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Meiotic drive and evolution of female choice

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As a special version of the good-genes hypothesis, it was recently proposed that females could benefit from choosing drive-resistant males in a meiotic drive system. Here, we examine with a three-locus, six-allele population genetic model whether female choice for drive resistance can evolve. An allele leading to female preference for drive-resistant males was introduced at low frequency into a population polymorphic for meiotic drive and drive resistance. Our simulations show that female choice of drive-resistant males is disadvantageous when resistance is Y-linked. This disadvantage occurs because, at equilibrium, drive-resistant males have lower reproductive success than drive-susceptible males. Thus, female choice of drive-susceptible males can evolve when resistance is Y-linked. When resistance is autosomal, selection on female choice for drive resistance is less strong and depends on the frequency of choice: female preference of resistant males is favoured when choice is rare and disadvantageous when choice is frequent, leading to a stable equilibrium at a low frequency of the choice allele. Independent of the location of drive resistance alleles, males with the non-driving allele always have above average reproductive success. Female choice is therefore beneficial when choosy females prefer males with the non-driving allele.

Keywords: drive resistance; numeric simulation; population genetics; selfish genes; sexual selection

1. INTRODUCTION

In many animal species, females choose their mates on the basis of morphological characters or courtship displays presented by males. Because females often seem to receive no direct benefits, it has been suggested that females can increase offspring fitness by mating with attractive males (for reviews, see Pomiankowski 1988; Kirkpatrick & Ryan 1991; Andersson 1994). According to the good-genes hypothesis, offspring with superior viability will result when females mate with attractive males of high quality. It has been suggested that females should be able to increase offspring viability when they choose parasite-resistant males or males with fewer deleterious mutations (Hamilton & Zuk 1982; Iwasa *et al.* 1991; Andersson 1994).

Recently, Wilkinson *et al.* (1998) suggested an additional mechanism by which females may benefit indirectly from choosing among males. According to their hypothesis, females should benefit by choosing males that are resistant to meiotic drive. Meiotic drive alleles, a special case of selfish genes, can manipulate their own representation among gametes (Sandler & Novitski 1957; Crow 1979). By increasing their representation in gametes above the level predicted by Mendel's laws, meiotic drive genes can spread, even if the individuals that express them have reduced fitness. Meiotic drive genes are especially likely to be linked to the sex chromosomes (Hamilton 1967; but see Charlesworth *et al.* 1993). Meiotic drive genes on the sex chromosomes bias the offspring sex ratio. When such genes increase in frequency they cause a biased population sex ratio that reduces the fitness of individuals expressing the drive genes. As a consequence, selection will increase the frequency of genes that lead to meiotic drive resistance, as soon as such alleles are produced by mutation. When a polymorphism exists for drive and resistance, it has been suggested that females can benefit from choosing drive-resistant males because resistant males produce more sons (Wilkinson *et al.* 1998; Hurst & Pomiankowski 1998).

What is the empirical basis for this suggestion? Wilkinson *et al.* (1998) described a remarkable genetic correlation between selfish and sexually selected genes. The existence of such a genetic correlation was inferred from correlated responses to selection for increased and decreased size of eye stalks in stalk-eyed flies. Artificial selection for larger male eye span increased resistance to meiotic drive (Presgraves *et al.* 1997; Wilkinson *et al.* 1998). Since females preferentially mate with males having a long eye span (Burkhardt & de la Motte 1988; Wilkinson & Reillo 1994), female choice was inferred to lead to increased drive resistance. It was consequently suggested that female preference for males with long eye stalks evolved because these males have increased drive resistance (Wilkinson *et al.* 1998; Hurst & Pomiankowski 1998).

