Original article

Familial *versus* mass selection in small populations

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Abstract – We used diffusion approximations and a Markov-chain approach to investigate the consequences of familial selection on the viability of small populations both in the short and in the long term. The outcome of familial selection was compared to the case of a random mating population under mass selection. In small populations, the higher effective size, associated with familial selection, resulted in higher fitness for slightly deleterious and/or highly recessive alleles. Conversely, because familial selection leads to a lower rate of directional selection, a lower fitness was observed for more detrimental genes that are not highly recessive, and with high population sizes. However, in the long term, genetic load was almost identical for both mass and familial selection for populations of up to 200 individuals. In terms of mean time to extinction, familial selection did not have any negative effect at least for small populations ($N \leq 50$). Overall, familial selection could be proposed for use in management programs of small populations since it increases genetic variability and short-term viability without impairing the overall persistence times.

familial selection / deleterious mutation / genetic load / extinction / genetic variation

1. INTRODUCTION

Haldane [17] defined familial selection as the selective regime under which each family in a population contributes the same number of adults in the next generation. Selection acts among offspring within families and not among the entire set of offspring produced in the population as in the case of mass or ordinary selection.

Such a selection may occur in mammals when embryonic deaths increase the probability of survival of their sibs in the same litter, or in plants with restricted seed dispersal [8]. However, the exact realization of this selective

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regime in nature is restricted [22], and the main interest in studying familial selection resides in the potential applications of familial selection in captive breeding programs.

The property of familial selection to nearly double the effective size of a population [9] leads to both a slower rate of inbreeding and genetic drift. As a result, a population under familial selection retains high genetic variability and therefore preserves the potential of future adaptations [14].

Moreover, familial selection leads to a slower rate of directional selection relative to mass (or ordinary) selection [17, 22]. This could be advantageous for captive populations because it retards adaptation to captivity [1, 13]. However, for such populations, one could argue that the lower efficiency of familial selection will lead to a higher frequency of deleterious mutations and hence a loss of fitness. Indeed, for large populations at mutation-selection balance, familial selection is expected to double the genetic load relative to mass selection [7].

However, when small populations are considered, the outcome of familial selection will depend on the trade-off between the lower efficiency of selection and the slower rate of genetic drift. Recently, Fernández and Caballero [11] carried out some simulations to evaluate the effect of familial selection on population fitness in the first generations after the implementation of this regime. According to their findings, genetic load in small populations will be almost the same under both mass and familial selection in the short-term. However, it is not clear in their analysis whether a threshold population size exists after which familial selection becomes significantly less efficient and should not therefore be proposed for management of endangered populations. Furthermore, we feel that, as long as uncertainty concerning the values of mutation parameters persists, a more thorough analysis of the joint effect of the population size and the strength of selection (Ns) on the relative outcome of the two selective regimes is needed.

Furthermore, conservation programs of endangered populations should also be concerned with the effects of management measures on the long-term persistence of these populations.

The goal of this study was therefore to examine the effect of familial selection on the genetic load of small populations both in the short and in the long term. For this purpose, we, first, investigated the effect of familial selection on the genetic load of the populations in the first twenty generations after the implementation of this selective regime. Second, to assess the relative outcome of familial and mass selection in the long run, we calculated the genetic load of populations at the mutation-drift-selection balance. Finally, in order to directly evaluate the overall effect of familial selection on population persistence, an estimation of the mean time to extinction due to deleterious mutations was carried out for both mass and familial selection.

2. MATERIALS AND METHODS

We considered a two allele model per locus, A being the wild-type allele and a an unconditionally deleterious and partially recessive allele. We denote as D, H and R the frequency of the AA, Aa and aa genotypes. The relative fitness of the AA, Aa and aa genotypes are 1, $1 - hs$, and $1 - s$ respectively, where s is the selection coefficient and h the dominance coefficient of the deleterious allele.

In order to study the effect of familial selection on the genetic load during the first generations a Markov-chain approach was used (from now on referred to as the transition matrix approach). Although the transition matrix approach is regarded as the most accurate mathematical method dealing with this problem [10,26], it presents some serious computational limitations in particular when population size increases. Diffusion approximations allow us to overcome these limitations, and they will be used to calculate the long-term genetic load (populations at mutation-drift-selection balance) and times to extinction.

For a full description of the transition matrix approach in the case of mass selection, the reader may refer to Ewens [10], Schoen *et al.* [31] and Theodorou and Couvet [32] among others. Here, we will only develop the case of familial selection.

2.1. Genetic load at equilibrium

To find the frequency distribution of the deleterious allele at equilibrium, we used the general formula [9]

$$\phi(x) = \frac{C}{V_{\delta x}} \exp \left(2 \int \frac{M_{\delta x}}{V_{\delta x}} \mathrm{d}x \right) \tag{1}$$

where x is the frequency of the deleterious allele ($0 \leq x \leq 1$), $M_{\delta x}$ the mean rate of change in x per generation, $V_{\delta x}$ the variance in δx due to random sampling of the gametes; in a population of effective size N_e:

$$V_{\delta x} = \frac{x(1 - x)}{2N_e}; \tag{2}$$

C is a constant which is adjusted so that

$$\int_0^1 \phi(x)\mathrm{d}x = 1. \tag{3}$$

The expected load per locus in the population is given by the integral

$$L = \int_0^1 l(x)\phi(x)\mathrm{d}x \tag{4}$$

where $l(x)$ is the mean contribution to genetic load of a mutant of frequency x.

