Published in final edited form as:

Theor Popul Biol. 2007 June ; 71(4): 445–453.

Cytonuclear dynamics in selfing populations under selection

Renyi Liu* and Marjorie A. Asmussen

Department of Genetics, University of Georgia, Athens, GA 30602, USA

Abstract

We develop a mathematical model to delimit the role of natural selection in maintaining nuclear and cytoplasmic polymorphisms in selfing populations. We provide explicit time-dependent solutions for joint cytonuclear frequencies under any combination of constant fertility, viability, and gametic selection and exact analytical conditions for the maintenance of polymorphisms under joint cytonuclear selection. The equilibrium structure is determined by the relative magnitude of echo fitnesses, defined as the rate at which individuals survive and produce offspring with their own genotype. Both nuclear and cytoplasmic polymorphisms can be maintained under biologically meaningful conditions, although the majority of the parameter combinations will lead to fixation. The theoretical framework developed here should be very useful in formally dissecting the form and strength of selection on cytonuclear genotypes in populations with negligible levels of outcrossing.

Keywords

Cytonuclear; Polymorphism; Selfing; Selection; Model

1. Introduction

One of the major issues in evolutionary genetics is to understand the mechanisms responsible for the maintenance of genetic variation (Hedrick, 1998). Recent advances in molecular marker and DNA sequencing technology have revealed a vast amount of genetic variation in both nuclear and cytoplasmic genomes (Weinreich and Rand, 2000). Although recent evidence has strongly suggested that the evolution of mitochondrial DNA (mtDNA) is nonneutral (Gerber et al., 2001; Rand, 2001), it is not clear what role natural selection plays in the maintenance of the extensive cytoplasmic polymorphisms observed in natural and experimental populations. In fact, it cannot be achieved by simple directional constant selection, since when this acts solely on haploid genomes such as mitochondrial (mt) and chloroplast (cp) DNA in isolated populations, all but the most fit type will be eliminated. Here, we explore the possibility of maintaining cytoplasmic polymorphism by joint nuclear–cytoplasmic selection favoring one cytonuclear genotype over another.

Extensive cytonuclear interactions and coevolution have been demonstrated by both molecular experiments and fitness assays (for reviews, see Gerber et al., 2001; Rand, 2001; Rand et al., 2004). Cytoplasmic male sterility (CMS) is a classic example in which male fertility depends on joint nuclear and mitochondrial molecules, which has been observed in over 150 plant species, including many crops (Saumitoullaprade et al., 1994; Schnable and Wise, 1998). Another good example is the coadaptation between mtDNA encoded subunits of cytochrome oxidase (*COX*) and its substrate, the nuclear DNA encoded cytochrome *c* (*CYC*) as suggested by enzyme activity experiments (Burton et al., 1999; Edmands and Burton, 1999) and sequence

*Corresponding author. Department of Biochemistry and Molecular Biophysics, University of Arizona, Tucson, AZ 85721, USA. Fax: +1 520 621 3709. E-mail address: rliu@email.arizona.edu (R. Liu).
Dedicated to Marjorie A. Asmussen, who died on January 19, 2004

comparison (Schmidt et al., 2001). And in fact, it was recently shown that in copepod *Tigriopus californicus* populations, the viability of *CYC* genotypes depends on cytoplasmic backgrounds (Willett and Burton, 2001). Cytonuclear interactions are also suggested by the variable frequency dynamics of mtDNA haplotypes, when competed on mixed nuclear backgrounds in lab populations of *Drosophila* (Fos et al., 1990; Hutter and Rand, 1995; Kilpatrick and Rand, 1995; Macrae and Anderson, 1988).

The conditions under which selection on cytonuclear genotypes will maintain cytoplasmic or joint cytonuclear polymorphisms has proved to be unexpectedly difficult to determine. The first theoretical treatment of this issue demonstrated that a permanent cytoplasmic polymorphism is not even possible in random mating populations under standard deterministic forms of constant viability or fertility selection (Clark, 1984). Subsequent simulations showed that this can occur in both random and mixed mating populations, when there is differential selection between the two sexes (Babcock and Asmussen, 1996, 1998; Gregorius and Ross, 1984; Ross and Gregorius, 1985), and in random mating populations when the nuclear marker is X-linked (Rand et al., 2001).