Here, we examine the hypothesis that female choice of males that are resistant to meiotic drive is adaptive. For the proposed mechanism, a polymorphism involving meiotic drive and drive resistance is necessary. With a population genetics model, we describe conditions that lead to such a polymorphism. We model the evolution of female preference for drive-resistant males by introducing an allele causing female choice in low frequency into a population at a polymorphic equilibrium between meiotic drive and drive resistance. We can show that the fitness of resistant and susceptible males differs at equilibrium when resistance is Y-linked: males without the drive allele

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produce the same number of surviving sons, but a lower number of daughters. Females choosing resistant males thus have lower reproductive success and the proposed mechanism for the evolution of female choice cannot work. However, our model demonstrates that female choice can evolve when choosy females prefer to mate with drive-free or drive-susceptible males.

2. THE MODEL

We examined the proposed hypothesis—evolution of a female mating preference for drive resistance—with a population genetics model assuming a diploid organism with discrete generations and infinite population size. Inspired by the meiotic drive system found in stalk-eyed flies (Presgraves *et al.* 1997; Wilkinson *et al.* 1998), six alleles at three loci were assumed to influence the following three traits: female choice, meiotic drive and drive resistance. An X-linked locus of meiotic drive in males assumed a driving allele X^d and a non-driving allele X^+. A Y-linked locus was assumed to influence resistance to meiotic drive. Males having the allele Y^m were modelled to be resistant to meiotic drive, and males with allele Y^+ were assumed to be drive-susceptible. Males with the genotype X^dY^+ were assumed to produce only female offspring, whereas X^dY^m males and males with the X^+ allele were assumed to produce an even sex ratio. With additional simulations we verified that similar results were obtained when assuming less biased offspring ratios of X^dY^+ males and male-biased offspring sex ratios of X^dY^m males. In additional simulations, drive resistance was assumed to be influenced by an autosomal locus: an allele R^m causing meiotic drive resistance and an allele R^+ leading to drive-susceptible males. Here, similar results were obtained with dominant and recessive autosomal drive resistance. In all simulations female choice was assumed to be influenced by an unlinked autosomal locus. Females expressing the choice allele A^c were assumed to mate preferentially with males of a specific genotype, and females expressing the random mating allele A^+ were assumed to mate randomly with respect to male genotype. The female choice allele A^c was modelled to be either recessive or dominant to the no-choice allele A^+. The strength of female choice was varied according to Kirkpatrick's (1982) model of 'relative female preference'.

We introduced A^c at low frequency into a population polymorphic for meiotic drive and drive resistance and observed changes in the frequencies of the choice allele. Choosy females were assumed to base mate preference on (i) the Y^m and Y^+ allele, (ii) the R^m and R^+ allele, and thus on drive resistance and susceptibility, and on (iii) the X^+ and X^d alleles.

In theory, the evolution of meiotic drive can cause the extinction of populations when drive increases to unity (Hamilton 1967; Lyttle 1977). Moreover, when resistance to meiotic drive evolves, this may lead to the elimination of meiotic drive when the frequency of drive resistance increases to unity. But when there are costs to meiotic drive and drive resistance, conditions for a protected polymorphism are not unduly restrictive (Curtsinger & Feldman 1980; Clark 1987; Carvalho *et al.* 1997; Jaenike 1999). To achieve a polymorphic equilibrium, we assumed fitness costs associated with meiotic drive and meiotic drive resistance. Based on fitness costs associated with meiotic drive and drive resistance in *Drosophila* (Beckenbach 1978, 1983; Wu 1983; Wu *et al.* 1989; Cazemajor *et al.* 1997), Y^m males and females homozygous for X^d were assumed to have reduced fertility. Fertility of Y^m (or R^m) males was reduced by a factor of $1-c$ $(0<c<1)$ relative to the fertility of Y^+ (or R^+) males, whereas fertility of females homozygous for X^d was reduced by a factor of $1-f$ $(0<f<1)$. Without such a fertility cost associated with drive and drive resistance, either X^d or Y^m would increase to fixation. In additional simulations we assumed a viability cost instead of a fertility cost for Y^m males and X^dX^d females and obtained identical results.

