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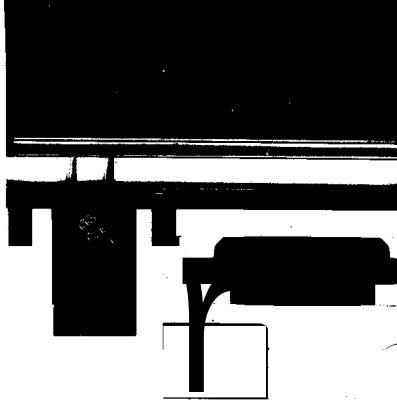

The Coevolution of Autosomal and Cytoplasmic Sex Ratio Factors

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It is generally believed that the presence of cytoplasmic sex ratio distorters in a population causes selective pressure on autosomal genes *for* a compensatory shift in the sex ratio. Investigations reveal that when within lineage transmission of a cytoplasmic distorter of the primary sex ratio is 100%, no compensatory autosomal sex ratio shift is favored. When transmission is less than 100%, a synergistic interaction occurs between autosomal and cytoplasmic sex ratio factors which results in a polymorphic population with individuals producing either 100% sons (autosomal) or 100% daughters (cytoplasmic). The outcome will only occur if there is sufficient autosomal sex ratio variability in the population for 100% ~on production. Some cytoplasmic factors cause male larval death, rather than a shift in the primary sex ratio. Such factors have no effect upon autosomal sex ratio selection, and therefore no compensatory sex ratio shift is expected. Even low levels of inbreeding can selectively favor male-killing cytoplasmic factors. Basic models of cytoplasmic sex ratio distortion suggest that cytoplasmic distorters (with high transmission) should increase to or near fixation, thus potentially driving a population to extinction. Models indicate that haplodiploid species are less vulnerable to this population level selection than are diplodiploid species. Among diplodiploid species, cytoplasmic distorters with incomplete transmission will achieve lower frequencies in species without autosomal sex ratio variability.

Introduction

Most models of sex ratio evolution either implicitly or explicitly assume nuclear genetic control over the sex ratio. Autosomal nuclear genes are transmitted to future generations through both sexes, and therefore selection favors a balance between production of male and female offspring. In panmictic populations a 1:1 ratio is typically favored (Fisher, *1930;* Chamov, *1982).* In contrast, cytoplasmic genes are typically inherited through egg cytoplasm and therefore are transmitted to future generations only through females (Grun, *1976;* Birky, *1976).* This assymmetric transmission creates strong selective pressure for cytoplasmic genes that distort sex ratio toward female production, since this is the only sex which transmits the cytoplasmic gene (Lewis, *1941; Bull, 1983).* Cytoplasmically inherited factors which either distort the primary sex ratio, alter sex determination, or cause male lethality, are found in many diverse taxa, including mites, isopods, mosquitoes, fruitflies, butterflies, parasitic wasps and plants (Grun, *1976;* Uyenoyama & Feldman, *1978;* Werren *et al., 1986).*

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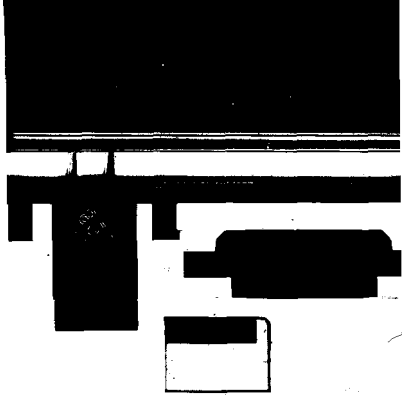


Fisher's theory predicts that autosomal sex ratio selection in the absence of cytoplasmic sex ratio distorters favors a 1:1 sex ratio in panmictic populations. Therefore, the presence of a cytoplasmic sex ratio distorter in a population would cause a deviation in the population sex ratio from 1 :1 and may create compensatory selective pressures on autosomal genes to restore the 1:1 ratio (Johnson, 1977; Uyenoyama & Feldman, 1978; Bull, 1983; Charnov, 1982). For example, if 30% of the females in a population carry a cytoplasmic "all-female" factor, then a compensatory overproduction of males might be expected. To determine whether such a compensatory shift would actually be selected for, it is useful to consider the different ways that autosomal genes can affect the sex ratio of a species. Two distinct categories are sex ratio genes and sex determination genes. As defined here, sex ratio genes are genetic elements which operate in parents to influence the sex ratio among their offspring. Sex determination genes are genetic elements which operate in an individual to determine its sex. The distinction of where the gene operates can be important in determining dynamics of the genetic element. A third general category should be considered in reference to the coevolution of autosomal and cytoplasmic genes. Resistance genes modify expression and/or transmission of cytoplasmic factors. Such genes would not normally alter sex ratio in "uninfected" individuals, but they influence sex ratio "indirectly" via their effects on cytoplasmic factors. It is important to distinguish these different categories because they may differ in dynamics and because it is coevolution of the entire system which determines what we observe in nature.

Studies of parts of this coevolutionary system have been performed. Uyenoyama & Feldman (1978) have demonstrated that selection on an autosomal locus controlling resistance to maternal transmission of a sex ratio distorter generally favors evolution of resistance and restoration of the primary sex ratio toward 1:1. Bull (1983) analyzed the interactions between extrachromosomal and autosomal sex determination genes. He concluded that the presence of a female determining cytoplasmic factor selectively favors increase of male determining autosomal factors. He further observed that this compensatory selection should lead to the evolution of monogeny.

No studies have investigated the effect of cytoplasmic sex ratio distorters upon autosomal loci which directly control the sex ratio produced by parents. The issue is relevant to several biological systems. For example, there is no evidence of autosomal compensation in Culex salinarius mosquitoe populations, even though a microsporidian sex ratio distorter occurs at frequencies ranging from 6 to 17% (Andreadis & Hall, 1979). Similarly, there is no evidence of sex ratio compensation in Nasonia vitripennis, where sex ratio distorters comprise up to 26% of individuals in natural populations (Skinner, 1983), nor in various Drosophila species which have extrachromosomal sex ratio distorters (Williamson & Poulson, 1979).

