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Cytoplasmic genetics under inbreeding and outbreeding

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SUMMARY

Selfish cytoplasmic factors that gain overrepresentation within an individual at a cost to individual fitness can invade a population only if they are biparentally transmitted. It has been hypothesized that the spread of these selfish genomes provides the conditions for the spread of nuclear genes that enforce uniparental inheritance of cytoplasmic genes. However, not all cell fusions result in uniparental inheritance. By using the same logic as the above hypothesis it is shown that, depending on the rate of in- and outbreeding, a variety of transmission patterns of cytoplasmic factors may be expected. Two selective pressures are considered separately. First, selection on nuclear enforcement of uniparental inheritance. If this enforcement is costly then it is not expected where, in a population with biparental inheritance, either selfish cytoplasmic genes cannot spread, or the cost of those that do spread is always below the cost of nuclear suppression. These conditions are met when the rate of inbreeding is adequately high. Biparental inheritance may thus be expected in fusions between closely related cells. This expectation is consistent with data from sexual fusions in inbred fungi and with somatic cell fusions in diverse taxa. Secondly, in an outbred species with enforced uniparental inheritance, a cytoplasmic factor that resists attempts to prevent its transmission may spread. In contrast, in the inbred condition the optimal strategy is for a cytoplasmic factor to allow its relative to be transmitted free of cost. If such resistance is possible then, in contrast to the above expectations, biparental (or paternal) inheritance may be associated with outbreeding, whereas homothallic or selfing species could have relatively strict uniparental transmission. This expectation is consistent with data on cytoplasmic inheritance in higher plants and chlorophyte algae. Thus all four possible states are found: both uni- and biparental inheritance are associated both with in- and outbreeding. We may conclude that those general models that cannot predict this much variation in cytoplasmic genetics are falsified by the data. The broad diversity of resolutions is consistent with the hypothesis that there exists a conflict between nuclear and cytoplasmic genes over the transmission of the latter. However, as the conflict hypothesis is compatible with any outcome, no set of comparative data can directly falsify the model in the absence of extra information. It would hence be useful to be able to predict the conditions under which any of the four states is to be found. Possible relevant parameters, both biological and historical, are discussed. The most robust prediction is that somatic fusion between close relatives, as guaranteed by compatibility at highly polymorphic loci, is expected to provide the conditions for biparental inheritance.

1. INTRODUCTION

When two organisms reside in the same territory, competition between them is expected to be commonplace. Similarly, biparental inheritance of cytoplasmic heritable factors (organelles, symbionts etc.) after the fusion of two cells provides the conditions for competition between these factors (Eberhard 1980). Competition between two organisms in a territory could be expressed indirectly by one tending to monopolize resources (exploitation competition), or by one directly hindering the other (interference competition). So too with cytoplasmic factors. We may consider fast-replicating mitochondrial genomes as one form of exploitative cytoplasmic factor. Such over-replicating mitochondria have been reported in fungi (e.g. petite mutants of yeast) and are suspected in animals (see Rand & Harrison 1989; Wallace 1992). Alternatively, we may envisage 'killer' organelles that specifically eliminate their competitors derived from the other parent. Only circumstantial evidence can be provided for the existence of such organelles (Anderson 1968; Chiang 1976; Eberhard 1980; Koslowsky & Waaland 1987). There exist, however, numerous precedents for such directed spite by cytoplasmic factors, e.g. cytoplasmic incompatibility factors in arthropods (Rousset & Raymond 1991), ciliate cytoplasmic mate killers (Beale & Jurand 1966), and cytoplasmic killer factors in yeast (Somers & Bevan 1969) and in *Ustilago* (Puhalla 1968). Plasmid-encoded colicin factors (Eberhard 1990) constitute a prokaryote analogue of the above.

The spread of a costly ultracompetitive cytoplasmic factor could, it is argued, provide the conditions for the spread of nuclear genes that act to coordinate the inheritance of cytoplasmic factors to prevent this

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competition and hence curtail the spread of the factor (Hoekstra 1987, 1990; Hurst 1990; Hastings 1992*a*; Hurst & Hamilton 1992; Law & Hutson 1992) (for related ideas see also Grun 1976; Cosmides & Tooby 1981; Coleman 1982; Charlesworth 1983). The spreading cytoplasmic factor may be considered a selfish factor (alias selfish genetic element). As the selfish cytoplasmic factor and the nuclear control allele have opposing interests, they are said to be in conflict. I shall hence refer to the above idea as the conflict hypothesis. From this point of view, uniparental inheritance of cytoplasmic factors is interpreted as a means to prevent intra-organism competition between potential antagonists.

The conflict hypothesis is supported by several forms of evidence. First, the hypothesis predicts that uniparental inheritance will be coordinated by the action of nuclear genes. In numerous isogamous organisms nuclear genes do, as predicted, coordinate cytoplasmic inheritance and mediate the process of destruction of organelles of a given type from one of the two parents. Typically the nuclear control genes are tightly linked to the mating type alleles (see, for example, Kawano & Kuroiwa 1989; Armbrust *et al.* 1993) (but see Silliker & Collins 1988). Furthermore, in both mice and flies, rates of paternal inheritance of mitochondria are higher in hybrid than in intra-specific crosses (Kondo *et al.* 1990; Gyllensten *et al.* 1991). This is consistent with the notion that coevolving active control of cytoplasmic inheritance is exercised in anisogamous species as well (Gyllensten *et al.* 1991).

Secondly, the hypothesis predicts that selection could favour alternative means to prevent cytoplasmic mixing. This expectation is borne out by genetical and anatomical analysis of organisms that do not fuse cytoplasms during conjugation. The best-studied example is the ciliate *Paramecium* (Jurand & Selman 1969). Here the nuclear genes that are exchanged are tightly packed, the gap through which they are exchanged between partners is very small, and the nuclear package must constrict to get through this gap. Cytoplasmic genes do not typically move from one partner to the other, and the system is consistent with selection to prevent this movement (Hurst 1990). Similarly, in numerous basidiomycetes, limited hyphal fusion allows nuclear transfer but cytoplasmic transfer is strictly limited (May & Taylor 1988). This too is consistent with selection opposing the mixing of cytoplasmic components (Hurst & Hamilton 1992).

Thirdly, the hypothesis predicts that even if the prevention of cytoplasmic mixing is costly it should none the less be performed (but see below). The stripping of cytoplasm away from the male gamete before fusion with the egg is widely reported (Eberhard 1990; Sears 1980; Whatley 1982) and directly contradicts the usual assumption (see, for example, Parker *et al.* 1972) that selection always acts to maximize zygote size. It is hence reasonable to suppose that there must be some advantage to the elimination of paternally derived cytoplasm.

The above evidence is consistent with any of the hypotheses, of which the conflict hypothesis is one, which propose that uniparental inheritance is the product of selection on nuclear genes (reviewed in Hoekstra 1990). In addition, however, the conflict hypothesis predicts uniparental transmission rather than uniparental inheritance and in the best-studied instance of biparental inheritance in animals this is indeed what is found (Skibinski *et al.* 1994; Zouros *et al.* 1994). In the mussel, *Mytilus*, two different mitochondrial genomes (types F and M) can be detected (Fisher & Skibinski 1990; Hoeh *et al.* 1991). Whereas females usually (if not always) have only the F genome, males harbour both M and F genomes (Fisher & Skibinski 1990). This is the result of a bias in transmission of mitochondrial types dependent upon the sex of the offspring (Skibinski *et al.* 1994; Zouros *et al.* 1994). Sons receive M-type mitochondria from fathers and F-type from their mothers. Daughters in contrast usually receive F-type from their mothers only. Hence, *Mytilus*'s mitochondria are functionally differentiated into two uniparentally transmitted lineages: F mitochondria are transmitted down a maternal lineage, whereas M mitochondria are transmitted down a paternal line. A selfish mitochondrial mutant cannot spread in either lineage.