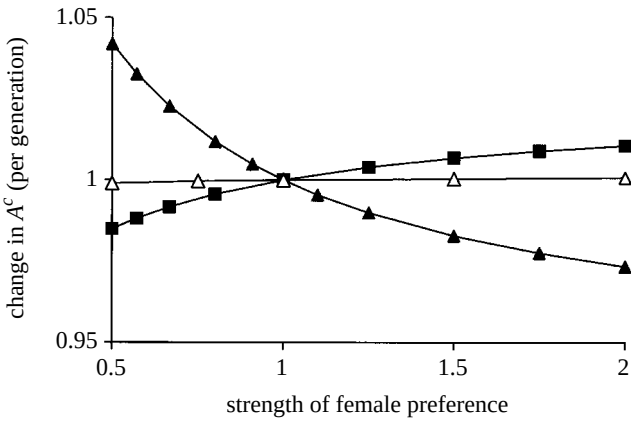

Figure 1. Frequency change per generation for a rare female choice allele A^c (frequency of choice $< 10^{-5}$) when preference is based on Y-linked drive resistance (filled triangles) (preference of males with allele Y^m against males with Y^+), autosomal drive resistance (open triangles) (preference of males with allele R^m against males with R^+), and the meiotic drive locus (filled squares) (preference of males with allele X^+ against males with X^d). For values with a relative female preference smaller than one, females are assumed to avoid mating with the respective males and thus mate preferentially with males having the alternative allele. For the figured cases, moderate costs of drive and resistance were assumed $(f=c=0.3)$. Similar changes in the frequency A^c resulted for all values of f and c that led to a polymorphism between X^d and Y^m.

3. RESULTS

(a) *Conditions for stable polymorphism*

A polymorphism for both the drive–non-drive and drive susceptibility–drive resistance alleles occurred over a wide area when different combinations of values for the fitness costs c and f were examined. With large fitness costs associated with meiotic drive and drive resistance, the frequency of drive resistance decreased to zero, and a polymorphism between the driving and the non-driving allele remained. For all values with a moderate fitness cost to the Y-linked or the autosomal drive resistance, a polymorphism between drive resistance and meiotic drive resulted. With a large cost to Y-linked resistance $(c>0.5)$ and moderate values for a fitness cost $(f<0.25)$ to females homozygous for the meiotic drive allele, stable limit cycles and a protected polymorphism with all four alleles occurred. The wide area with a polymorphism between the four alleles allows examination of the