The purpose of this paper is to investigate the influence of extrachromosomal sex ratio distorters (ESRs) on autosomal sex ratio genes (ASRs) controlling the primary sex ratio produced by parents. A general model is developed for diplodiploid species. The model reveals that little or no sex ratio compensation is selectively favored under certain circumstances. The model is then applied to haplodiploid species and

analyzed with respect to the specific ESR system found in Nasonia vitripennis, which is a complex of three different ESRs occurring in natural populations (Werren et al., 1981, 1986; Skinner, 1982, 1983, 1985; Werren & Assem, 1986).

General Model

The optimal sex ratio for an autosomal locus in a population containing an ESR is determined by local stability analysis, or the "ESS technique" (Maynard Smith, 1976; Uyenoyama & Bengtsson, 1982). Consider a large random mating population which has an extrachromosomal sex ratio distorter that occurs at polymorphic equilibrium in the population. Further consider an autosomal sex ratio locus with two alleles (A and a). The "a" allele is near fixation, but the dominant "A" allele occurs in the population at low frequency. These alleles influence sex ratio in "uninfected" females, but their expression is overridden by the extrachromosomal factor in "infected" females. The optimal sex ratio is determined by finding that sex ratio which when produced by the "a" allele, results in the "a" allele being uninvadeable by an "A" producing any other sex ratio. The following terms are defined:

p = frequency of the cytoplasmic sex ratio distorter (ESR) in adult females

W = fitness of ESR females relative to uninfected females

x_A = proportion of daughters produced by Aa females

x_s = proportion of daughters produced by ESR females

x = proportion of daughters produced by as females

a = proportion of ESR daughters which inherit ESR

ε_1 = frequency of Aa among adult males

ε_2 = frequency of Aa among adult non-infected females

ε_3 = frequency of Aa among adult ESR females

Since it is assumed that the cytoplasmic factor overrides expression of the autosomal sex ratio locus, any female which carries ESR will express the x_s sex ratio regardless of autosomal genotype. When the A allele is rare, homozygous AA individuals and heterozygous Aa x Aa matings are extremely rare and have negligible effect upon frequencies of the allele in the next generation. Therefore, the transmission dynamics of the A allele can omit these matings and is approximately described by the following matrix

$$\begin{pmatrix} \frac{1}{2} & \frac{(1-xa)(1-P)}{2M} & \frac{(1-x_s)P}{2M} \\ \frac{1}{2} & \frac{x_A(1-p)}{2F} & \frac{px_s(1-a)}{2F} \\ \frac{1}{2} & 0 & \frac{1}{2} \end{pmatrix} \begin{pmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \varepsilon_3 \end{pmatrix}$$

where

$$F_{\bullet\bullet}=(1-p)x+pxs(1-a) \quad (2)$$

$$M=(1-p)(1-x)+p(1-xs). \quad (3)$$

The characteristic equation (C) for this matrix is

$$0=(1/2-A)^2[xa(1-p)/2F_{\bullet\bullet}-AI-[(1/2-A)/2-pxs(1-a)/4F_{\bullet\bullet}] \times (1-p)(1-xA)/2M - [(I-p)xal2F.-k]p(1-xs)/4M \quad (4)$$

The ESS sex ratio is determined by setting dc/dx =0, then setting A = 1, and solving for x. The solution is a weak form ESS as defined by Uyenoyama & Bengtsson (1982). The ESS sex ratio in the presence of a cytoplasmic factor producing x_s females ($x_s > x$) is

$$x^* = 1/2-(1-a)pxsl(1-p). \quad (5)$$

This equation has several interesting characteristics. First, the equilibrium sex ratio (x*) is a function of the of ESR frequency (p), sex ratio of the ESR (x,) and transmission frequency of the ESR (a). As expected, in the absence of the ESR (p = 0), $x^* = 1/2$ as predicted by Fisher (1930). However, a surprising result is that if an *ESR* has complete transmission (a=1), then the presence of the *ESR* has no effect upon selection for *ASR* genes (x*=1/2). Thus, even if the ESR were very common, e.g. p = 0.90, there would be no compensatory selection for ASR genes to produce more males. An intuitive explanation for this result is that when the factor has complete transmission, ESR females are in a separate subpopulation from normal females. Although they receive chromosomal genes from the normal subpopulation they have little gene flow back into the normal subpopulation because of the high within ESR transmission. As a result the ESR subpopulation has no effect on sex ratio selection in the normal subpopulation.

At intermediate transmission frequencies, the ESR can affect ASR selection, as shown in Fig. 1, since there is input of normal females from the ESR female population due to incomplete transmission.

FREQUENCY OF ESR

In natural populations, frequency of an ESR can be affected by a variety of factors, such as frequency dependent fitness effects and population structure. Let us consider the frequency of the ESR in a panmictic population, assuming constant fitness and transmission. First consider the conditions which permit an ESR to successfully invade a panmictic population, i.e. to increase when rare. Given that x =proportion females produced by normal females, then the frequency of an ESR from one generation (p) to the next generation (p') when rare is

$$p'=px,Wa/x. \quad (6)$$

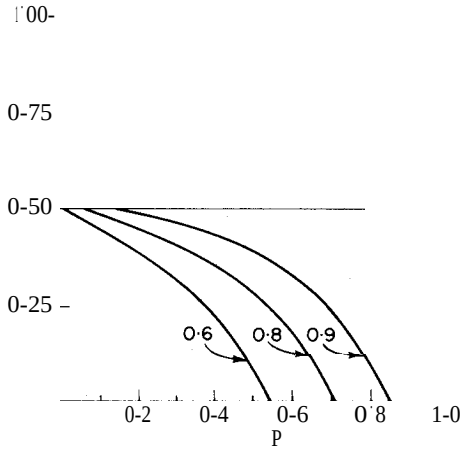


FiG. 1. The influence of an ESR which produces 100% females of equal fitness to normal females, upon ASP, selection, is shown for different transmission rates (a). The higher transmission, the less effect the ESR subpopulation has upon the optimal proportion daughters (x*), because the ESR subpopulation has less genetic input to the normal subpopulation. With complete transmission, ESR has no influence on the optimal sex ratio.