Here we extend these investigations to the effects of joint cytonuclear selection in selfing populations, for which a complete analytical analysis is possible. Although predominantly selfing species often have less genetic variation than cross-fertilizing species in nuclear genome (Baudry et al., 2001; Graustein et al., 2002; Hamrick and Godt, 1996; Liu et al., 1999, 1998; Savolainen et al., 2000; but see Wright et al., 2002), substantial genetic variations do exist in highly selfing populations (Hedrick, 1998). The maintenance of nuclear polymorphisms has been the subject of a few studies and the exact conditions have been obtained (Asmussen et al., 1998; Hedrick, 1998). Mitochondrial diversity in selfing species is also reduced, but the reduction is much less than that for the nuclear genome (Graustein et al., 2002). Here, we delimit the role of natural selection in maintaining cytonuclear polymorphisms under selfing, by presenting explicit time-dependent solutions for joint cytonuclear frequencies in a selfing population under any combination of constant fertility, viability, and gametic selection on a diallelic, autosomal nuclear locus and a diallelic, haploid, cytoplasmic locus. The results provide the first exact analytical conditions for the maintenance of polymorphisms under joint cytonuclear selection. In addition to providing valuable qualitative predictions, this framework allows formal, empirical estimates for selection components by fitting the dynamical solutions for cytonuclear frequencies obtained here to multigenerational data, as recently demonstrated under a purely nuclear system (Asmussen et al., 1998; Liu et al., 2003). As in the nuclear case, the theoretical framework developed here can also be applied with reasonable accuracy to populations with a negligible outcrossing rate, such as those involving the model organism *Arabidopsis thaliana*.

2. The cytonuclear system

We consider a purely selfing, diploid population censused as adults with two alleles (A and a) at an autosomal nuclear locus, and two alleles (C and c) at a uniparentally inherited, haploid cytoplasmic locus. We assume that the population has discrete, nonoverlapping generations and no mutation or gene flow, and is large enough to preclude the effects of random genetic drift. The frequencies of the six possible cytonuclear genotypes in adults are specified in Table 1 together with the marginal genotypic frequencies at each individual locus. The genotypes are subject to constant fertility (f_i), viability (ϕ_i), and gametic selection (m_i) as shown in Table 2, where the subscript i ranges from 1 to 6 corresponding to the six possible joint genotypes AA/C , Aa/C , aa/C , AA/c , Aa/c , and aa/c , respectively.

The fertility parameter f_i denotes the average number of offspring produced when an individual of cytonuclear genotype i selfs, while the viability parameter ϕ_i denotes the average fraction

of the newly formed zygotes of cytonuclear genotype i that survive to reproduce. Gametic selection occurs via meiotic drive as the deviation from 50:50 Mendelian ratios in gametes produced by the two nuclear heterozygotes (Aa/C and Aa/c). For the C cytotype, this is incorporated by the three gametic parameters m_1 , m_2 , and m_3 , which are nonnegative numbers that sum to 1 ($m_1 + m_2 + m_3 = 1$) and represent the average fractions of progeny that are AA/C , Aa/C , and aa/C , respectively, when an Aa/C individual selfs; m_4 , m_5 , and m_6 have similar meanings for heterozygotes with the c cytotype.

3. Cytonuclear frequency dynamics

3.1. Derivation of recursions

To obtain the time-dependent solutions for the cytonuclear frequencies, we first need to derive the recursions for the changes in adult frequencies between two successive generations. These are readily determined by working through a complete generation cycle. Although population size is not monitored in the model, the frequency dynamics are most easily derived by tracing the number of each cytonuclear genotype through the successive life stages. Letting N denote the total number of reproducing adults in the current generation, the number of AA/C zygotes, for instance, is $(f_1 u_1 + f_2 m_1 v_1)N$, where $f_1 u_1 N$ is the number of new AA/C zygotes produced when the $u_1 N$ adults of type AA/C self, and $f_2 m_1 v_1 N$ is the number produced by the $v_1 N$ Aa/C heterozygotes. These zygotes are subject to viability selection, after which the number of new AA/C adults is $(f_1 \phi_1 u_1 + f_2 m_1 \phi_1 v_1)N$. Similar reasoning yields the number of new adults of the other five cytonuclear genotypes.

We then obtain the recursions for the adult frequencies of each joint cytonuclear genotype simply by dividing each genotypic count by the total number of new adults ($\bar{w}$):

$$\begin{aligned} u_1' &= \frac{(f_1 \phi_1)u_1 + (f_2 m_1 \phi_1)v_1}{\bar{w}}, \\ v_1' &= \frac{(f_2 m_2 \phi_2)v_1}{\bar{w}}, \\ w_1' &= \frac{(f_3 \phi_3)w_1 + (f_2 m_3 \phi_3)v_1}{\bar{w}}, \\ u_2' &= \frac{(f_4 \phi_4)u_2 + (f_5 m_4 \phi_4)v_2}{\bar{w}}, \\ v_2' &= \frac{(f_5 m_5 \phi_5)v_2}{\bar{w}}, \\ w_2' &= \frac{(f_6 \phi_6)w_2 + (f_5 m_6 \phi_6)v_2}{\bar{w}}, \end{aligned} \quad (1)$$

$$\bar{w} = (f_1 \phi_1)u_1 + f_2(m_1 \phi_1 + m_2 \phi_2 + m_3 \phi_3)v_1 + (f_3 \phi_3)w_1 + (f_4 \phi_4)u_2 + f_5(m_4 \phi_4 + m_5 \phi_5 + m_6 \phi_6)v_2 + (f_6 \phi_6)w_2 \quad (2)$$

is the average fitness in the previous generation.