The above example is possibly not unique. The basidiomycete *Ustilago violacea* mates by the anastomizing, via a conjugation tube, of two equal-sized 'yeast-like' cells of opposite mating type (a1 and a2). The resulting dikaryons can then be induced to bud-off haploid cells. These too are either of type a1 or type a2. Those progeny of mating type a2 contain almost exclusively (94%) the mitochondria from the a2 parent, whereas those of mating type a1 have mitochondria from either parent (Wilch *et al.* 1992). Hence a1 mitochondria are transmitted only to a1 progeny (cf. *Mytilus*'s M genome) and a2 progeny typically receive their mitochondria from a2 parents (cf. F genome). Unlike *Mytilus*, each haploid a1 cell usually contains mitochondria from only one parent, hence the a1 mitochondria will not be transmitted to all a1 grand-progeny. If this is the natural state then the mitochondria in the a2 type would be expected to spread to fixation.

Any hypothesis that predicts the evolution of uniparental transmission (as opposed to inheritance) of cytoplasmic factors is consistent with the *Mytilus* and *Ustilago* data. Other than the conflict hypothesis, only one other hypothesis predicts the evolution of uniparental transmission (Godelle & Reboud 1995*a*). In anisogamous organisms, organelles are considered to be able to specialize at transmission through one sex. Fixation of specialist organelles can result in their uniparental inheritance (Godelle & Reboud 1995*a*). This hypothesis need not evoke a necessity for nuclear control of organelle inheritance. For the anisogamous case this hypothesis is alternative to, but not incompatible with, the conflict hypothesis. The hypothesis does not attempt to explain uniparental inheritance in isogamous organisms.

In short, to the best of this author's knowledge, only the conflict hypothesis is consistent with all of the above data. It does not follow that other explanations are wrong, just that they cannot function as general explanations. Uniparental transmission is, however,

not the only pattern of organelle inheritance (Sears 1980; Whatley 1982; Milligan 1992; Reboud & Zeyl 1994). In higher plants, for instance, some degree of biparental transmission of organelle genomes is comparatively common. Assuming the validity of the conflict hypothesis, is it possible to make predictions about the phylogenetic occurrence of bi- and uniparental inheritance? As the spread of selfish genes is most probable under conditions of outbreeding (see, for example, Hickey & Rose 1988; Hickey 1993), we might expect variation in the inheritance of organelles as a function of inbreeding rate. Below I discuss separately two effects of selection on the inheritance of cytoplasmic genomes and show that they have opposing effects on the expected rate of biparental inheritance as the rate of inbreeding changes (see also Reboud & Zeyl 1994).

2. UNDER INBREEDING NUCLEAR CONTROL, IF COSTLY, MIGHT DECAY: INBREEDERS COULD HAVE BIPARENTAL INHERITANCE

(*a*) *A model*

Biparental inheritance of cytoplasmic organelles can be a stable state if fusions are always between closely related cells (Hurst & Hamilton 1992). Imagine that nuclear genes coordinate to force cytoplasmic genomes to be uniparentally inherited. Imagine also that there is a cost to this process. Let us then suppose that a nuclear mutant arrives (a mutant version of one of the control genes) that relaxes controls on cytoplasmic inheritance and allows biparental inheritance. Will this mutant invade and persist? Consider that it did spread (due to reduction in costs), the important question then, and the one I analyse here, is whether a new selfish cytoplasmic factor would be able to invade? Were invasion possible, then the conditions for the spread of a nuclear mutant that enforces uniparental inheritance could also be provided (Hoekstra 1990; Hastings 1992*a*; Hurst & Hamilton 1992; Law & Hutson 1992).

Under what conditions will the invasion of a selfish cytoplasmic factor be possible? Let us consider a hermaphroditic organism. Let p be the frequency of the selfish cytoplasmic factor and q be the frequency of the competing wild-type cytoplasmic factor. As always, $p+q=1$. The competing cytoplasmic factors can hence be considered as two alleles at a cytoplasmic locus. On entering the zygote the selfish factor attempts to gain overrepresentation (either by killing the competing factor or replicating faster than it). If successful it excludes competitor genomes within the same individual. It is successful a proportion, β, of the time. If unsuccessful, however, it too is completely excluded and only the wild-type factor is transmitted to the following generation. Note that the genome is overrepresented only if $\beta > 0.5$.

Two costs on individual fitness are considered to accompany overrepresentation. First, there is the cost to the act of attempted overrepresentation. This cost is t if selfish factor is received from only one of the two parents. If, however, the factor is received from both parents then the fitness will be lower still. The fitness of such individuals I shall assume to be approximately $(1-t)^2$. These costs are even enforced on those zygotes in which the overrepresentation was not successful. Secondly, possession of the selfish factor has a cost U on adult fitness (as it is homoplasmic if successful this cost is the same for all inheritors of the allele). For fast-replicating cytoplasmic factors it is this latter form of cost that is possibly the more significant, whereas for 'killer' factors both costs may be realistic. If the inbreeding rate is F (in the perfectly inbred condition $F=1$) then the frequency of the selfish cytoplasmic factor in the next generation (p') is given by:

$$p' = \langle (1-U)\{Fp(1-t)^2 + (1-F)[p^2(1-t)^2 + 2pq\beta(1-t)]\}\rangle / \bar{W}, \quad (1)$$

where

$$\bar{W} = F[q + p(1-U)(1-t)^2] + (1-F) \times [p^2(1-U)(1-t)^2 + 2pq(1-t)(1-U\beta) + q^2].$$

Invasion will be possible if $\mathrm{d}p'/\mathrm{d}p > 1$ at $p=0$ is satisfied. This resolves to the condition that

$$F < [1-2(1-t)(1-U)\beta]/\{(1-U) \times [(1-t)^2 - 2\beta(1-t)]\} \quad (2)$$

must be satisfied. A graph of these conditions is given in figure 1. The above solutions are special cases of the general ones derived by Wade (1985) (see also Godelle & Reboud 1995*b*) which in turn are extensions of Price's (1970, 1972) covariance method. For simplicity, inbreeding depression is not considered.

As would be expected (Reboud & Zeyl 1994), as F tends to unity so the conditions for the invasion of selfish organelles become increasingly restrictive: in inbred lineages the costs a selfish cytoplasmic gene imposes are enforced on itself. Consider then all the possible functions relating U, t, and β such that costs increase as β increases. There exist forms of the function such that invasion is possible if outbred but that are inconsistent with invasion in an inbred population (for F near but not equal to unity). Hence, in general, inbred populations are less vulnerable to selfish cytoplasmic factors than are outbred ones.

It is possible to ask about the cases when, at a given inbreeding rate, the trade-off function is such that invasion is possible. Solving $p'=p$ for the above relations reveals equilibrium at $p^*=0$, $p^*=1$ and $p^*=f(U,t,\beta,F)$. If the inequality given in equation (2) is satisfied, the latter term is always less than zero. Hence invasion is always followed by fixation (note, however, that this conclusion is vulnerable to alterations in assumptions about homoplasmic fitness) (cf. figure 3.9 in Wright 1969; see Godelle & Reboud 1995*b*). Once fixed, however, the relative fitness of an individual with the fast-replicating factor will be unity, although the absolute fitness will have declined. Will this provide the conditions for the invasion of a new selfish factor, and will the process carry on reiterating itself?