Increase occurs when p'/ p > 1. The conditions for increase are $x_S Wa - x > 0$. In other words, for the ESR to increase it must effectively produce more ESR females than a normal female produces normal females (Bull, 1983). Since in a panmictic population x =1/2, $x_S Wa > I/2$ is necessary for the ESR to increase. As ESR becomes more common in the population its frequency becomes defined by

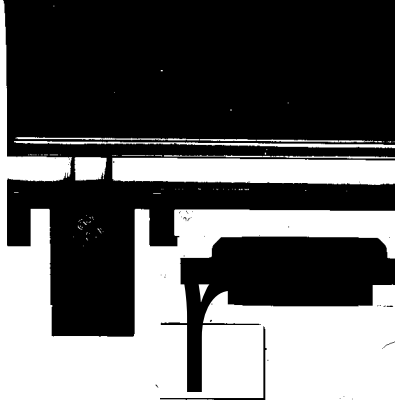
$$p'=px,Wa/[px,Wa+(1-p)x+px_s(1-a)] \quad (7)$$

and the equilibrium frequency p* is

$$p^* = [x_S Wa - x]/[xS\ Wa - x + x_5(1-a)]. \quad (8)$$

When a = 1 (complete transmission) this equation simplifies to p = 1. So an ESR will go to fixation in this simple model whenever $Wx_s a > 1/2$ and a = 1. This presents the paradox that an ESR with complete transmission can go to fixation in the population, but this would probably drive the population to extinction because of an absence of males (Heuch, 1978).

It is useful to investigate what forces might prevent an ESR with complete transmission from going to fixation. In general, for a polymorphic equilibrium to occur, one of the parameters governing frequency of the ESR must vary in a frequency dependent fashion such that increase of the factor is limited as it becomes more common. Several possibilities exist. For example, frequency dependent selection for autosomal suppressors could result in polymorphic equilibria, as has been suggested for cytoplasmic male sterility factors in plants (Charlesworth & Ganders, 1979). Alternatively, the fitness of ESR females (W) could decline with increasing frequency of the ESR factor. Such an effect would occur if males tended to discriminate against ESR females for mating. As the ESR factor increased in



frequency males would become scarce and mate discrimination would result in decreased ESR female fitness.

Assuming that an all-female producing ESR has complete transmission, it is easy to show that the factor will continue to increase so long as W > x and will decrease when W < x. Prior to invasion of the ESR, the equilibrium autosomal sex ratio was 1/2, and formula (5) shows that the optimal autosomal sex ratio when such a factor is at equilibrium in the population is also 1/2. If we can assume that the formula also applies when frequency of the ESR is dynamic, then a polymorphic equilibrium will be achieved at that p for which W = 1/2.

COEVOLUTION OF ESR AND ASR

When transmission is less than complete, (a < 1) and there are no frequency dependent fitness effects, the ESR achieves an intermediate equilibrium indicated in equation (8). The formula shows that this equilibrium frequency is dependent upon the sex ratio produced by ASR females. Similarly, the optimal x is dependent upon ESR frequency. The outcome of this interaction (for 0 < x < 1) is determined by substituting formula (5) into formula (8) and solving for p*. This provides

$$(p-1)(1/2-x,Wa)=0. \tag{9}$$

Two solutions are possible. Either $Wx_s a = 1/2$ or p = 1. In order for the ESR to initially invade the population, $Wx_s a > 1/2$. Therefore, unless there are frequency dependent effects, the inequality will remain over the range of p. The second solution is p =1, i.e. the ESR is at fixation. It is easy to show that the ESR will increase toward fixation by deriving the conditions for increase of p when x = x*. P increases so long as x > 0 and $x_s Wa > 1/2$. Once x* = 0, the positive feedback ends and the equilibrium conditions for the system are then

$$x^* \to 0 \tag{10}$$

$$p^* - Wa/(1-a+Wa). \tag{11}$$

The result indicates that when ASR is allowed to evolve (i.e. there is genetic variability) in the presence of an ESR with incomplete transmission, there is a positive feedback between ASR and ESR which eventually drives the autosomal sex ratio to 100% sons. At this point ESR achieves polymorphic equilibrium at Wa/ (1- a + Wa). Since there is strong selection upon any ESR to produce 100% daughters (Bull, 1983), the system would tend to evolve to a polymorphic equilibrium with two kinds of females producing single sex broods, (1) ESR all-female producers and (2) ASR all-male producers. An overall female bias in the population will result so long as p > 1/2.

This synergistic interaction between ESR and ASR occurs only if a < 1 and there is genetic variability in the sex ratio sufficient for ASR to go to 100% male. In a species with no such genetic variability, x* remains at 1/2 and the ESR obtains the equilibrium indicated in equation (8). These two situations are contrasted in Fig. 2. When the ASR is not free to evolve, p attains a lower equilibrium frequency

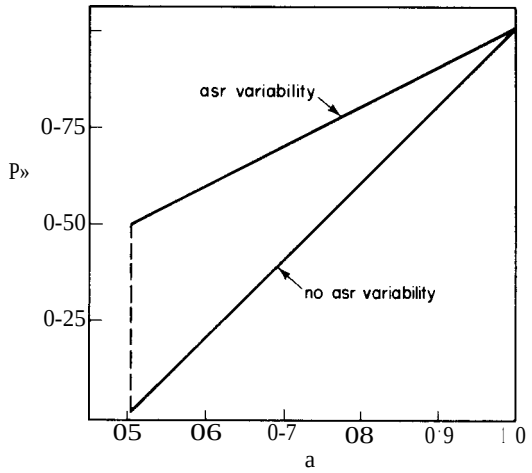
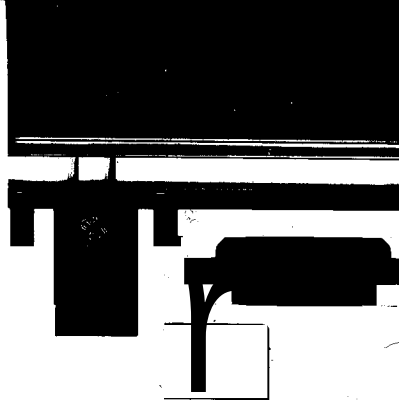


FIG. 2. The equilibrium frequency of an ESR (p*) which produces 100% females of equal fitness to normal females is shown for a species with autosomal sex ratio variability and a species without such variability. In species with ASR variability, a positive feedback occurs which drives x* to 0% daughters and allows the ESR to reach higher equilibrium values.

than when ASR can evolve. One difficulty with the coevolutionary scenario is that the ASR formula (5) assumes that ESR is at equilibrium in the population. The model can reasonably be applied to coevolution if it is assumed that the ESR goes to equilibrium very rapidly relative to ASR evolution. Therefore, at any point in time the ESR is likely to be in equilibrium. However, it is not known whether the same dynamics of sex ratio alleles apply when the ESR is not in equilibrium.