3.2. Time-dependent solutions

As in the purely nuclear system (Asmussen et al., 1998), the dynamical analysis is facilitated by a change of variables, in this case to the five independent variables, $x_1 = u_1/v_2$, $x_2 = w_1/v_2$, $x_3 = u_2/v_2$, $x_4 = w_2/v_2$, and $x_5 = v_1/v_2$. These represent the ratios of the frequencies of the other five cytonuclear genotypes to that of the Aa/c heterozygote and the complicated denominator $\bar{w}$ in the frequency equations is eliminated. Their recursions have the advantage of being simple, linear equations:

$$x_i' = \begin{cases} a_i x_i + b_i x_5 & \text{for } i = 1, 2, \\ a_i x_i + b_i & \text{for } i = 3, 4, \\ a_i x_i & \text{for } i = 5, \end{cases} \quad (3)$$

where

$$\begin{aligned} a_1 &= \frac{f_1 \phi_1}{f_5 m_5 \phi_5}, & b_1 &= \frac{f_2 m_1 \phi_1}{f_5 m_5 \phi_5}, \\ a_2 &= \frac{f_3 \phi_3}{f_5 m_5 \phi_5}, & b_2 &= \frac{f_2 m_3 \phi_3}{f_5 m_5 \phi_5}, \\ a_3 &= \frac{f_4 \phi_4}{f_5 m_5 \phi_5}, & b_3 &= \frac{m_4 \phi_4}{m_5 \phi_5}, \\ a_4 &= \frac{f_6 \phi_6}{f_5 m_5 \phi_5}, & b_4 &= \frac{m_6 \phi_6}{m_5 \phi_5}, \\ a_5 &= \frac{f_2 m_2 \phi_2}{f_5 m_5 \phi_5}. \end{aligned} \quad (4)$$

Their dynamical solutions in each generation $t = 1, 2, \dots$, are easily found to be

$$x_i^{(t)} = \begin{cases} (a_i)^t (x_i^{(0)} - x_i^*) + (a_5)^t x_i^* & \text{if } a_i \neq a_5, \\ (a_i)^t x_i^{(0)} + (a_i)^{t-1} b_i x_5^{(0)} & \text{if } a_i = a_5 \end{cases} \quad (5)$$

for $i = 1, 2$, where $x_i^* = b_i x_5^{(0)} / (a_5 - a_i)$;

$$x_i^{(t)} = \begin{cases} (a_i)^t (x_i^{(0)} - x_i^*) + x_i^* & \text{if } a_i \neq 1, \\ x_i^{(0)} + b_i t & \text{if } a_i = 1 \end{cases} \quad (6)$$

for $i = 3, 4$, where $x_i^* = b_i / (1 - a_i)$; and

$$x_5^{(t)} = (a_5)^t x_5^{(0)}. \quad (7)$$

Finally, since the frequencies of all six genotypes sum to 1 at each generation t , we have equation $u_1^{(t)} + v_1^{(t)} + w_1^{(t)} + u_2^{(t)} + v_2^{(t)} + w_2^{(t)} = 1$. Division of this equation by $v_2^{(t)}$ followed by an inversion yields $v_2^{(t)} = 1 / (1 + x_1^{(t)} + x_2^{(t)} + x_3^{(t)} + x_4^{(t)} + x_5^{(t)})$, which is the frequency of genotype Aa/c . The time-dependent solutions for other five genotypic frequencies can be recovered via the relationships

$$u_1^{(t)} = x_1^{(t)} v_2^{(t)}, \quad v_1^{(t)} = x_5^{(t)} v_2^{(t)}, \quad w_1^{(t)} = x_2^{(t)} v_2^{(t)}, \quad u_2^{(t)} = x_3^{(t)} v_2^{(t)}, \quad w_2^{(t)} = x_4^{(t)} v_2^{(t)} \quad (8)$$

for every generation $t = 0, 1, 2, \dots$

3.3. Equilibrium behavior

The equilibrium behavior of this cytonuclear selfing model depends on the relative magnitudes of 1 and the five geometric terms a_1, a_2, a_3, a_4, a_5 , defined in (4). Biologically, the cytonuclear dynamics are governed by the relative magnitudes of the *echo fitnesses* of each of the six cytonuclear genotypes, defined here as the rate at which individuals contribute offspring with their own genotype to the next generation. For homozygotes, the echo fitness is simply the product of their fertility and viability ($f_i \phi_i$) since they only produce offspring of their own

genotype when they self-fertilize. For Aa/C and Aa/c heterozygotes, who produce three different types of progeny, the echo fitness is $m_2 f_2 \phi_2$ and $m_5 f_5 \phi_5$, respectively.