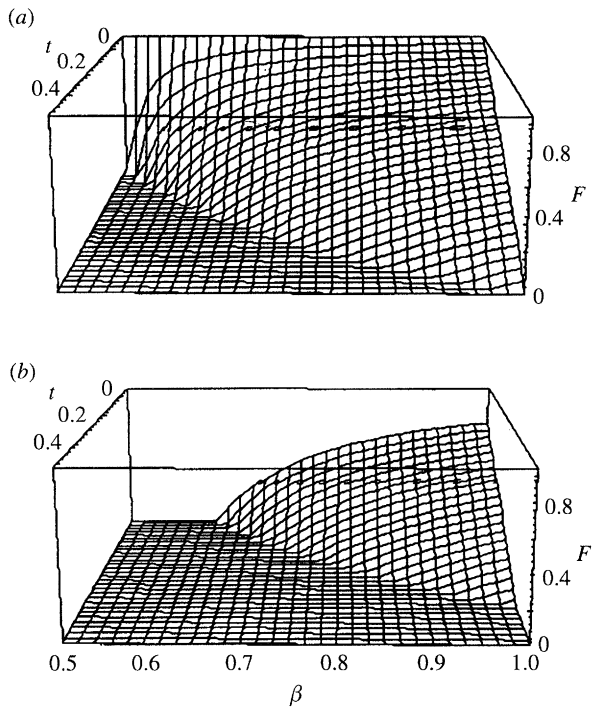

Figure 1. Invasion conditions for a selfish cytoplasmic genome. For invasion the relevant parameters must lie below the surface; β is the rate of transmission through a heteroplasmic host, and t is the cost to such overrepresentation. (*a*) The plot assuming there to be no cost to possession of the selfish gene (aside from a cost due to attempts to force overrepresentation), i.e. $U = 0$. (*b*) This assumes a cost, $U = 0.2$. Note, as F tends to unity (inbreeding rate going up) so the conditions for the invasion of selfish organelles become increasingly difficult. If $U > 0$ is satisfied then some outbreeding is required for invasion.

Consider that the selfish factor is in fact a fast-replicating genome. I shall hence ignore the cost t and consider only the relation between U and β. To understand whether a novel overreplicating genome can always invade we must know the form of the curve relating these two parameters as a function of the absolute replication rate. This will be found by consideration of two functions. First, that relating the absolute fitness of an individual (W_a) with a given cytoplasmic genome, with the absolute replication rate (R) of that cytoplasmic genome (above the mininum necessary replication rate). Secondly, that relating the transmission advantage β to the difference in replication rate between the invading factor (R_2) and the resident factor (R_1). The difference in replication rate is hence $\Delta R = R_2 - R_1$. The transmission advantage may be simply a function of the absolute difference in replication rate or some function of the relative difference, $\Delta R/R_1$. If the organelle genome that is presently at fixation confers absolute fitness W_{a1} on its host, and the invading genome confers fitness W_{a2}, then the cost in relative fitness suffered by the invading factor will be given by:

$$U = (W_{a1} - W_{a2})/W_{a1}. \quad (3)$$

Invasion of a faster replicating genome will not be possible if the above cost is greater than or equal to that consistent with invasion (from equation (2)). If invasion was initially possible (when $R_1 = 0$, $W_{a1} = 1$), then there must have existed a value of β and associated U consistent with invasion. Consider now a new mutant with the same value of β as that which initially invaded. For this given value of β, the cost may be less than, equal to or greater than that initially suffered. If the first two conditions are always true then recurrent invasions are always possible (but absolute fitness cannot reach zero). This form of the curve, however, is very unlikely. More realistically, the cost per unit transmission advantage would increase as the absolute replication rate tends to infinity. If this is so there will exist a maximum rate of replication consistent with invasion. This conclusion is not affected by considering β as a variable. The maximum value of U consistent with invasion is negatively correlated with F. Inbred populations that are susceptible to invasion by a selfish cytoplasmic factor will thus tend to have a smaller decline in absolute fitness (compared with $W_{a1} = 1$), due to recurrent invasions of ever faster replicators, than would outbred populations. For a particular example of the above in which β is a function of the absolute difference in replication rate, see Appendix 1. For further treatment of the above problem, see Godelle & Reboud (1995*a*, *b*).

All possible relations between β, U and R will be composites of the above forms: costs per unit transmission advantage can either increase, decrease or stay the same. If the direction of costs is changing, however, behaviour of the system is difficult to analyse unless we assume ΔR to always be infinitely small. This assumption, however, may provide unrealistic results, even if the differential is always in the same direction (see Appendix 1).

In those cases in which invasion of a selfish factor is possible, collapse can be avoided through the spread of a nuclear allele enforcing uniparental inheritance (Hoekstra 1987, 1990; Hurst 1990; Hastings 1992*a*; Hurst & Hamilton 1992; Law & Hutson 1992). If the only costs considered are those of possession (U) then the selfish gene must be spreading for the nuclear modifier to invade (Hastings 1992*a*). If, however, the zygotes that are homoplasmic for the selfish factor have lower fitness than heteroplasmic ones (as considered for the cost of overrepresentation, t), then fixation of the selfish gene also allows the spread of the modifier (Hurst & Hamilton 1992). However, if costly, such a nuclear allele can only spread if the cost immediately associated with not forcing uniparental inheritance is higher than the cost associated with suppression (assuming an absence of group selection and multiple selfish factors in the same population). In inbred populations this might be the case as the maximum decrement in fitness which allows invasion is relatively small. In contrast, in the outbred condition relatively costly selfish genes can spread, and hence the spread of a costly suppressor is more likely.

(*b*) *The data*

A variety of inbred species seem to have relaxed controls on organelle inheritance. Yeasts, for instance, are almost certainly inbred (extrapolated from the fact

of mating type switching) and have biparental inheritance of mitochondrial genomes (Dujon 1981). This biparental inheritance is, however, associated with relatively rapid sequestration of mitochondria into homoplasmic lineages. Some of this homoplasmization may be random, but some may also be enforced (e.g. those of the first buds from the mother cell) (for discussion see Hurst & Hamilton (1992)).

Somatic or vegetative fusion of cells is reported in a variety of taxa. These fusions are typically between extremely closely related cells, and there is no evidence of nuclear control of cytoplasmic factors. Controls preventing fusion between unrelated cells do, however, exist. It is probably the existence of these controls that ensures that cytoplasmic inheritance need not be regulated if fusion is allowed (see discussion). Genetic evidence demonstrates biparental transmission after somatic cell fusion in ascomycete fungi (see, for example, Jinks 1964; Gunatilleke *et al.* 1975). Cytological evidence suggests biparental transmission of organelles in somatic cell fusion in myxomycetes (M. Carlile, personal communication, reported in Hurst & Hamilton (1992)). Cytological evidence also demonstrates an absence of plastid degradation in naturally occurring intra-strain fusion in *Griffithsia* (red algae) (Goff & Coleman 1990). Perhaps significantly, artificial fusions between somatic cells of *Griffithsia* result in unilateral chloroplast destruction in between-strain fusions, although this is not witnessed in within-strain artificial fusions (see Koslowsky & Waaland 1984, 1987; Goff & Coleman 1990). It is, however, unclear as to whether the natural fusions in *Griffithsia* are of somatic or sexual function.

3. UNDER INBREEDING, CYTOPLASMIC RESISTANCE TO ELIMINATION, IF COSTLY, COULD DECAY: INBREEDERS COULD HAVE UNIPARENTAL INHERITANCE

(*a*) *A model*

Let us consider an outbred species with gametic fusion and with some means to bias organelle inheritance towards those organelles derived from one of the two sexes. The bias I assume to be enforced by nuclear genes, but the cytoplasmic factors in the sex that transmits its cytoplasmic genes have more or less the same set of interests. Typically, the transmitting sex is the mother and the non-transmitting sex the father. Here I shall refer to mother and father as a shorthand for transmitter and non-transmitter, respectively. The theory is equally valid, however, for isogamous organisms with imposed uniparental inheritance and for those species with paternal inheritance. We might imagine that, because of this control, the nuclear genes prevent transmission of the organelles derived from sperm and hence maternal inheritance is imposed. But what if a novel cytoplasmic mutant were to arrive that could resist these attempts to prevent its transmission? Will this invade?

Consider a hermaphroditic organism and that, at a frequency F, a gamete from such an organism will mate with another gamete from the same organism. Consider also that if a cytoplasmic factor resists destruction when passed into a zygote through sperm, then at a frequency α of these occasions it will take over the zygote. At a frequeny $1-\alpha$ it will be fully eliminated. Similarly then, at a frequency $1-\alpha$ the competing cytoplasmic factor will be transmitted if it is inherited from a female and the resisting type is inherited from the male. All individuals hence produce gametes containing only one of the two competing cytoplasmic factors. Although this is not fully realistic, it is to first approximation adequate.