In contrast to an ESR with incomplete transmission, where a synergistic interaction can occur, no such effect occurs when the ESR has complete transmission. An ESR with complete transmission will go to fixation unless a frequency dependent fitness effect results in a polymorphic equilibrium. If a polymorphic equilibrium is achieved, then p* proportion of the females will be all-female producers, but the remaining 1-p* females will continue to produce 1/2 sons. Thus, the selective outcome of interactions between a primary sex ratio distorter and autosomal sex ratio genes is strongly dependent upon (1) transmission frequency of the ESR and (2) whether sufficient genetic variability is present for autosomal sex ratio to evolve.

The model suggests a dramatic breakpoint. With 100% transmission there is no coevolution, with transmission less than 100%, the synergistic reaction results in all-female producers and all-male producers. An obvious question is "What happens when transmission is close to but not at 100% T For example, if transmission were 99-9% would monogeny still evolve? The mathematical result indicates that it would. However, in a real biological system the force of selection favoring a decrease in sex ratio may be so weak that the synergistic reaction would effectively never take place. As mentioned, low sex ratio heritability would further reduce the likelihood of a synergistic reaction. However, the influence of these factors has not been investigated in detail in this study.



MALE LETHAL ESRS

The majority of ESRs so far discovered do not distort the primary sex ratio, but rather cause lethality of male offspring (Williamson & Poulson, 1979; Andreadis & Hall, 1979; Werren *et al.*, 1986). These are maternally inherited and are usually caused by micro-organisms. Such factors have been identified in *Drosophila* species of the willistoni group, *Culex* mosquitoes, certain butterflies and parasitic wasps (Uyenoyama & Feldman, 1978; Clarke *et al.*, 1975; Werren *et al.*, 1986). The effect of a male lethal ESR upon ASR selection was investigated following the same procedures as above.

Assume that the ESR is maternally transmitted at frequency a to female offspring and there is no contagious transmission. Further assume that ESR and normal females produce the same primary sex ratio, but that *"d* - proportion of males from an ESR female's brood die from effects of the factor. The proportion surviving, S, equals 1- *d.* Male lethality may impart a fitness advantage to ESR females. For example, there may be more food for developing ESR females when their male siblings die, thus raising their fitness (W) (Skinner, 1985; Werren *et* al., 1986). All other parameters are defined as before. A simplifying assumption is made that only the ESR females gain a fitness benefit from male death. The characteristic equation for a male lethal distorter is

$$0=(1/2-A)(x,a(1-p)/2F,,-A)(xA/2x-A)-(1-xA)(1-p)/2M \quad (12)$$

where

$$M=PS(1-x)+(1-p)(1-x) \quad (13)$$

$$F,,=px(l-a)+(1-p)x. \quad (14)$$

Following the previous method, equilibrium ASR is

$$x^* = 1/2. \quad (15)$$

A male lethal cytoplasmic factor has no effect upon autosomal selection for the primary sex ratio. No compensation is favored. This result is not too surprising when it is realized that a male lethal factor does not distort the primary sex ratio, but rather alters the secondary sex ratio. Thus the result is consistent with the general finding that differential sexual mortality after the period of parental investment does not affect primary sex ratio selection (Fisher, 1930).

POPULATION DYNAMICS OF MALE LETHAL ESRS

For a male lethal ESR to initially invade a population, Wa > 1 (where W is fitness of "infected" females). In other words, male lethality must effectively increase the fitness times number of ESR females relative to normal females. Since transmission is never greater than 1, this means that the male lethal distorter must effectively increase the fitness of ESR females to exist in a population (W > 1). The dynamics of a male lethal ESR are

$$p'=pWa/[pWa-pa+l) \quad (16)$$

and equilibrium frequency is

$$p^*=(Wa-1)/(Wa-a). \quad (17)$$

Under complete transmission *(a =1),* the male lethal ESR goes to fixation in the absence of frequency dependent effects. As with a primary ESR, a frequency dependent effect on W can lead to a polymorphic equilibrium if W declines with increasing p. For example, if ESR females were less likely to be mated than normals, and the probability decreased with increasing frequency of ESR, then an equilibrium could result. The equilibrium occurs at that p for which W =1.

A polymorphic equilibrium also occurs when transmission in not complete. A synergistic interaction does not occur between a male lethal ESR and ASR genes because p* is not a function of x*, as it is for the primary ESR.

FITNESS EFFECTS OF MALE LETHAL ESRS

In order for the male lethal to invade, male death must impart some fitness advantage to the ESR females. This is in contrast to the primary ESR which need only produce more females to be selectively favored when rare. It has been observed that male lethal distorters cannot persist in a population via cytoplasmic inheritance unless some other effect enhances transmission of the factor (Andreadis & Hall, 1979). Since most male lethal ESR's are caused by micro-organisms, various workers speculate that dead males provide an inocula for the infective spread of the micro-organisms (Andreadis & Hall, 1979). However, there is currently no evidence of natural infective transmission in many systems where male lethal distorters have been discovered. Yet, in these species male lethal ESRS can occur at frequencies ranging from l to 40% (Williamson & Poulson, 1979; Andreadis & Hall, 1979). In certain other species, such as Nasonia vitripennis, infectious transmission of male lethals has been documented (Skinner, 1985).