A comprehensive analysis of the cytonuclear dynamics under all numerical orderings of a_1, a_2, a_3, a_4, a_5 , and 1 shows that all four basic types of evolutionary outcomes are possible in terms of whether a nuclear and/or cytoplasmic polymorphism is maintained, assuming that the population starts with all six cytonuclear genotypes present. These subsume 24 types of outcomes in terms of which of the six genotypes are present at equilibrium. A brief description of the analysis and a complete summary of these results are given in Appendix A. Here we only discuss the cases whose conditions do not involve highly restrictive equalities in echo fitnesses that seem unlikely to happen in real populations. These twelve outcomes and the corresponding selection conditions are listed in Table 3, and the sample trajectories for allelic frequencies are provided in Fig. 1.

The first (and as shown below, most likely) outcome is for selection to eliminate all variation, resulting in only one type of nuclear homozygote in one cytoplasmic background, for example, AA/C , being maintained. This happens when that cytonuclear homozygote has a strictly greater echo fitness than all the other five genotypes. The population becomes fixed for AA/C , for instance, if

$$f_1 \phi_1 > m_2 f_2 \phi_2, f_3 \phi_3, f_4 \phi_4, m_5 f_5 \phi_5, f_6 \phi_6$$

(Fig. 1A) and for AA/c , aa/C , or aa/c if the corresponding echo fitness $f_3 \phi_3, f_4 \phi_4$, or $f_6 \phi_6$ exceeds that of all others.

The second possible evolutionary outcome is to maintain only a nuclear polymorphism, with the cytoplasmic variation eliminated. This occurs when the echo fitness of one of the two cytonuclear heterozygotes exceeds that of the five other cytonuclear genotypes, either Aa/C ,

$$m_2 f_2 \phi_2 > f_1 \phi_1, f_3 \phi_3, f_4 \phi_4, m_5 f_5 \phi_5, f_6 \phi_6$$

or Aa/c ,

$$m_5 f_5 \phi_5 > f_1 \phi_1, m_2 f_2 \phi_2, f_3 \phi_3, f_4 \phi_4, f_6 \phi_6$$

In either case, only the three cytonuclear genotypes with the cytoplasmic background of the selectively favored heterozygote are retained (AA/C , Aa/C and aa/C in the first case or AA/c , Aa/c , and aa/c in the second) (Fig. 1B). With pure selfing, nuclear polymorphism can also be maintained with only homozygotes present and no heterozygotes. This occurs in our cytonuclear system when the two homozygotes with the same cytoplasmic background have exactly the same echo fitness and this common value exceeds that of all other four cytonuclear genotypes. Under these conditions, only the two favored cytonuclear homozygotes remain at equilibrium (Fig. 1C).

Third, only a cytoplasmic polymorphism may be maintained via a single nuclear homozygous genotype with both cytoplasmic backgrounds. This third possibility happens when the echo fitness of the favored homozygote is not affected by its cytoplasmic background and exceeds those of the other four genotypes. i.e.

$$f_1 \phi_1 = f_4 \phi_4 > m_2 f_2 \phi_2, f_3 \phi_3, m_5 f_5 \phi_5, f_6 \phi_6$$

which preserves AA/C and AA/c (Fig. 1D), or

$$f_3 \phi_3 = f_6 \phi_6 > f_1 \phi_1, m_2 f_2 \phi_2, f_4 \phi_4, m_5 f_5 \phi_5$$

, which preserves aa/C and aa/c .

Fourth and lastly, a purely selfing population will converge to a joint polymorphic equilibrium for both the nuclear and cytoplasmic loci, with all six cytonuclear genotypes present, if and only if the echo fitness of Aa heterozygotes is not affected by their cytoplasmic background and exceeds those of the four homozygotes ($m_2f_2\phi_2 = m_5f_5\phi_5 > f_1\phi_1, f_3\phi_3, f_4\phi_4, f_6\phi_6$) (Fig. 1E). This requires that the usual net fitness of the two heterozygotes (Aa/C and Aa/c), given by the product of their fertility and viability ($f_2\phi_2$ and $f_5\phi_5$) exceed those of the four homozygotes ($f_i\phi_i$, for $i = 1, 3, 4, 6$) by a factor of $1/m_2 < 1$ and $1/m_5 < 1$, respectively. In the special case of Mendelian segregation, a joint cytonuclear polymorphism is maintained if and only if the two cytonuclear heterozygotes have the same net fitness and there is *double overdominance*, with each heterozygote more than twice as fit as each homozygote in net fitness ($f_2\phi_2 = f_5\phi_5 < 2f_1\phi_1, 2f_3\phi_3, 2f_4\phi_4, 2f_6\phi_6$). This is analogous to the conditions for the maintenance of a nuclear polymorphism under purely nuclear selection (Asmussen et al., 1998). Under pure selfing, nuclear and cytoplasmic polymorphisms can also be maintained simultaneously with only the four homozygotes present and no heterozygotes when the homozygotes all have the same echo fitness and this exceeds those of the two heterozygotes ($f_1\phi_1 = f_3\phi_3 = f_4\phi_4 = f_6\phi_6 < m_2f_2\phi_2, m_5f_5\phi_5$) (Fig. 1F).