Let us assume that the mutant cytoplasmic factor 'knows' that it is in a male or a female gamete and attempts to prevent its destruction only if being transmitted through a male gamete. There exist two cytoplasmic factors in the population. One, at a frequency $1-p$, resists destruction and receives transmission at a rate α_1 when transmitted from a male. The other, at frequency p, resists destruction and receives transmission when coming in from males at a rate α_2 (greater than α_1) but at a cost. As before, two costs on individual fitness will be considered. First, a cost due to attempted resistance. Even if an organelle is not transmitted but attempts to resist, the host none the less suffers this cost s. Second, there is a cost u, to the possession of the resisting allele. This cost is suffered if the adult contains the more resistant factor. As individuals are assumed to be approximately homoplasmic for most of their lifetime, it is assumed that this cost is independent of the initial zygotic organelle constituents. The frequency of the factor 2 in the next generation (p') will be given by:

$$p' = (1-u)\langle Fp(1-s) + (1-F)\{p^2(1-s) + pq[(1-\alpha_1)+\alpha_2(1-s)]\}\rangle/\bar{W}), \quad (4)$$

where

$$\bar{W} = (1-u)\langle Fp(1-s) + (1-F)\{p^2(1-s) + pq[(1-\alpha_1)+\alpha_2(1-s)\}\rangle + \langle Fq + (1-F)\{q^2 + pq[(1-\alpha_2)(1-s)+\alpha_1]\}\rangle.$$

Invasion will be possible if $dp'/dp > 1$ at $p = 0$ is satisfied. This resolves to

$$F < \{1+(1-u)[\alpha_1-\alpha_2(1-s)-1]\}/\{(1-u) \times [\alpha_1-\alpha_2(1-s)-s]\}. \quad (5)$$

For the first possible invasion event, $\alpha_1 = 0$, hence invasion is possible if

$$F < \{1-(1-u)[(1-s)\alpha_2+1]\}/(1-u)[(s-1)\alpha_2-s]$$

is true. The plot of these conditions is provided in figure 2. As might be expected, as the level of inbreeding tends to unity so the invasion conditions become increasingly restrictive. It can be noted that, in the above model, invasion conditions are quite relaxed in the outbred condition. If resistance to destruction is conditional upon being in the non-transmitting sex, in the outbred condition any resisting organelle has little to lose. In contrast, in the inbred condition a resisting cytoplasm gains nothing as the transmitted factor is its clonal relative. Hence, as the level of inbreeding

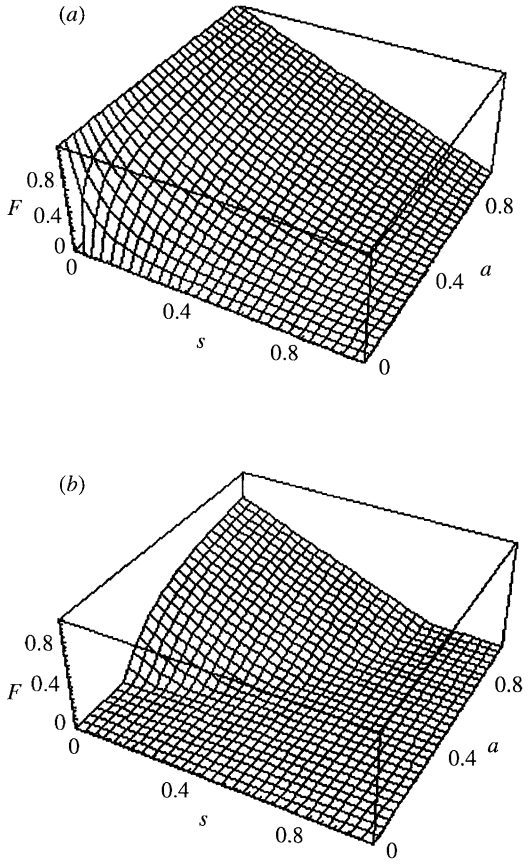

Figure 2. Invasion conditions for a cytoplasmic mutant that resists destruction when it finds itself in the gamete whose organelles are due for destruction. For invasion, points must lie below the sheet. Here α is the rate of transmission of the resisting organelle, and s is the cost suffered. (*a*) The condition in which the cost of possessing the resisting cytoplasm is zero ($u = 0$); (*b*) $u = 0.2$ is assumed. Limiting conditions for invasion are that $\alpha > 0$, $u < 0.5$, $s < 1$, $F < 1$ must all be true.

increases, selection may favour less costly resistance and hence uniparental inheritance (Reboud & Zeyl 1994). What is unknown, however, is what realistic values of the three parameters, u, s and α might be. It could, for instance, be the case that, depending upon the cost of biparental inheritance, nuclear suppression may be very tightly enforced in which case, even in the outbred condition, invasion of a resisting cytoplasmic factor may not be possible.

As before, however, it is possible to ask not only about the conditions preventing invasion but also the fate of systems in which invasion is initially possible. Solving equation 4 for $p' = p$ reveals that invasion is followed by fixation ($p^* = 0$, 1, or is less than 0 (when invasion conditions are satisfied)). Will fixation of a resisting factor in turn pave the way for a new, more resistant factor reducing absolute fitness still further? The answer to the latter question is dependent upon the form of the relation between cost per unit transmission advantage and α_1. If the costs per unit transmission advantage either stay the same or decrease as α_1 increases, then we might expect that, if invasion is initially possible at a given value of F, α will go to its maximum value of 1 (i.e. paternal inheritance). If costs go up as α_1 increases then stable biparental transmission can be possible if invasion is ever possible. The equilibrium can lie at $\alpha = 1$. The equilibrium solutions will lie closer to $\alpha = 0$ as F tends to unity. For equilibrium conditions in which $0 < \alpha < 1$, although one genotype has gone to fixation, biparental inheritance will still be found.

(*b*) *The data*

The above models predict that cytoplasmic resistance to imposed destruction should be increased on outbreeding. Data from higher plants and algae are consistent with this expectation. Selfing angiosperms, for instance, typically have most of their organelles transmitted from their mother only, whereas outbred ones are more likely to have significant levels of biparental inheritance (Reboud & Zeyl 1994). The same difference in organelle inheritance has been observed in comparison between inbred and outbred *Chlamydomonas* species (Van Winkle-Swift *et al.* 1994): in homothallic species uniparental inheritance seems to be very strict (i.e. very little leakage if any), whereas in heterothallic (hence outbred) species (e.g. *C. reinhardtii*) up to about 5–10% leakage is reported. Similarly, cytological data from homothallic (inbred) species of *Spirogyra* show that chloroplast inheritance is uniparental (see Margulis *et al.* 1990). Although the comparison within the algae is based on few data points, it does suggest that this pattern may be independent of gamete size asymmetry.

The models also predict that paternal inheritance of cytoplasmic factors may be associated with a history of outbreeding ($\alpha \to 1$ as $F \to 0$). It may then be significant that: (i) the two genera of angiosperm with paternal inheritance of plastids are outbred ones (*Daucus* and *Medicago*; see table 3 in Reboud & Zeyl (1994)); and (ii) in gymnosperms, which are usually assumed to be some of the most outbred of all species, paternal inheritance of plastids is reported in at least eight species, whereas significant biparental inheritance is found in a further three, and maternal inheritance has yet to be reported is any species (table 4 in Reboud & Zeyl (1994)). Further support comes from the finding that in bananas, which are expected to be outbred (see Itino *et al.* 1991), mitochondria are paternally inherited (Faure *et al.* 1994) (but note also that the chloroplasts are maternally derived). Alternative explanations may, of course, be provided for these findings. In those species (such as angiosperms and gymnosperms) in which differential investment in (and/or abortion of) progeny is possible, paternal inheritance may be favoured as it allows maternal selection between embryos differing in their cytoplasmic fitness. A higher variance in plastid, rather than mitochondrial, derived fitness components could explain why the former are more often paternally transmitted than the latter.