Given that infective transmission does not occur in any particular system, we are left with the quandary, "How does male lethality enhance fitness of ESR females over non ESR females?". One distinct possibility is that of inbreeding avoidance (Lewis, 1941). Sibling mating is not possible in families with complete male death. It can be shown that even very low levels of inbreeding can favor the initial increase of a complete male lethal ESR with high transmission frequency. Defining I = frequency of sib-mating (inbreeding), D = inbreeding depression or proportional decrease in fitness of female offspring from sib-matings, then W =fitness of ESR females relative to ASR females, defined in terms of daughter production, is

$$W=1/(1-ID). \quad (18)$$

Substituting this equation in (21) for a complete male killer gives

$$p^*=[a+ID-1]/aID. \quad (19)$$

The simplifying assumption is made that only ESR females gain a fitness benefit from male death. Formula (19) shows that a male lethal ESR can be maintained in a population even when inbreeding occurs at low frequency. For the isopod Venezillo

evergladensis, which has cytoplasmic sex ratio distorters, inbreeding depression for full sibmating is approximately *0-22* (Johnson, 1977). Figure *3* shows the frequency of an ESR for a from 0-95 to 0-99 and various inbreeding levels. Several conclusions are possible; (1) even when the occurrence of sib mating inbreeding depression is less than 0-01 it can be sufficient to maintain an ESR in the population, (2) the frequency of p is very sensitive to slight changes in a. This observation is consistent with observations on *Drosophila* "sex ratio" factors which occur at frequencies of 0 to 40% (Williamson & Poulson, 1979).

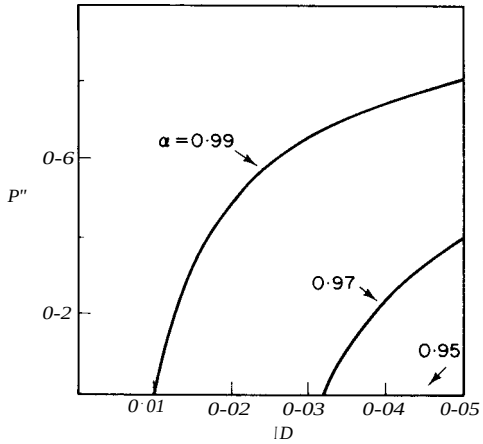


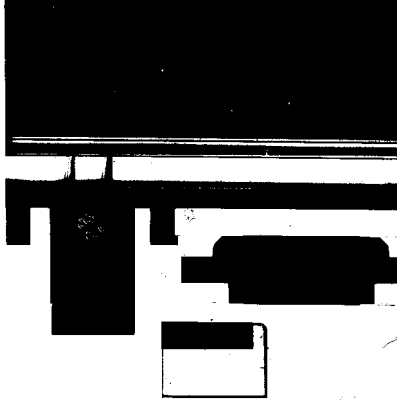
FiG. 3. The relationship is shown between equilibrium frequency of the male-killing ESR and the average cost of inbreeding (I x D). The ESR can occur even with small inbreeding costs, so long as transmission (a) is high. Equilibrium frequency is very sensitive to small changes in transmission frequency of the factor.

It is important to note that male death would not be an adaptation on the part of the insect for inbreeding avoidance. The fitness of individual insects is severely reduced by ESRs causing male death, since half their offspring die. In contrast, the lethality does not negatively affect transmission of the ESR since the ESR is only transmitted by females. Therefore, even a slight advantage of inbreeding avoidance could selectively favor an ESR to induce male lethality.

Haplodiploid Species

The dynamics of ESRs and their coevolution with ASRs may be quite different in haplodiploid species. Haplodiploid species differ in two important respects. Since females develop from fertilized eggs and males from unfertilized eggs (1) transmission of autosomal genes differs from that in diplodiploid species and (2) unmated haplodiploid females can still produce all-male families and therefore they are still fecund and can also alter the primary sex ratio of a population.

The following sections consider the coevolution of ESRs and ASRs in haplodiploid species. First, maternally transmitted ESRs which cause female biased sex ratios



are considered. In addition, paternally transmitted ESRs which cause male biased sex ratios are investigated, since such factors have been discovered in Nasonia vitripennis (Werren et al., 1981; Werren & Assem, 1986). Finally, the haplodiploid models are applied to the sex ratio system of Nasonia vitripennis.

MATERNAL SEX RATIO DISTORTERS

Since males in haplodiploid species transmit chromosomal genes to female progeny of their mates without meiotic reduction, but transmit no chromosomal genes to male offspring, the transmission patterns of ASR alleles are different in these species from that of diplodiploid species. Do these differences affect the equilibrium frequency of maternal ESRs?

Following the definitions used previously, the equilibrium sex ratio is

$$x^*=1/2-px,(1-a)/(i-p). \quad (20)$$

The equation is identical to that for diplodiploid species (5). In addition, equilibrium frequency for the ESR is also identical (8). Therefore, the same synergistic interactions may be expected between ESR and ASR which favors increase of the ESR, causes monogeny, and potentially causes extinction of the population. However, there is a fundamental difference between haplodiploid species and diplodiploid species which may alter this relationship. Although unmated diplodiploid females are infertile, unmated haplodiploid females still produce male offspring from their unfertilized eggs. As a result, the increase of an ESR is less likely to cause a high incidence of infertility due to the absence of males.

THE EFFECT OF UNMATED FEMALES

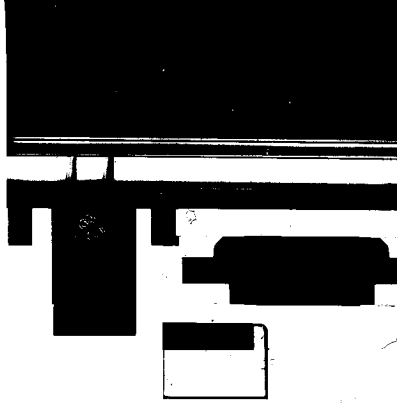
The derivation above can be modified to introduce the influence of unmated haplodiploid females. Assume that the probability of being mated (z) is independent of sex ratio genotype. Then the equilibrium ASR is

$$x^* =1/2z-px,(1- a)/(I - p). \quad (21)$$

A more female-biased sex ratio produced by mated females is favored in response to the presence of unmated females in a population. Conditions for equilibrium of ESR are independent of z and the same as before (8)

$$p^* = [x.Wa -x]/[x_s Wa -x+x,(1- a)]. \quad (22)$$

In a population with no ESR the equilibrium sex ratio is 1/2z. As a result it is more difficult for an ESR to invade a population with unmated females because the conditions for increase of the distorter when rare are Wax, > 1/2z. Once established within a population; however, the ESR will cause a synergistic interaction with ASR genes similar to that observed in populations without unmated females. The ASR will decrease and ESR frequency will increase and the interaction will continue until (1)x*=0 or (2) genetic variability in the sex ratio is exhausted.