4. Numerical studies

4.1. Probability of maintaining polymorphism

Computer simulations provide further insight into the potential for maintaining polymorphisms in this selfing system in terms of the size of the region of parameter space that does this. Ideally, this measure would be based on the true distribution of the selection parameters in the populations being studied. Since this is not known, for simulation purposes we used randomly generated selection parameters from a uniform distribution on the interval (0, 1). To ensure that each set of three gametic selection parameters (with the same cytoplasmic background) sum to 1, we used the “broken stick” method. This involved generating two random numbers to divide the interval (0, 1) into three pieces, and then assigning the three gametic parameters to be the lengths of these three subintervals. Each run of the program included one million complete sets of 18 selection parameters.

The results show that for the majority of random parameter sets (93.5%), the population loses both cytoplasmic and nuclear variation, and in the remaining parameter sets (6.5%), only a nuclear polymorphism is maintained. With completely random selection parameters, the potential for maintaining cytoplasmic or joint cytonuclear polymorphism is zero, because these outcomes require exact equalities of echo fitnesses, which are products of random variables with a continuous distribution.

In some special cases, however, the necessary exact equalities of echo fitnesses are biologically reasonable. It is therefore of interest to ask how often the relevant genotypes are selectively favored (and cytoplasmic or joint cytoplasmic polymorphism maintained) subject to such constraints. When the nuclear genotypes have the same fitness, then the echo fitnesses of two homozygotes with the same cytoplasmic background are equal ($f_1\phi_1 = f_3\phi_3$ or $f_4\phi_4 = f_6\phi_6$). Our simulation shows that with either of the two equalities satisfied, the probability that these two echo fitnesses are strictly greater than those of all other four genotypes is 30%. The evolutionary result for these conditions is only these two genotypes are present at equilibrium and thus only nuclear variation is maintained. When the echo fitnesses are not affected by the cytoplasmic background, the two homozygotes with the same nuclear genotype but different cytotypes have the same echo fitness ($f_1\phi_1 = f_4\phi_4$ or $f_3\phi_3 = f_6\phi_6$). The probability that these two equal echo fitnesses exceed that of the other four genotypes is also 30%. With these conditions, the two genotypes with the equal and strictly greatest echo fitnesses are preserved, and only

cytoplasmic polymorphism is maintained. The equality of the echo fitnesses of the two heterozygotes requires that both the usual net fitnesses and the meiotic drive are not affected by cytoplasmic background. With this equality holds, the probability that the echo fitnesses of the two heterozygotes strictly exceed that of all the four homozygotes is 3.5%. All six cytonuclear genotypes are present at equilibrium and both cytoplasmic and nuclear polymorphisms are maintained. If the echo fitnesses of the four homozygotes are equal, which means the fitness is not affected by the type of nuclear allele or cytoplasmic background, the probability that their echo fitnesses are strictly greater than that of the two heterozygotes is 64.9%. Both cytoplasmic and nuclear polymorphisms are maintained and only four homozygotes are present at equilibrium.

4.2. Time to reach equilibrium

If the time to reach equilibrium is long, a polymorphism is effectively maintained in this process, even though it will be lost eventually. Our simulation shows that there is a significant correlation between the number of generations to reach equilibrium and the difference of the top two echo fitnesses. The smaller the difference is, the longer it takes to reach equilibrium (Fig. 2). Since it is a selfing population, a genotype with the maximum echo fitness (thus produce most offspring of the same genotype) will win the competition. The difference between the top two echo fitnesses reflects the degree of dominance of the best-fit genotype. The larger the difference is, the quicker that the best-fit genotype will take over the population.

5. Discussion

The comprehensive analysis here provides explicit time-dependent solutions for cytonuclear genotype frequencies and exact analytical conditions that maintain genetic polymorphism at a diploid, diallelic nuclear locus and a haploid, diallelic cytoplasmic locus in purely selfing populations subject to any combination of viability, fertility, and gametic selection via meiotic drive.

The equilibrium behavior is determined by the relative magnitude of echo fitnesses. Numerically, there is no chance to maintain cytoplasmic, or joint cytonuclear polymorphism, since it requires exact equalities of echo fitnesses. However, the cytoplasmic or joint cytonuclear polymorphism may still be observed in natural or experimental populations due to the following reasons: (1) The equalities of echo fitnesses are sometimes biologically meaningful. For example, if the cytoplasmic locus is selectively neutral, the individual with same nuclear genotype will have equal echo fitness regardless of their cytoplasmic genotype. (2) If the difference between the top two echo fitnesses is small, it takes a long time for the population to reach equilibrium and the polymorphisms are effectively maintained.