Above I assumed that cytoplasmic factors could 'know' whether they were being maternally or paternally transmitted. This need not be so. If cytoplasmic factors could not express sex-specific conditionality then conditions for invasion are more restrictive. Invasion conditions for the first possible such resisting factor (i.e. when $\alpha_1 = 0$) can be described

Table 1. *Possible conflict-based explanations of patterns of uniparental and biparental inheritance of cytoplasmic genes as a function of the rate of in- or outbreeding and groups that fit each state*

(This table is not exhaustive. The assignment of taxa to a given box is not supposed to imply that the explanation provided for that state need apply to the group concerned.)

		inbreeding	outbreeding
Uniparental inheritance (including low-level leakage)		Cytoplasmic resistance to nuclear enforcement of uniparental inheritance selectively unfavourable	Nuclear control of selfish organelle inheritance is absolute
	examples	Plastids and mitochondria in selfing angiosperms[a] and in homothallic green algae[b]	Probably mitochondria in most outbred animals[c] and numerous outbred angiosperms[a]
Biparental inheritance		Absence of nuclear control of cytoplasmic inheritance (selfish organelles cannot spread)	Organelles resist elimination
	examples	Mitochondria in yeast[d], mitochondria in somatic cell fusions in myxomycetes[e] and ascomycetes[f], plastids in cell fusions in rhodophytes[g]	Plastids and mitochondria in some outbreeding angiosperms and gymnosperms[a], plastids in heterothallic green algae[b]

References.
[a] Reboud & Zeyl (1994).
[b] VanWinkle-Swift *et al.* (1994).
[c] Avise & Lansman (1983).
[d] Dujon (1981).
[e] M. Carlile in Hurst & Hamilton (1992).
[f] Jinks (1964).
[g] Goff & Coleman (1990).

by the plot given in figure 1 if $2\beta = 1 + \alpha_2$, $t = s$ and $U = u$. As mitochondrial genomes in plants can express sex-specific conditionality (e.g. in the form of cytoplasmic male sterility), it is to be expected that they could just as well have resistance to destruction expressed only when transmitted through pollen. Similarly, the chloroplast genes of *Chlamydomonas reinhardtii* are methylated depending upon whether they are derived from + or − type (for references see Matagne (1987)). Animal mitochondria in contrast never distort sex ratios (Hurst 1993) and, to the best of this author's knowledge, do not show differential methylation and hence may not have sex-specific conditionality. One reason for this (Hurst 1993) may be that the genome of animal mitochondria is typically an order of magnitude smaller than that of plant mitochondria. It may hence be too small to contain the necessary instructions for conditional activity. This could in principle go some way to explaining why plant mitochondria seem to be biparentally transmitted much more often than animal mitochondria. This fact, however, could equally well be explained by a variety of other factors (see discussion), not least a vast difference in mutation rate.

4. DISCUSSION

The above models suggest that two antagonistic forces could determine the rate of biparental inheritance of cytoplasmic factors (see also Reboud & Zeyl 1994). If populations are affected by resisting cytoplasmic genes then the above analysis suggests that inbred organisms might have uniparental inheritance (cytoplasmic genes are under selection not to resist destruction in inbred populations). Outbreeding conditions can select for organalles that resist suppression and hence force biparental inheritance (although at the extreme they may revert to uniparental inheritance, albeit paternal inheritance). In contrast, if nuclear suppression is costly then we might also predict that selection could favour the absence of controls over cytoplasmic inheritance in inbred populations. This logic would suggest that inbred organisms could have biparental inheritance whereas outbred ones tend to have uniparental inheritance. The antagonism of these two forces (cytoplasmic resistance and nuclear suppression) is symptomatic of a conflict of interest between cytoplasmic genes and nuclear genes in the outbred condition.

Empirical evidence is compatible with both of the antagonistic forces (see table 1 and above). Fusions between closely related cells may result in either relatively strict uniparental or unbiased biparental inheritance. Fusions between distantly related cells may give uniparental inheritance or some degree of biparental transmission. Any model not competent to explain the above diversity of data cannot be a generally valid model. Those models that argue, for instance, that uniparental inheritance is a means to prevent recombination between organelle genomes (Sager 1977) would predict that outbreeders would always have higher rates of uniparental inheritance than inbreeders. Other models might prefer that uniparental inheritance is a side consequence of other factors such as anisogamy (Birky 1983; Godelle & Reboud 1995*a*). Why then do yeast and *Chlamydomonas*, both isogamous, have different patterns of inheritance, and why is there biparental inheritance in *Mytilus*?

VanWinkle-Swift and colleagues (see VanWinkle-Swift 1978; Sears & VanWinkle-Swift 1994; VanWinkle-Swift *et al.* 1994) have suggested that uniparental inheritance might be an adaptation to allow the recycling of organelle DNA following its zygotic digestion. Biparental inheritance is hence expected in those organisms with a relative abundance of nutrients. That yeast have biparental inheritance but *Chlamydomonas* has uniparental inheritance may be consistent with the model. Yeast do not encyst after zygote formation (and are hence liable to the same nutrient constraints as before zygote formation). *Chlamydomonas*, in contrast, encysts immediately after zygote formation and hence may have reduced nutrient input and so may not be able to sustain a high titre of organellar DNA. Variation within and between *Chlamydomonas* species is predicted to vary as a function of nutrient status. The model, however, is relevant only to eukaryotes that have coupled sex with sporulation and dormancy (Sears & VanWinkle-Swift 1994) and cannot explain uniparental inheritance in those cases where organelles are excluded rather than digested. Furthermore, the model is not necessarily one of uniparental inheritance as the recycling of DNA from both parents could in principle be equally efficient. However, one can postulate possible problems in coordination of such destruction (VanWinkle-Swift & Aubert 1983). If so, unilateral destruction may be the most efficient means of coordination. This model is for uniparental inheritance, not transmission, and hence fails to explain the *Mytilus* and *Ustilago* data.

The conflict model is consistent with all the available data. One might imagine that this consistency constitutes strong evidence in support of the conflict-based models. This is not so, however, for any finding could be incorporated (see table 1). If comparative tests are to be used to falsify the conflict model, it is necessary to be able to predict under which circumstance one resolution rather than the other might be found. Making these predictions is not simple.

Consider, for instance, the fact that mammalian mitochondria have a high mutation rate, a very small genome, and free replication in the cell cycle. As a consequence of the small genome size (every base pair is needed), we might expect that any deletion resulting in fast replication would be very disadvantageous ($U \rightarrow 1$) and hence the necessary replication advantage may be impossible to achieve (if $U > 0.5$, β must be greater than 1, which it cannot be). Yeast's petite mutants are probably of this nature. These indeed are only described because yeast can respire anaerobically. Were this not so, selection at the cellular level would prevent the spread of the factors through the population. So perhaps animals should not have a problem with selfish organelles, as between-cell selection within a germ line, or between germ-line (individual) selection, would prevent their spread even under outbreeding. We might expect an absence of nuclear controls. However, by virtue of the free replication in the cell cycle, β might also be high (this is only relevant for $U < 0.5$). If this is so we might expect strict nuclear controls on uniparental inheritance as the selfish factors that could invade would also be highly deleterious. Unless we knew more precisely the relation between cost and overreplication, we cannot *a priori* predict the host's response.

Similar problems beset attempts to predict the rate of biparental inheritance as a function of any input bias. A role for an input bias in determining uniparental inheritance has often been noted (see, for example, Cosmides & Tooby 1981; Birky 1983; Godelle & Reboud 1995*a*). Anisogamy provides such a bias. Consider then a species with an output bias of organelle genomes into a zygote and nuclear genes that attempt to reinforce this bias. If a bias exists then the marginal gains of a resisting organelle could be expected to be less than the gains received in the absence of such a bias. Perhaps then, we might expect that outbred isogamous organisms are more likely to have biparental inheritance of cytoplasmic organelles than comparable anisogamous ones. However, the converse argument can also be made. If the advantage to organelles in resisting elimination is low in anisogamous species then the marginal costs to nuclear genes of reducing control of organelle inheritance might also be low (so promoting leakage). Outbred isogamous organisms might hence be expected to have particularly strong controls on cytoplasmic inheritance. It is in principle difficult to predict which force (cytoplasmic resistance or nuclear suppression) is the stronger in any given situation.