Another important difference with haplodiploid species is that even if the ESR goes to fixation, the population will not necessarily be driven to extinction, as it would' in a diplodiploid species. However, there is a potential instability in the system, as pointed out by Hamilton (1967). If all females are mated in a population and they all produce 100% daughters, then those daughters will have no males to mate with and the population will go extinct the next generation. The lack of mates in the daughter generation will cause them to produce 100% males. Such a scenario seems unlikely for large natural populations. Some females will inevitably fail to mate, or will produce offspring prior to mating, and thus males should always be available. For example, certain parasitic wasp species produce only males prior to mating and then only females after mating (Flanders, 1956). It is possible that an ESR factor has become fixed in such species. In species for which an ESR has become fixed, sex ratios will either be cyclic (Hamilton, 1967) or achieve an equilibrium (Werren, manuscript), depending upon the particular relationship between population sex ratio and mating success.

PATERNALLY INHERITED ESRS

An ESR has been discovered in the parasitic wasp, *Nasonia vitripennis,* which is unique from others so far known in that it is paternally transmitted. The psr (paternal sex ratio) factor causes carrier males to produce all-male broods, and is transmitted to fertilized eggs but not to unfertilized eggs of the brood (Werren *et aL,* 1981; Werren & Assem, 1986). Although the mechanism is currently unknown, the factor causes loss of the paternal chromosomes from fertilized eggs, resulting in haploid male offspring which develop into the psr males. Since no systematic examination of haplodiploid species for ESR's has been conducted, it is unknown how common psr-type factors may be.

Following the usual procedures, the characteristic equation for an ASR gene in a population with psr is

$$o = XAA^2/^2x - A^a + [(l - p)(1 - xA) + p(l+a)]A/2M. \quad (23)$$

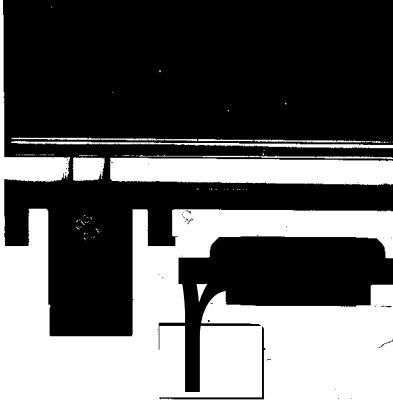
Since the psr is transmitted only to fertilized eggs, transmission frequency is positively increasing with the female sex ratio produced. Defining /3 as the proportion of fertilized eggs which inherit psr, then fix; is the transmission of psr in genotype i and x; is the sex ratio produced by that genotype. The equilibrium ASR is

$$x^* = 1/2(1-p+,Qp). \quad (24)$$

Notice that when ,0 = 1, psr has no effect upon ASR selection. Assuming that psr and normal males have equal fitness, then

$$p^* = [x(/3+1)-1]/x. \quad (25)$$

For a psr factor to initially invade a population, x > 1 / (1 +,6). In other words, a female biased sex ratio is necessary for psr to become established in a panmictic population. Even when transmission is complete (,Q =1), x > 1/2 is necessary for psr establishment. This finding presents a paradox since panmictic populations



normally produce x=1/2 and therefore psr could not invade. Several different circumstances might create the female-biased sex ratios which would then allow a psr factor to become established: (1) the population structure may be demic, thus favoring female-biased sex ratios (Hamilton, 1967), (2) female-biased ESRs may be present in the population, thus enhancing transmission of psr. The second possibility will be considered in the next section.

Finally, it should be noted that when a proportion of the females in a population go unmated, then (assuming a =1)

$$= 1/2z(1 - p+ap) \quad (26)$$

$$p^* = [x(1 +z)+z-2]/[x+z-1]. \quad (27)$$

As a result, it is even more difficult for a psr factor to become established in populations with unmated females. The reason is two-fold. First, psr is not transmitted via unmated females, and second, unmated females produce males which compete with psr males for mates.

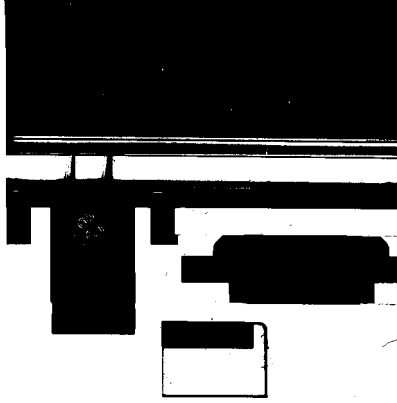
APPLICATION TO THE NASONIA ESR SYSTEM

The parasitic wasp *Nasonia vitripennis* has an assemblage of three known ESRs that occur in natural populations, each distorting the sex ratio in a different manner. Although *Nasonia* has a demic population structure in nature, the panmictic models derived in this paper can be used in a preliminary test to determine how well the models predict (1) ESR frequencies, and (2) autosomal sex ratio produced by *Nasonia vitripennis* under panmictic population situations. First, some background information on the wasp is presented.

Nasonia vitripennis is a small (-~3 mm) chalcidoid wasp which parasitizes the pupae of various fly species (Whiting, 1967). The wasp is typically found in bird nests and around carcasses where it lays its eggs in the pupae of sarcophagid and calliphorid flies (Werren, 1983). From 10 to 40 wasps routinely develop in a single fly puparium. Male wasps have vestigial wings and are incapable of flight: females are winged and disperse after mating in search of hosts. Mating typically occurs on or near the host puparium. Due to the flightlessness of males and patchy distribution of hosts, the wasp has a demic population structure of local mating populations, and *Nasonia vitripennis is* known to alter sex ratio in response to variable deme size (Walker, 1967; Werren 1980, 1983; Skinner, 1983).