The probability of maintaining nuclear polymorphism in this system is less than those in two related selfing models. In a purely selfing model with a single nuclear, diallelic locus, the probability of maintaining a nuclear polymorphism is 8.3% when only viability selection (Overath and Asmussen, 1998), and 10.0% when all three selection forces are considered (the model was developed by Asmussen et al. (1998), and we obtained the probability of maintaining polymorphism here with the simulation method described above).

The theoretical framework developed here can be used to obtain formal maximum likelihood estimates for the set of fertility, viability, and gametic selection parameters from multigenerational genotypic counts, using a similar approach as in the purely nuclear system (Liu et al., 2003). Those estimates reveal not only the form and strength of natural selection, but also the nature of the interaction between cytoplasmic and nuclear genomes.

Acknowledgements

We thank two anonymous reviewers for valuable comments. This work was supported by the National Institute of Health (NIH) grant GM-48528 to M.A.A.

Appendix A

The equilibrium behavior of cytonuclear genotypic frequencies can be obtained by comparing the a_1, a_2, a_3, a_4, a_5 , and 1 to find the dominant term(s), which determines the limiting values of the genotypic frequencies as generation $t \rightarrow \infty$. For example, under the condition $a_1 > a_2, a_3, a_4, a_5, 1$, the limiting value of the AA/C frequency $u_1^{(t)}$ can be evaluated to 1 by dividing the nominator and denominator with the dominant term $a_1^{(t)}$. The results are summarized in Table A1. In the table, each condition is expressed as the maximum term(s) of echo fitnesses. This can be achieved by multiplying a_1, a_2, a_3, a_4, a_5 , and 1 with $m_5 f_5 \phi_5$.

Table A1

The equilibrium behavior of a selfing population under fertility, viability, and gametic selection

Nuclear and/or cytoplasmic polymorphism	Equilibrium frequencies ^a			Maximum term(s) of echo fitnesses ^b
Neither	1	0	0	$f_1\phi_1; f_1\phi_1 = m_2f_2\phi_2; f_1\phi_1 = m_2f_2\phi_2 = m_5f_5\phi_5;$ $f_1\phi_1 = m_2f_2\phi_2 = f_4\phi_4;$
	0	0	0	$f_1\phi_1 = m_2f_2\phi_2 = f_6\phi_6;$ or $f_1\phi_1 = m_2f_2\phi_2 = f_4\phi_4 = f_6\phi_6$
	0	0	1	$f_3\phi_3; f_3\phi_3 = m_2f_2\phi_2; f_3\phi_3 = m_2f_2\phi_2 = m_5f_5\phi_5;$ $f_3\phi_3 = m_2f_2\phi_2 = f_4\phi_4;$
	0	0	0	$f_3\phi_3 = m_2f_2\phi_2 = f_6\phi_6;$ or $f_3\phi_3 = m_2f_2\phi_2 = f_4\phi_4 = f_6\phi_6$
	0	0	0	$f_4\phi_4; f_4\phi_4 = m_5f_5\phi_5; f_4\phi_4 = m_5f_5\phi_5 = f_1\phi_1; f_4\phi_4 = m_5f_5\phi_5 = f_3\phi_3;$
	1	0	0	$f_4\phi_4 = m_5f_5\phi_5 = m_2f_2\phi_2;$ or $f_4\phi_4 = m_5f_5\phi_5 = f_1\phi_1 = f_3\phi_3$
	0	0	0	$f_6\phi_6; f_6\phi_6 = m_5f_5\phi_5; f_6\phi_6 = m_5f_5\phi_5 = f_1\phi_1; f_6\phi_6 = m_5f_5\phi_5 = f_3\phi_3;$
	0	0	1	$f_6\phi_6 = m_5f_5\phi_5 = m_2f_2\phi_2;$ or $f_6\phi_6 = m_5f_5\phi_5 = f_1\phi_1 = f_3\phi_3$
Nuclear only	+	+	+	$m_2f_2\phi_2$
	0	0	0	
	0	0	0	$m_5f_5\phi_5$
	+	+	+	
	+	0	+	$f_1\phi_1 = f_3\phi_3; f_1\phi_1 = f_3\phi_3 = m_2f_2\phi_2; f_1\phi_1 = f_3\phi_3 = m_2f_2\phi_2 = m_5f_5\phi_5;$ $f_1\phi_1 = f_3\phi_3 = m_2f_2\phi_2 = f_4\phi_4; f_1\phi_1 = f_3\phi_3 = m_2f_2\phi_2 = f_6\phi_6;$ or $f_1\phi_1 = f_3\phi_3 = m_2f_2\phi_2 = f_4\phi_4 = f_6\phi_6$
	0	0	0	
	0	0	0	$f_4\phi_4 = f_6\phi_6; f_4\phi_4 = f_6\phi_6 = m_5f_5\phi_5; f_4\phi_4 = f_6\phi_6 = m_2f_2\phi_2 = m_5f_5\phi_5;$ $f_4\phi_4 = f_6\phi_6 = m_5f_5\phi_5; f_1\phi_1; f_4\phi_4 = f_6\phi_6 = m_5f_5\phi_5 = f_3\phi_3;$ or $f_4\phi_4 = f_6\phi_6 = m_5f_5\phi_5 = f_1\phi_1 = f_3\phi_3$
	+	0	+	
Cytoplasmic only	+	0	0	$f_1\phi_1 = f_4\phi_4$ or $f_1\phi_1 = f_4\phi_4 = m_2f_2\phi_2 = m_5f_5\phi_5$
	+	0	0	
	0	0	+	$f_3\phi_3 = f_6\phi_6$ or $f_3\phi_3 = f_6\phi_6 = m_2f_2\phi_2 = m_5f_5\phi_5$
	0	0	+	
Both	+	0	0	$f_1\phi_1 = f_6\phi_6$ or $f_1\phi_1 = f_6\phi_6 = m_2f_2\phi_2 = m_5f_5\phi_5$
	0	0	+	
	0	0	+	$f_3\phi_3 = f_4\phi_4$ or $f_3\phi_3 = f_4\phi_4 = m_2f_2\phi_2 = m_5f_5\phi_5$
	+	0	0	