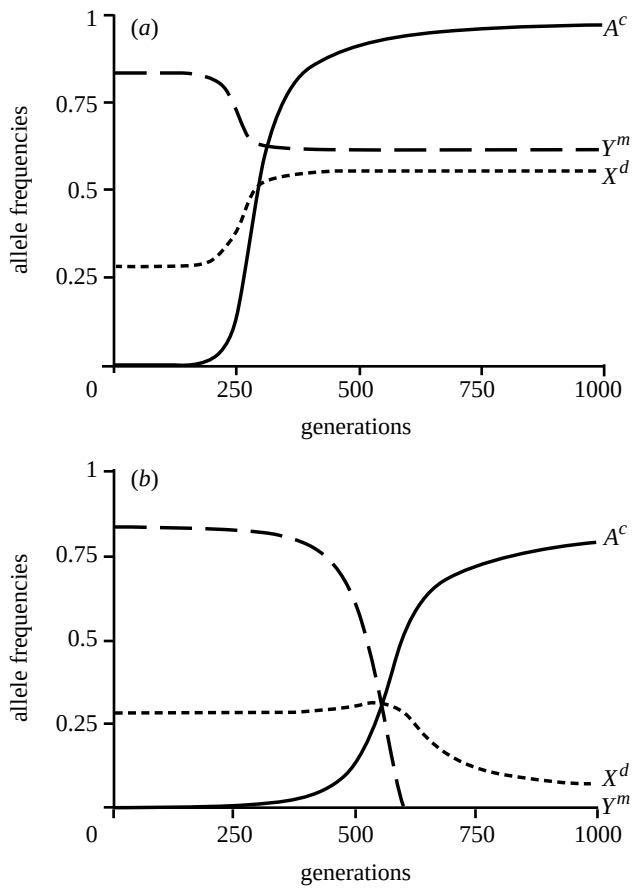

Figure 2. (*a*) Example of the trajectories for the frequencies of the meiotic drive allele X^d (dotted line), the drive resistance allele Y^m (thin line), and the female choice allele A^c (thick line), when choosy females were assumed to mate preferentially with drive-susceptible Y^+ males and when A^c was introduced at a low frequency. (*b*) Example of the trajectories for the frequencies of X^d (dotted line), Y^m (thin line), and A^c (thick line), when choosy females were assumed to mate preferentially with drive-free X^+ males and when A^c was introduced at a low frequency. ($f = c = 0.3$; strength of female preference = 2.)

hypothesis that female choice of drive resistant males is adaptive. To test this hypothesis, the fate of the allele A^c was examined when introduced in low frequency. For all cases examined, the outcome of the simulations regarding the fate of allele A^c was similar irrespective of the stability of the meiotic drive system.

(b) *Female preference based on drive resistance*

When females expressing A^c were assumed to mate preferentially with drive-resistant Y^m males, the frequency of the choice allele decreased rapidly (figure 1). A decrease in the frequency of the female choice allele could also be observed when only females carrying X^d or only those not carrying X^d were assumed to exhibit choice. Moreover, there was no threshold concerning the strength of female choice for the decrease in the female choice allele (figure 1). When choosy females were assumed to mate preferentially with drive-susceptible Y^+ males, the frequency of the choice allele increased, showing strong positive selection on female choice (figure 1). Owing to the female mating preference for drive-susceptible males, the frequency of the drive resistance allele Y^m decreased and the frequency of the drive allele X^d increased (figure 2*a*). When given enough time, either the female choice allele A^c increased to fixation or the frequency of the drive-resistant allele Y^m decreased to zero.

The fate of the female choice allele differed when resistance was assumed to be autosomal. When choosy females were assumed to prefer drive-resistant R^m males, selection on female choice was weak but positive when A^c occurred at very low frequency (figure 1). In all simulations where female choice was introduced into a polymorphic population, A^c increased until an equilibrium frequency of about 0.005–0.05 was reached. When choosy females were assumed to prefer drive-susceptible R^+ males, the frequency of allele A^c slowly decreased to zero.

(c) *Female preference based on meiotic drive*

When choosy females were assumed to mate preferentially with non-driving X^+ males, the frequency of female choice increased (figure 2*b*). This increase in the frequency of female choice of males with the non-driving allele occurred in all simulations, irrespective of the chosen values for f and c and the assumed linkage of the drive-resistance allele. The frequency of allele A^c even increased when meiotic drive resistance was absent. Female preference for drive-free males thus also seems to be adaptive in meiotic drive systems without resistance. Female preference for X^+ males decreased the frequency of the alleles Y^m and X^d, and when the strength of female choice was large enough, these alleles, causing meiotic drive and drive resistance, both disappeared (figure 2*b*).

When choosy females were assumed to mate preferentially with males having the drive allele X^d, the frequency of the female choice allele A^c decreased to zero. This decrease in the frequency of A^c occurred for autosomal and Y-linked resistance and with all chosen parameters for c and f and its speed increased with the strength of female choice.

4. DISCUSSION

In contrast to the suggested hypothesis, the frequency of female choice of drive-resistant males decreased in all simulations when Y-linked resistance was assumed. When autosomal resistance was assumed, selection led to a low equilibrium frequency of female choice of drive-resistant males. Thus, female choice of drive-resistant males is unlikely to be responsible for the evolution of female preference for large eye span in stalk-eyed flies. What are the reasons for this unexpected outcome of the simulations?