Although female-biased sex ratios are produced in smaller demes, approximately 50% females are produced in large demes, consistent with Hamilton's (1967) theory. This is observed both in field populations which contain all three sex ratio distorters and in non-ESR laboratory stocks derived from field populations (Werren, 1983; Skinner, 1983).

The observations are apparently paradoxical since it is generally believed that equilibrium ASR in large denies should be altered from 1/2 females in the presence of ESRs. The previously derived models can be used to address this problem. Two questions will be addressed. First, given the frequencies of ESRs, what equilibrium



ASR is predicted? Second, what is the predicted equilibrium frequencies of the ESRs?

Relevant characteristic of the ESRs are presented below. The data are from studies of Werren *et al.* (1981, 1986), Skinner (1983, 1985), Huger *et al.* (1985) and Werren & Assent (1986).

msr-(1) produces =95% female sex ratio.
(2) cytoplasmically transmitted through the female line.
(3) 100% of females inherit the trait.

sk-(1) causes death of 50-80% males.
(2) maternally transmitted to -~95% of daughters.
(3) can also be infectiously transmitted to other lineages in superparasitized hosts.
(4) the fitness advantage, if any, of male lethality to female offspring is unknown.
(5) causative agent is a Gram-negative bacterium.

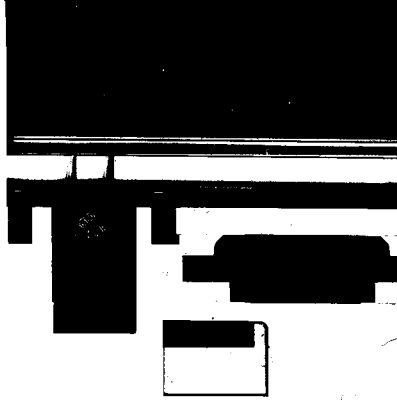
psr-(1) causes all-male broods, with rare occurrence of females.
(2) paternally transmitted to 100% of fertilized eggs; however, these eggs remain haploid.
overrides lethal effect of sk; in sk x psr matings an all-male brood is produced with no lethality.
(4) overrides sex ratio effect of msr; in psr x msr matings all-male broods are produced and around 95% of the males are psr. This result is a consequence of (2).

Table 1 shows the frequencies of ESR, virgin and normal females collected from field populations in Utah by Skinner (1983). Four percent of the females collected in the study were virgins. Assuming that virgins were equally likely to be ESR or normal (if mated), the actual frequencies of ESR and normal females can be

TABLE 1

Based on field data (Skinner, 1983), *the expected and observed frequencies of different ESRs in* Nasonia vitripennis, *and the optimal ASR sex ratios are presented. Adjusted frequencies are based upon the assumption that msr, sk and normal females are equally likely to go unmated. Adjusted frequency of these three types among females, and psr among males is shown. The expected frequency of each factor is based upon a model for* ***panmictic populations,*** *where* ***each factor is considered, given the*** *known frequencies of the other factors. Expected ASR, based upon the known frequencies of each factor, is also shown*

	psr	msr	sk	Normal	Virgin
Observed Frequency	0-07	0-17	0-02	0-70	0-04
Adjusted Frequency	0-07	0·19	0-02	0-72	
Expected Frequency	0-23	1·0	—	0	
Expected ASR	0500	0500	0500		



calculated as shown under "adjusted frequency" in Table 1. Also shown in the table are the expected ASR (x*) in the presence of each ESR. For each of these analyses shown below, z = 0-96.

(1) ASR & msr: Based upon equation (20), x* in the presence of an msr factor at frequency 0- 19 is x* =1/2. In other words, the presence of msr has no influence on autosomal sex ratio selection, because a =1; however, even if a = 0-9, ASR would be only slightly altered to x* = 0479.

(2) ASR & psr: Based upon equation (24), x* in the presence of a psr factor at frequency 0-07 is x* =1/2. Again, the presence of psr has no effect upon asr selection due to complete transmission ((3 =1) of the factor; however, even if 6 = 0-9 ASR is only slightly altered to x* = 0-504.

(3) ASR & sk: Based upon equation (15), x* in the presence of an sk factor at frequency 0-02 can be predicted. However, sk can be infectiously transmitted in superparasitized hosts, which has not been introduced in this model. Ignoring infectious transmission, the equilibrium x* = 0500 for any sk frequency. Again, negligible influence upon autosomal sex ratio occurs.

Although effect of the three ESRs has not been combined into a single equation, since each by itself has such a negligible influence upon ASR selection, it is reasonable to assume that in combination their influence would be insignificant. This is especially likely since the effects of msr and psr are counteracting.

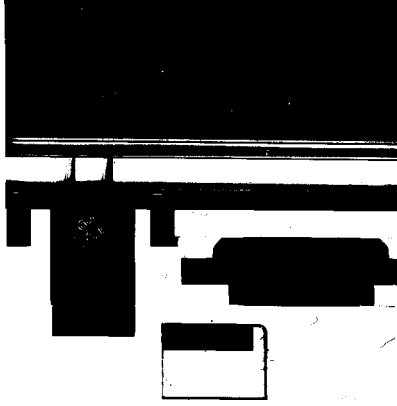
PREDICTING EQUILIBRIUM ESR FREQUENCIES

Previous derivations can now be utilized to determine how well the panmictic models predict equilibrium values of ESRs. Since the applicability of the model to sk is in question and as there are insufficient data for some of the parameters for sk, equilibrium frequencies for psr and msr only will be derived. Assuming the fitness of msr females is approximately 1, and defining q = frequency of psr and p = frequency of msr, then the observed and expected frequencies are

$$g_{obs} = 0\text{-}07 \qquad g_{exp} = 0\text{-}232$$

$$P_{obs} = 0'\,17 \qquad P_{exp} = 1.0$$

The prediction for each factor is derived by setting the other frequencies to those observed (Table 1) and then deriving the expected for the particular factor under study. Unfortunately, great confidence cannot be placed in these predictions because the data are tentative. Nevertheless, the panmictic model appears to be a rather poor predictor of psr and msr frequency. Given the frequency of msr in the population, psr should occur at three times the frequency it does. It is interesting to note that psr could not exist in this population without the presence of msr. The panmictic model also fails with respect to msr. Based upon the simple panmictic model, msr should go to fixation. This has not occurred to Utah populations. It is also interesting to note that if msr did approach fixation, then psr would rapidly increase to fixation (among males) because /3 = 1 in psr x msr matings. This could drive the population to extinction. Whereas an msr factor by itself in a haplodiploid



species is unlikely to drive a population to extinction, in the presence of a psr factor the population is likely to go extinct following fixation of the msr factor among females and the psr factor among males.