Nuclear and/or cytoplasmic polymorphism	Equilibrium frequencies ^a			Maximum term(s) of echo fitnesses ^b
	+	0	+	$f_1\phi_1 = f_3\phi_3 = f_4\phi_4$ or $f_1\phi_1 = f_3\phi_3 = f_4\phi_4 = m_2f_2\phi_2 = m_5f_5\phi_5$
	+	0	0	
	+	0	+	$f_1\phi_1 = f_3\phi_3 = f_6\phi_6$ or $f_1\phi_1 = f_3\phi_3 = f_6\phi_6 = m_2f_2\phi_2 = m_5f_5\phi_5$
	0	0	+	
	+	0	0	$f_1\phi_1 = f_4\phi_4 = f_6\phi_6$ or $f_1\phi_1 = f_4\phi_4 = f_6\phi_6 = m_2f_2\phi_2 = m_5f_5\phi_5$
	+	0	+	
	0	0	+	$f_3\phi_3 = f_4\phi_4 = f_6\phi_6$ or $f_3\phi_3 = f_4\phi_4 = f_6\phi_6 = m_2f_2\phi_2 = m_5f_5\phi_5$
	+	0	+	
	+	0	0	$f_1\phi_1 = m_5f_5\phi_5$
	+	+	+	
	0	0	+	$f_3\phi_3 = m_5f_5\phi_5$
	+	+	+	
	+	+	0	$m_2f_2\phi_2 = f_4\phi_4$
	+	0	+	$m_2f_2\phi_2 = f_6\phi_6$
	0	0	+	
	+	0	+	$f_1\phi_1 = f_3\phi_3 = f_4\phi_4 = f_6\phi_6$ or $f_1\phi_1 = f_3\phi_3 = f_4\phi_4 = f_6\phi_6 = m_2f_2\phi_2 = m_5f_5\phi_5$
	+	0	+	
	+	0	+	$f_1\phi_1 = f_3\phi_3 = m_5f_5\phi_5$
	+	+	+	
	+	+	+	$m_2f_2\phi_2 = f_4\phi_4 = f_6\phi_6$
	+	0	+	
	+	+	+	$m_2f_2\phi_2 = m_5f_5\phi_5$
	+	+	+	

^aThe equilibrium genotypic frequencies for AA/C , Aa/C , and aa/C are listed in the first row, and AA/c , Aa/c , and aa/c in the second row, in this order. “+” means that genotype is present at equilibrium with frequency between 0 and 1.

^bThe conditions are specified with the maximum term(s) of echo fitnesses. For example, $m_2f_2\phi_2 = m_5f_5\phi_5$, means $m_2f_2\phi_2 = m_5f_5\phi_5 > f_1\phi_1 = f_3\phi_3 = f_4\phi_4 = f_6\phi_6$, and the relative magnitudes of the last four terms do not matter.

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Fig. 1.

Sample trajectories of cytonuclear genotype and allele frequencies in a selfing population under fertility, viability, and gametic selection. Frequencies for the six joint genotypes and two alleles (nuclear allele A and cytoplasmic allele C) are calculated according to Eqs. (4)–(8) and plotted as a function of generation t for a large selfing population for 20 generations. The six genotypes have equal frequency at generation 0. The selection parameters are (if not specified, fertility and viability parameters have a value of 1 and meiotic drive parameters have Mendelian segregation values, i.e. $m_1 = m_3 = m_4 = m_6 = 0.25$, $m_2 = m_5 = 0.5$): (A) $\phi_2 = \phi_3 = \phi_4 = \phi_5 = \phi_6 = 0.8$, $m_4 = m_6 = 0.2$, $m_5 = 0.6$. (B) $\phi_1 = \phi_3 = \phi_4 = \phi_5 = \phi_6 = 0.8$, $\phi_2 = 2.4$. (C) $\phi_1 = \phi_3 = 1.2$, $\phi_4 = \phi_5 = 0.8$, $m_1 = m_3 = m_4 = m_5 = 0.2$, $m_2 = m_5 = 0.6$. (D) $\phi_3 = \phi_4 = \phi_5 = \phi_6 = f_1 = f_3 = f_5 = f_6 =$