Mating with drive-resistant males leads to an increased proportion of male offspring. Since the population sex ratio is female biased, an increased proportion of male offspring should lead to an increased number of grandoffspring. This benefit resulting from preferential mating with drive-resistant males is counterbalanced by the fertility cost assumed to be associated with drive resistance. With Y-linked resistance, drive-resistant Y^m males and drive-susceptible Y^+ males have to produce the same number of sons at equilibrium because otherwise Y^m would change in frequency. At the same time, drive-resistant Y^m males produce fewer daughters than Y^+ males because they produce a less biased sex ratio owing to

their resistance to meiotic drive. With an equal number of sons and a lower number of daughters the reproductive success of Y^m males is thus lower than that of Y^+ males. With A^c females choosing drive-resistant Y^m males, a linkage disequilibrium builds up between the alleles Y^m and A^c. As a consequence, the lower reproductive success of Y^m males leads to selection against female choice of drive-resistant males.

With autosomal drive resistance, the reproductive success of R^+ and R^m males has to be equal at equilibrium. When A^c is rare, the evolution of female choice is thus governed by the linkage disequilibrium with X^+ that builds up when females base mate choice on resistance. Since A^c, in comparison with A^+, will be less likely to occur together with the drive allele, female choice for resistance will initially increase in frequency. When female choice of resistant males increases in frequency, resistance increases above its equilibrium frequency, and increased viability selection against resistance together with a linkage disequilibrium between R^m and A^c results in an equilibrium frequency of the female choice allele.

Thus, the benefit from choosing drive-resistant males is at best very limited and the suggested reason for the evolution of female choice does not work. However, our simulations show that females can benefit from mate choice in a meiotic drive system. Female choice is likely to increase in frequency when choosy females prefer males with the non-driving X^+ allele or when they prefer males with the drive-susceptible Y^+ allele. In both cases, female choice has a large fitness advantage because males with these genotypes have above average reproductive success. When females preferentially mate with males having the non-drive allele X^+, they benefit (i) from a lower proportion of daughters that are homozygous for X^d, (ii) from a larger number of sons, which is the less frequent sex, and (iii) from a linkage disequilibrium with Y^+ when resistance is assumed to be Y-linked. For these reasons, females benefit from choosing X^+ males or from avoiding X^d males, both of which have an identical effect on mate choice. Regarding the evolution of female choice in meiotic drive systems, the existence of drive resistance is not necessary: choice of drive-free X^+ males is also advantageous when resistance to meiotic drive is absent (figure 2*b*). Moreover, female choice of drive-free males can also be expected to be advantageous when drive is autosomal since the reproductive success of driving and non-driving males has to differ at the equilibrium.

The results of the model presented here suggest that females should prefer to mate with drive-free males and with drive-susceptible males when resistance is Y-linked. Is there any empirical evidence for females choosing one of these two types of male? The sparse experimental evidence indeed suggests that females prefer males without driving alleles to males with meiotic drive. Non-virgin *Drosophila pseudoobscura* discriminate against males with X chromosomes having meiotic drive 'sex ratio' (Wu 1983; but see James & Jaenike 1992), and female mice heterozygous for the *t* allele discriminate against males with a driving *t* allele (Lenington *et al.* 1992; Williams & Lenington 1993; but see Lenington 1991). Meiotic drive can thus lead to the evolution of female choice, but a general role for meiotic drive in sexual selection seems unlikely because meiotic drive has been found almost exclusively in mice and flies.

Given that the suggested advantage of choosing drive-resistant males does not exist, why did drive resistance increase in stalk-eyed flies artificially selected for large eye span (Wilkinson *et al.* 1998)? Since eye span is condition dependent in stalk-eyed flies (David *et al.* 1998), males with large eye-stalks (i.e. males in good condition) may have a lower relative cost of drive resistance. As a consequence, the equilibrium should move towards a higher frequency of drive resistance in the lines selected for large eye span and vice versa. In stalk-eyed flies, female choice of males with large eye span may thus be consistent with a conventional indicator model (Andersson 1986; Iwasa *et al.* 1991).

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