The same problem confounds any variable that can predict the vulnerability to selfish cytoplasmic factors. Hastings (1992*a*, *b*), for instance, notes that the costs to biparental inheritance vary as a function of the number of asexual divisions between sexual cell fusions. The greater the number of asexual divisions between sexual fusions, the more heteroplasmic cells might randomly segregate out their cytoplasmic factors producing homoplasmic cells, and hence the more opportunity selection has to act on the deleterious, individual-level, fitness effects (this assumes that the initial divisions of a zygote are not so rapid as always to force homoplasmy and prevent any overreplication advantage (see Hurst 1990)). Thus, for a given rate of inbreeding, those populations that have few divisions between sexual cell fusions should be more vulnerable to selfish cytoplasmic factors. We do not, however, know whether a greater vulnerability means that nuclear suppression will be all the stronger or biparental inheritance will be all the more likely.

This unpredictability may be confounded by historical factors. It was assumed, for instance, that decay of nuclear suppression would be advantageous if selfish organelles could not re-invade. This may not be true. If coadaptation has occurred between these controls and other functions then decay may, in the short-term, be costly. If so we need not expect biparental inheritance on the switch towards inbreeding. Equally, the manner of response to selfish organelles may determine the ability for this to be relaxed on inbreeding. Tunicate sperm, for instance, is often forced by the ovule's micropyle to shed its cytoplasm. Maintenance of such a structure could prevent biparental inheritance on the switch to inbreeding.

Even if we knew all the forces, interpretation of data

may not be trivial. The balance of forces may be so delicate that slight alterations in inbreeding rate may affect the direction of evolution. Moderately inbred organisms, for instance, might be selected to maintain uniparental inheritance but heavily inbred ones might not. Levels of inbreeding could be high enough within populations to select against organelle resistance to destruction, whilst at the same time favouring the spread of the occasional selfish cytoplasmic factor were nuclear controls absent. Under these circumstances uniparental inheritance should be forced (nuclear decay should not occur), whilst decay of cytoplasmic resistance could occur. This would require that the costs per unit benefit suffered to resist destruction should be greater than the costs per unit benefit to enable spread in a population without nuclear controls. This in principle seems reasonable but would be very hard to test.

In one condition, however, most of the above problems do not apply. Somatic cell fusion, as described in myxomycetes, ascomycetes and possibly rhodophytes (see above), and also between muscle cells within developing animals, is usually restricted to cells that are very closely related. This may either be because the nearest neighbour is always a relative (as with muscle cells) or because fusion can only occur if cells are identical at highly polymorphic compatibility loci, as shown for ascomycetes and myxomycetes. To the best of my knowledge, this evidence is not available for *Griffithsia* (red alga), and the cell fusion discussed above may be a sexual process comparable to heterokaryon formation in basidiomycetes. High polymorphism is sufficient to guarantee that fusions usually only occur between extremely closely related individuals. In this sense these somatic compatability loci are true kin recognition systems (*sensu* Grafen 1990), and probably evolved so as to prevent parasitism by less related cells (Buss 1982; Cramptom & Hurst 1994). In a compatible fusion there is no history of enforcement of nuclear control of cytoplasmic inheritance, and there is only a very low probability that the fusing cells are not very closely related. In these systems then, when fusion is between compatible cells (rather than aggressive invasion (see, for example, Lane & Carlile 1979)), nuclear controls on cytoplasmic inheritance should be absent and biparental inheritance could be stably maintained. All instances in which this has been analysed are consistent with the expectation.

Thus if cell fusions are classified as those between closely related cells and those not between closely related cells, and if cytoplasmic genetics is described either as being uni- or biparental, four possible states (see table 1) could exist. All four states do exist. The notion that a conflict exists between cytoplasmic genes and nuclear genes over the rate of biparental transmission is consistent with this diversity of outcomes. To the best of my knowledge, the conflict hypothesis is unique in this regard. Those alternative models that cannot account for this diversity of states must be wrong as general explanations of cytoplasmic inheritance. However, the conflict hypothesis is poor at allowing prediction of which of the four possible states might exist in any given circumstance, the one exception to this inability being in the circumstance of somatic cell fusions mediated by highly polymorphic compatibility loci (or any other guarantee of very close relatedness between fusing partners) in which biparental inheritance is predicted and found. The difficulty in predicting is in large part because the two responses to a change in inbreeding rate that one might expect act in opposing directions, the parameters involved are hard to resolve, and historical factors may play a role. In brief, unless we know the power relations between nuclear genes and cytoplasmic genes, in most circumstances the outcome is difficult to predict.

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REFERENCES

Anderson, W. A. 1968 Structure and fate of the paternal mitochondrion during early embryogenesis of *Paracentrotus lividus*. *J. Ultrastruct. Res.* **24**, 311–321.

Armbrust, E. V., Ferris, P. J. & Goodenough, U. W. 1993 A mating type-linked gene cluster expressed in *Chlamydomonas* zygotes participates in the uniparental inheritance of the chloroplast genome. *Cell* **74**, 801–811.

Avise, J. C. & Lansman, R. A. 1983 Polymorphisms of mitochondrial DNA in populations of higher animals. In *Evolution of genes and proteins* (ed. M. Nei & R. K. Koehn), pp. 147–164. Sunderland, Massachusetts: Sinauer Associates.

Beale, G. H. & Jurand, A. 1966 Three different types of mate-killer (mu) particle in *Paramecium aurelia* (syngen 1). *J. Cell Sci.* **1**, 31–34.

Birky, C. W. J. 1983 Relaxed cellular controls on organelle heredity. *Science, Wash.* **222**, 468–475.

Buss, L. W. 1982 Somatic cell parasitism and the evolution of somatic tissue compatibility. *Proc. natn. Acad. Sci. U.S.A.* **79**, 5337–5341.

Charlesworth, B. 1983 Mating types and uniparental transmission of chloroplast genes. *Nature, Lond.* **304**, 211.

Chiang, K. S. 1976 On the search for a molecular mechanism of cytoplasmic inheritance. Past controversy, present progress and future outlook. In *Genetics and biogenesis of chloroplasts and mitochondria* (ed. L. Bucher, W. Neupert, W. Sebald & S. Werner), pp. 305–312. Amsterdam: North Holland.

Coleman, A. W. 1982 Sex is dangerous in a world of potential symbionts or the basis of selection for uniparental inheritance. *J. theor. Biol.* **97**, 367–369.

Cosmides, L. M. & Tooby, J. 1981 Cytoplasmic inheritance and intragenomic conflict. *J. theor. Biol.* **89**, 83–129.

Crampton, W. G. R. & Hurst, L. D. 1994 True kin recognition, in the form of somatic incompatibility, has multiple independent origins. *Anim. Behav.* **47**, 230–234.

Dujon, B. 1981 Mitochondrial genetics and functions. In *The molecular biology of the yeast saccaromyces* (ed. J. N. Strathern, E. W. Jones & J. R. Broach), pp. 505–635. New York: Cold Spring Harbor Laboratory Press.

Eberhard, W. G. 1980 Evolutionary consequences of intracellular organelle competition. *Q. Rev. Biol.* **55**, 231–249.

Eberhard, W. G. 1990 Evolution in bacterial plasmids and levels of selection. *Q. Rev. Biol.* **65**, 3–22.

Faure, S., Noyer, J.-L., Carreel, F., Horry, J. P., Bakry, F. &

Lanaud, C. 1994 Maternal inheritance of chloroplast genome and paternal inheritance of mitochondrial genome in bananas (*Musa acuminata*). *Curr. Genet.* **25**, 265–269.

