistence time of the polymorphism and the invasion probability of the SR allele to be insensitive to demographic details. Hatcher *et al.* (1999) reached similar conclusions in their study of the dynamics of feminizing parasites in finite populations. Demographic enhancement of the probability of loss of the driving chromosome will be most pronounced in large populations of species with small clutch sizes, and is consistent with the observation that sex chromosome meiotic drive has been documented most often in species with high fecundity (Jaenike 2001).

Dependence of population size on the population sex ratio could also influence the dynamics of X^{SR} in structured populations if migration between patches is density-dependent. In particular, if local population density increases with the number of mated females, then below the threshold frequency of X^{SR} (at which males become limiting for females) local population density will track the local frequency of X^{SR}. Transient increases in the local frequency of X^{SR} will result in increased migration of SR-bearing individuals into neighboring patches with smaller

X^{SR} frequencies and smaller population sizes. Migration will be asymmetric between these patches and may promote the spread of an instability through the metapopulation. The ultimate fate of both local and global populations will still depend on what happens to population size when males, and consequently mated females, become rare. Depending on the demographics at different frequencies of X^{SR} and on the structure of the population, frequency-dependent population size and density-dependent migration could either promote or prevent fixation of the driving chromosome.

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