Discussion

Several interesting findings arise from the analysis. First, when extrachromosomal sex ratio distorters with high transmission rates exist in a population, *there is no selection for autosomal genes to compensate by distorting sex ratio in the opposite direction.* This finding runs counter to the general view, and is dependent upon high (around 100%) transmission rate for the sex ratio distorters. Since there is very strong selection on ESRs to have high transmission rates, sex ratio compensation is unlikely in most systems. Indeed, an ESR with too low a transmission rate (e.g. 50%) could not exist unless it also imparted a significant fitness advantage to carrier females. A difficulty with the result is that for simple panmictic models, an ESR with complete transmission is expected to go to fixation, in which case ASR selection is irrelevant. Therefore, the finding is most relevant to systems which have some form of frequency dependent selection (e.g. frequency dependent fitness) which prevents the ESR from going to fixation. High transmission rates (between 95-100%) are found for the ESRs of *Drosophila* (Williamson & Poulson, 1979), *Culex mos*quitoes (Andreadis & Hall, 1979) and parasitic wasps (Skinner, 1983; Werren & Assem, 1986) without these factors going to fixation. Whether the models presented here are relevant to the particular biological characteristics of these systems is currently not known. An application of the models to the *Nasonia vitripennis* system suggests that little autosomal sex ratio compensation is expected.

Many ESRs have evolved from symbiotic or pathogenic micro-organisms (Grun, 1976; Uyenoyama & Feldman, 1978). It is possible that during the initial evolution of the microbes to sex ratio distortion that they had significantly lower transmission. If such an ESR had incomplete transmission *and* there was genetic variability in autosomal sex ratio in the host species, then the analysis reveals a second interesting effect. A positive feedback interaction would occur which would push the autosomal sex ratio toward 100% son production, and the female-biasing ESR to fixation. This process would continue until (1) the autosomal sex ratio variability was depleted, (2) a frequency dependent effect intervened or (3) ASR production went to 100% and ESR frequency was limited by its incomplete transmission. In the latter case the population would then be composed of two type females, 100% (ASR) male producers and 100% (ESR) female producers. Bull (1983) described a similar positive feedback leading to monogeny when he considered the coevolution of autosomal and extrachromosomal sex determination factors. Monogenous females have been described in many species such as sciarid flies (Metz, 1938), *Chrysomya* blowflies (Ullerich, 1975) and isopods (Johnson, 1977). As pointed out by Bull (1983), these systems could have resulted from invasion by a cytoplasmic factor, followed by evolution of an autosomal gene conferring resistance.

A basic problem in any ESR system, when transmission is nearly complete, is "What limits the ESR from going to fixation?" In diplodiploid species this would

result in a severe scarcity of males, and could drive the population to extinction. In this respect ESRs are similar to meiotic drive systems, which can also have detrimental population level effects (Hamilton, 1967; Lewontin, 1962).

Several possible mechanism may stabilize these systems over evolutionary time. First, there is autosomal selection for resistance to ESRs (Uyenoyama & Feldman, 1978). In certain circumstances, stable equilibria may exist between resistance genes and extrachromosomal sex ratio distorters. Genetic variability in susceptibility to sex ratio micro-organisms has been found in some *Drosophila* populations (Williamson & Poulson, 1979), but is not known for mosquitoes or parasitic wasps. Analogous models for the interaction between cytoplasmic male sterility in plants and autosomal repressors also show that stable polymorphism can occur (Charlesworth & Ganders, 1979; Charlesworth, 1981; Delanney et *al.*, 1981). To date no models have been developed which simultaneously consider the coevolution of autosomal sex ratio (or sex determination) alleles, cytoplasmic distorters and autosomal repressors. Presumably, rather complicated interactions could result. The outcome in a natural system would be strongly influenced by amount of genetic variability for the different characters.

A second mechanism which may act to limit ESRs is population level selection. The extinction of local demes in which ESRs have gone to fixation could limit increase of ESRs in diplodiploid species. However, such group extinction processes require rather specific rates of extinction and recolonization for an equilibrium to result (Heuch, 1978). Less stringent conditions for equilibria occur if the productivity of local demes is a negative function of the frequency of ESR in the demes (Werren, in preparation).

A third general mechanism potentially limiting increase of ESRs would be frequency dependent changes in one of the parameters regulating frequency of the factor in panmictic populations. For example, either transmission rate (a), ESR sex ratio (x_s) or ESR female fitness (W) could be declining functions of ESR frequency.

Species level selection may also operate on sex ratio distorters. For example, results of this study suggest that diplodiploid species are much more vulnerable to extinction via fixation of an ESR than are haplodiploid species. This result occurs simply because unmated diplodiploid females are unfecund, reducing reproductive potential of the population. In contrast, unmated haplodiploid females are fecund and produce male offspring, thus alleviating a potential shortage of males. Since autosomal sex ratio variability can facilitate the establishment of sex ratio distorters, it is possible that those diplodiploid species and genera with genetic sex ratio variability were historically more subject to extinction. Although difficult to investigate empirically, such species level selection may explain why most diplodiploid species so far studied have little (Curtsinger, 1981) or no autosomal variability in the primary sex ratio (Falconer, 1960; Toro & Charlesworth, 1982; Williams, 1979).

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