Fisher, C. & Skibinski, D. O. F. 1990 Sex biased mitochondrial DNA heteroplasmy in the marine mussel. *Mytilus*. *Proc. R. Soc. Lond.* B **242**, 149–156.

Godelle, B. & Reboud, X. 1995*a* Why are organelles uniparentally inherited? *Proc. R. Soc. Lond.* B. **259**. (In the press.)

Godelle, B. & Reboud, X. 1995*b* The evolutionary dynamics of selfish replicators: cyclical evolution or synthetic fitness. *J. theor. Biol.* (Submitted.)

Goff, L. J. & Coleman, A. W. 1990 DNA: Microspectrofluorometric studies. In *Biology of the red algae* (ed. K. M. Cole & R. G. Sheath), pp. 43–71. Cambridge University Press.

Grafen, A. 1990 Do animals really recognise kin? *Anim. Behav.* **39**, 42–54.

Grun, P. 1976 *Cytoplasmic genetics and evolution*. New York: Columbia University Press.

Gunatilleke, I. A. U. N., Scazzocchio, C. & Arst, H. N. Jr 1975 Cytoplasmic and nuclear mutations to chloramphenicol resistance in *Aspergillus nidulans*. *Molec. gen. Genet.* **137**, 269–276.

Gyllensten, U., Wharton, D., Josefsson, A. & Wilson, A. C. 1991 Paternal inheritance of mitochondrial DNA in mice. *Nature, Lond.* **352**, 255–257.

Hastings, I. M. 1992*a* Population genetic aspects of deleterious cytoplasmic genomes and their effect on the evolution of sexual reproduction. *Genet. Res.* **59**, 215–225.

Hastings, I. M. 1992*b* Why is sex so frequent? *Trends Ecol. Evol.* **7**, 278–279.

Hickey, D. A. 1993 Molecular symbionts and the evolution of sex. *J. Hered.* **84**, 410–414.

Hickey, D. A. & Rose, M. R. 1988 The role of gene transfer in the evolution of eukaryotic sex. In *The evolution of sex: an examination of current ideas*. (ed. R. E. Michod & B. R. Levin), pp. 161–175. Sunderland, Massachusetts: Sinauer Associates.

Hoeh, W. R., Blakley, K. H. & Brown, W. M. 1991 Heteroplasmy suggests limited biparental inheritance of *Mytilus* mitochondrial DNA. *Science, Wash.* **251**, 1488–1490.

Hoekstra, R. F. 1987 The evolution of sexes. In *The evolution of sex and its consequences* (ed. S. C. Stearns), pp. 59–91. Basel: Birkhauser.

Hoekstra, R. F. 1990 Evolution of uniparental inheritance of cytoplasmic DNA. In *Organisational constraints on the dynamics of evolution* (ed. J. Maynard Smith & G. Vida), pp. 269–278. Manchester University Press.

Hurst, L. D. 1990 Parasite diversity and the evolution of diploidy, multicellularity and anisogamy. *J. theor. Biol.* **144**, 429–443.

Hurst, L. D. 1993 The incidences, mechanisms and evolution of cytoplasmic sex ratio distorters in animals. *Biol. Rev.* **68**, 121–193.

Hurst, L. D. & Hamilton, W. D. 1992 Cytoplasmic fusion and the nature of sexes. *Proc. R. Soc. Lond.* B **247**, 189–194.

Itino, T., Kato, M. & Hotta, M. 1991 Pollination ecology of the two wild bananas, *Musa acuminata* subsp *halabanensis* and *M. salaccensis* – chiropterophily and ornithophily. *Biotropica* **23**, 151–158.

Jinks, J. L. 1964 *Extrachromosomal inheritance*. Englewood Cliffs, New Jersey: Prentice Hall.

Jurand, A. & Selman, G. G. 1969 *The Anatomy of Paramecium*. London: Macmillan St. Martin's Press.

Kawano, S. & Kuroiwa, T. 1989 Transmission pattern of mitochondrial DNA during plasmodium formation in *Physarum polycephalum*. *J. gen. Microbiol.* **135**, 1559–1566.

Kondo, R., Setta, Y., Matsuura, E. T., Ishiwa, H., Takahata, N. & Chigusa, S. I. 1990 Incomplete maternal transmission of mitochondrial DNA in *Drosophila*. *Genetics* **126**, 657–663.

Koslowsky, D. J. & Waaland, S. D. 1984 Cytoplasmic incompatibility following somatic cell fusion in *Griffithsia pacifica* Kylin, a red alga. *Protoplasma* **123**, 8–17.

Koslowsky, D. J. & Waaland, S. D. 1987 Ultrastructure of selective chloroplast destruction in *Griffithsia pacifica* Kyl. *J. Phycol.* **23**, 638–648.

Lane, E. B. & Carlile, M. 1979 Post-fusion somatic incompatibility in plasmodia of *Physarum polycephalum*. *J. Cell. Sci.* **35**, 339–354.

Law, R. & Hutson, V. 1992 Intracellular symbionts and the evolution of uniparental cytoplasmic inheritance. *Proc. R. Soc. Lond.* B **248**, 69–77.

Margulis, L, Corliss, J. O., Melkonian, M. & Chapman, D. J. 1990 *Handbook of Protoctista*. Boston: Jones and Bartlett.

Matagne, R. F. 1987 Chloroplast gene transmission in *Chlamydomonas reinhardtii*. A model for its control by the mating-type locus. *Curr. Genet.* **12**, 251–256.

May, G. & Taylor, J. W. 1988 Patterns of mating and mitochondrial DNA inheritance in the agaric basidiomycete *Coprinus cinereus*. *Genetics* **118**, 213–220.

Milligan, B. G. 1992 Is organelle DNA strictly maternally inherited? Power analysis of a binomial distribution. *Am. J. Bot.* **79**, 1325–1328.

Parker, G. A., Barker, R. R. & Smith, V. G. F. 1972 The origin and evolution of gamete dimorphism and the male–female phenomenon. *J. theor. Biol.* **36**, 181–198.

Price, G. R. 1970 Selection and covariance. *Nature, Lond.* **227**, 520–521.

Price, G. R. 1972 Extension of covariance selection mathematics. *Ann. hum. Genet.* **35**, 485–490.

Puhalla, J. E. 1968 Compatibility reactions on solid medium and interstrain inhibition in *Ustilago maydis*. *Genetics* **60**, 461–477.

Rand, D. M. & Harrison, R. G. 1989 Molecular population genetics of mtDNA size variation in crickets. *Genetics* **121**, 551–569.

Reboud, X. & Zeyl, C. 1994 Organelle inheritance in plants. *Heredity* **72**, 132–140.

Rousset, F. & Raymond, M. 1991 Cytoplasmic incompatibility in insects: why sterilize females? *Trends Ecol. Evol.* **6**, 54–57.

Sager, R. 1977 Genetic analysis of chloroplast DNA in *Chlamydomonas*. *Adv. Genet.* **19**, 287–340.

Sears, B. B. 1980 Elimination of plasmids during spermatogenesis and fertilization in the plant kingdom. *Plasmid* **4**, 233–255.

Sears, B. B. & VanWinkle-Swift, K. 1994 The Salvage-Turnover-Repair (STOR) model for uniparental inheritance in *Chlamydomonas*: DNA as a source of sustenance. *J. Hered.* **85**, 366–376.

Silliker, M. E. & Collins, O. R. 1988 Non-Mendelian inheritance of mitochondrial DNA and ribosomal DNA in the myxomycete. *Didymium iridis*. *Molec. gen. Genet.* **213**, 370–378.

Skibinski, D. O., Gallagher, C. & Beynon, C. M. 1994 Mitochondrial DNA inheritance. *Nature, Lond.* **368**, 817–818.

Somers, J. M. & Bevan, E. A. 1969 The inheritance of the killer character in yeast. *Genet. Res.* **13**, 71–83.