0.8. (E) $\varphi_1 = \varphi_6 = 0.8$, $\varphi_2 = f_5 = 2.4$. (F) $\varphi_4 = \varphi_6 = f_1 = f_3 = 0.8$, $m_1 = 0.2$, $m_3 = m_4 = m_6 = 0.3$, $m_5 = 0.4$.

Fig. 2.

The number of generations for a selfing population to reach equilibrium is negatively correlated with the difference of the two largest echo fitnesses. The figure shows 1000 runs with randomly generated fertility, viability, and meiotic drive parameters. All populations start with equal frequencies for all six genotypes. The equilibrium is reached if the sum of absolute changes in the six genotypic frequencies is at most 10^{-7} in a single generation.

Table 1

Frequencies of joint cytonuclear genotypes in adults

Cytotype	Nuclear genotype			
	<i>AA</i>	<i>Aa</i>	<i>aa</i>	
<i>C</i>	u_1	v_1	w_1	x
<i>c</i>	u_2	v_2	w_2	y
Total	u	v	w	1.0

Table 2
Fertility (f_i), viability (φ_i) and gametic (m_i) selection parameters

Cytotype	Nuclear genotype		
	<i>AA</i>	<i>Aa</i>	<i>aa</i>
<i>C</i>	f_1, φ_1, m_1	f_2, φ_2, m_2	f_3, φ_3, m_3
<i>c</i>	f_4, φ_4, m_4	f_5, φ_5, m_5	f_6, φ_6, m_6

Table 3
Cytonuclear genotypic frequencies at equilibrium under biologically meaningful selection conditions in a selfing population

Nuclear and/or cytoplasmic polymorphism	Selection conditions	Cytonuclear genotypes ^a				Sample trajectory ^b		
		AA/C	Aa/C	aa/C	AA/c	Aa/c	aa/c	
Neither	$f_1\phi_1 > m_2f_2\phi_2, f_3\phi_3, f_4\phi_4, m_5f_5\phi_5, f_6\phi_6$	1	0	0	0	0	0	A
	$f_3\phi_3 > f_1\phi_1 > m_2f_2\phi_2, f_4\phi_4, m_5f_5\phi_5, f_6\phi_6$	0	0	1	0	0	0	
	$f_4\phi_4 > f_1\phi_1 > m_2f_2\phi_2, f_3\phi_3, m_5f_5\phi_5, f_6\phi_6$	0	0	0	1	0	0	
	$f_6\phi_6 > f_1\phi_1 > m_2f_2\phi_2, f_3\phi_3, f_4\phi_4, m_5f_5\phi_5$	0	0	0	0	0	1	
Nuclear only	$m_2f_2\phi_2 > f_1\phi_1, f_3\phi_3, f_4\phi_4, m_5f_5\phi_5, f_6\phi_6$	+	+	+	0	0	0	B
	$m_5f_5\phi_5 > f_1\phi_1, m_2f_2\phi_2, f_3\phi_3, f_4\phi_4, f_6\phi_6$	0	0	0	+	+	+	
	$f_1\phi_1 = f_3\phi_3 > m_2f_2\phi_2, f_4\phi_4, m_5f_5\phi_5, f_6\phi_6$	+	0	+	0	0	0	
	$f_4\phi_4 = f_6\phi_6 > f_1\phi_1, m_2f_2\phi_2, f_3\phi_3, m_5f_5\phi_5$	0	0	0	+	0	+	
Cytoplasmic only	$f_1\phi_1 = f_4\phi_4 > m_2f_2\phi_2, f_3\phi_3, m_5f_5\phi_5, f_6\phi_6$	+	0	0	+	0	0	D
	$f_3\phi_3 = f_6\phi_6 > f_1\phi_1, m_2f_2\phi_2, f_4\phi_4, m_5f_5\phi_5$	0	0	+	0	0	+	
Both	$m_2f_2\phi_2 = m_5f_5\phi_5 > f_1\phi_1, f_3\phi_3, f_4\phi_4, f_6\phi_6$	+	+	+	+	+	+	E F
	$f_1\phi_1 = f_3\phi_3 = f_4\phi_4 = f_6\phi_6 > m_2f_2\phi_2, m_5f_5\phi_5$	+	0	+	+	0	+	

^aThe equilibrium frequency for each genotype is classified as 0 (absent), 1 (the only genotype present), or "+" (present at a frequency <1).

^bCorresponding sample trajectories shown in Fig. 1