VanWinkle-Swift, K., Hoffman, R., Shi, L. & Parker, S. 1994 A suppressor of a mating-type limited zygotic lethal allele also suppresses uniparental chloroplast gene transmission in *Chlamydomonas monoica*. *Genetics* **136**, 867–877.

VanWinkle-Swift, K. P. 1978 Uniparental inheritance is

promoted by delayed division of the zygote in *Chlamydomonas*. *Nature, Lond.* **275**, 749–751.
VanWinkle-Swift, K. P. & Aubert, B. 1983 Uniparental inheritance in a homothallic alga. *Nature, Lond.* **303**, 167–169.
Wade, M. J. 1985 Soft selection, hard selection, kin selection, and group selection. *Am. Nat.* **125**, 61–73.
Wallace, D. C. 1992 Mitochondrial genetics: a paradigm for aging and degenerative diseases? *Science, Wash.* **256**, 628–632.
Whatley, J. 1982 Ultrastructure of plastid inheritance: green algae to angiosperms. *Biol. Rev.* **57**, 527–569.
Wilch, G., Ward, S. & Castle, A. 1992 Transmission of mitochondrial DNA in *Ustilago violacea*. *Curr. Genet.* **22**, 135–140.
Wright, S. 1969 *Evolution and the genetics of populations: the theory of gene frequencies*. Chicago University Press.
Zouros, E., Ball, A. O., Saavedra, C. & Freeman, K. R. 1994 Mitochondrial DNA inheritance. *Nature, Lond.* **368**, 818.

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APPENDIX 1

Consider a population of single-celled organisms with biparental inheritance of a particular class of cytoplasmic genes. There exists a minimum replication rate of the organelle genome at which fitness is maximal. Above this replication rate a cytoplasmic genome has a replication rate R. At any given instant it shall be assumed that the population is at fixation for a cytoplasmic genome (type 1) with replication rate R_1. At the very start of evolution, $R_1 = 0$.

Into a population at fixation for type 1 comes a mutant genome (type 2) with a higher replication rate, R_2. The excess replication rate of this mutant is $\Delta R = R_2 - R_1$. When a cell homoplasmic for genome 2 mates with one homoplasmic for genome 1, an excess of the progeny inherit the faster replicating genome. The frequency of progeny cells with the faster genome from such matings is β (if $\beta = 0.5$ there is no excess). This in turn is a function of the excess replication rate. In general one can consider that the transmission advantage is a function of the relative increment in replication rate:

$$\beta = 0.5 + (1 - e^{-\Delta R/(\lambda R_1 + \Phi)})/2, \quad \text{(A 1)}$$

where λ and Φ are non-negative constants. If $\lambda = 0$ then the transmission advantage is a simple function of the absolute difference in replication rate. It is this case that I consider here.

Cells that are homoplasmic for a given mutant have a fitness determined by the rate of replication of the mutant. I shall consider that the absolute fitness (W_a) of a cell with an organelle genome that replicates at a rate R is given by

$$W_a = 1 - (R/\epsilon)^2, \quad \text{(A 2)}$$

where ϵ is a constant. This is probably a realistic form of the relation. An individual with the mutant genome has an absolute fitness W_{a2}, whereas those with type 1 have an absolute fitness W_{a1}. At invasion, an individual with the mutant genome suffers a cost U as shown in equation (3), i.e.

$$U = (W_{a1} - W_{a2})/W_{a1}.$$

Note, here I ignore cost t considered previously. However, as established in equation (2), for invasion the cost must be below some value determined by the inbreeding rate F, i.e.

$$U_{max} < 1 - 1/(1 - \psi), \quad \text{(A 3)}$$

where $\psi = (1 - 2\beta)(1 - F)$ and $\beta = f(\Delta R)$ as above (equation (A 1) with $\lambda = 0$), must be satisfied. Invasion is impossible if the cost suffered by a mutant is greater than U_{max}. The intersection can be found from solving $U = U_{max}$. Solving this for R gives

$$\hat{R} = [-b \pm \sqrt{(b^2 - 4ac)}]/2a, \quad \text{(A 4)}$$

where $a = \psi$, $b = 2\Delta R(\psi - 1)$, and $c = (\psi - 1)\Delta R^2 - \epsilon^2\psi$.

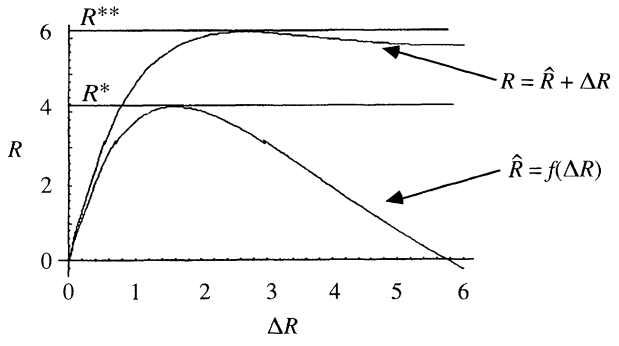

Figure 3. A plot of the values of the increment in replication rate (ΔR) against the absolute replication rate that are consistent with invasion of a mutant fast-replicating cytoplasmic genome. This comes from the solution of $U = U_{max}$. Invasion is possible if, at a given value of R, ΔR is between the minimum and maximum value described by the urve $\hat{R} = f(\Delta R)$. There exists a maximum value of R compatible with invasion that is given as R^*. This, however, is not the limit to R that may invade and persist. At any value of R, the limits of the value of R that the invading genome may possess is given by $R = \hat{R} + \Delta R$. This curve is also plotted. It has a maximum at $R = R^{**}$. Between the curve described by $R = \hat{R} + \Delta R$ and $R = R^*$ exists a space that is accessible. If at any time the invading mutant has a value of R within this space and can invade (dependent upon the lower curve) then a population with this genome will be uninvadable by a faster replicator. Parameters for the above plots are set at $F = 0.5$, $\epsilon = 10$ and $\Phi = 2$.

Only the positive solution for $\hat{R}$ is relevant. This is plotted in figure 3. At any given value of R there hence exist only particular values of ΔR compatible with invasion. As these values do not necessarily lie close to zero, consideration of only infinitely small increments in ΔR is not adequate. At any given value of F there exists a value of R beyond which there exist no values of ΔR compatible with invasion. This upper limit to R shall henceforth be called R^* (see figure 3). However, from values below R^* there exist values of ΔR compatible with invasion which ensure that the replication rate of the invading genome (i.e. $R_2 = R_1 + \Delta R$) is higher than R^*. $\hat{R} + \Delta R$, however, has an upper limit. This upper limit occurs at R^{**} (see figure 3). It follows that there exists a space between R^* and the curve describing $\hat{R} + \Delta R$ for which, once a population is at fixation for a genome with a replication rate within this space, further evolution of faster genomes is impossible (as no ΔR is compatible with invasion if $R > R^*$ is true). Hence within the space a halt to the decay of a cytoplasmic genome occurs.

If slower replicating genomes are always excluded by intracellular competition, thus preventing the production of cells homoplasmic for slower replicators, then the above stopping positions are stable equilibria. If slower replicators can ever invade then the above represent the upper limits that R might ever achieve. From equation (A 4), the values of R^* and R^{**} tend towards zero as F tends to unity. The absolute fitness at the equilibrium position can be found by substituting for R into equation (A 2). This tends to unity as

F tends to unity. The maximum value of ΔR also tends to zero as F tends to unity. Hence the maximum possible increment in cost is reduced as F tends to unity, thereby making the invasion of a costly suppressor less likely as the level of inbreeding goes up. The limit to absolute fitness can never descend below zero. This is trivially shown by considering the extreme cost that allows invasion as being 0.5 (i.e. if $F = 0$). As $U = 1 - W_{a2}/W_{a1}$, with W_{a1} positive, which it must initially be, if W_{a2}, is ever equal to or less than zero, U would be equal to or greater than one and this is not consistent with invasion. Hence an equilibrium value of W_{a2} must be greater than zero.

Because this paper exceeds the maximum length normally considered for publication in *Proceedings* B, the author has agreed to make a contribution to production costs.