Next, we derive the expressions of $M_{\delta x}$, $\phi(x)$ and $l(x)$ for the case of mass and familial selection.

2.1.1. Mass selection

The mean change in allele frequency due to mass selection is

$$M_{\delta x} = -sx(1 - x)[h + (1 - 2h)x] \tag{5}$$

and the stationary distribution of the allele frequency ([9], p. 445)

$$\phi(x) = C \exp\left[-2N_e sx(x + 2h(1 - x))\right]x^{4N_e u - 1}(1 - x)^{4N_e v - 1} \tag{6}$$

where u is the mutation rate per locus per generation from the A to a allele, and v is the reverse mutation rate.

The mean contribution to genetic load of a mutant gene with frequency x is:

$$l(x) = 2hsx(1 - x) + sx^2. \tag{7}$$

2.1.2. Familial selection

King [22] gives some approximate relationships for the mean change of allele frequency per generation for some special classes of mutations. We extended his analysis for the general case of arbitrary dominance.

From Table I, the mean genotype frequencies after selection are:

$$D' = D^2 + H\left[\frac{2D}{2 - hs} + \frac{H}{4 - 2hs - s}\right]; \tag{8a}$$

$$H' = 2DR + 2(1 - hs)H\left[\frac{D}{2 - hs} + \frac{H}{4 - 2hs - s} + \frac{R}{2 - hs - s}\right]; \tag{8b}$$

$$R' = R^2 + (1 - s)H\left[\frac{H}{4 - 2hs - s} + \frac{2D}{2 - hs - s}\right]. \tag{8c}$$

The corresponding allele frequency is $q' = R' + H'/2$.

Making the approximation, $H \approx 2x(1 - x)$, and after some rearrangements, the mean change in allele frequency due to selection, $M_{\delta x} = q' - q$, becomes:

$$M_{\delta x} \approx -sx(1 - x)[a + 2(bx + cx^2)] \tag{9}$$

where

$$a = \frac{h}{2 - hs}; \tag{9a}$$

$$b = \frac{1}{4 - 2hs - s} - \frac{h}{2 - hs}; \tag{9b}$$

$$c = \frac{1}{s(2 - hs)} - \frac{1}{4 - 2hs - s} - \frac{1 - s}{s(2 - hs - s)}. \tag{9c}$$

Table I. Genotypes surviving with familial selection.

Genotype of parents	Frequency of crosses	Frequency of offspring within each family		
		AA	*Aa*	*Aa*
$AA \times AA$	D^2	$f_{11} = 1$	$f_{12} = 0$	$f_{13} = 0$
$AA \times Aa$	$2DH$	$f_{21} = 1/(2 - hs)$	$f_{22} = (1 - hs)/(2 - hs)$	$f_{23} = 0$
$AA \times aa$	$2DR$	$f_{31} = 0$	$f_{32} = 1$	$f_{33} = 0$
$Aa \times Aa$	H^2	$f_{41} = 1/(4 - 2hs - s)$	$f_{42} = (2 - 2hs)/(4 - 2hs - s)$	$f_{43} = (1 - s)/(4 - 2hs - s)$
$Aa \times aa$	$2HR$	$f_{51} = 0$	$f_{52} = (1 - hs)/(2 - hs - s)$	$f_{53} = (1 - s)/(2 - hs - s)$
$aa \times aa$	R^2	$f_{61} = 0$	$f_{62} = 0$	$f_{63} = 1$

Hence, from equations (1), (2) and (9), the stationary distribution of the allele frequency is:

$$\phi(x) = \exp\left[-4N_e s\left(ax + bx^2 + c\frac{x^3}{3}\right)\right] x^{4N_e u - 1}(1-x)^{4N_e v - 1} \tag{10}$$

with $N_e = 2N - 1$. Notice that for the values of s used in this study the term $cx^3/3 \ll bx^2$ and can be neglected.

The mean contribution to the genetic load of a mutant with frequency x can be calculated by equation (7).

2.2. Mean time to extinction

An estimation of the mean time to extinction due to deleterious mutations can be derived by means of diffusion approximations.

As noted by Lynch *et al.* [25,26], the process of mutation accumulation in a population, which initially consists of mutation-free individuals, can be divided into three phases. During phase 1, mutations accumulate until a balance between mutation, drift and selection arises. This balance marks the beginning of phase 2 during which segregating mutations reach a steady state and fixations occur at a constant rate. Although mean fitness declines, we assume that population size remains constant and equal to the carrying capacity of the environment, K. Finally, in phase 3, the accumulation of deleterious mutations causes populations to decline in size until ultimate extinction occurs.

To estimate the length of phase 1, we followed the analysis of Ohta and Kimura [20] and Caballero and Hill [4] whereas the length of phase 2 and 3 was calculated as in Lynch *et al.* [26].

2.3. Mutational models

The rate of the accumulation of deleterious mutations in a population would depend jointly on the mutation rate, the selection coefficient and the level of dominance of deleterious alleles. Although most of these parameters are not adequately known, several studies concerning *Drosophila melanogaster* suggest that the majority of mutations are slightly deleterious ($\bar{s} = 0.01 - 0.03$) with mutation rates per diploid genome of $U = 1$ and a mean dominance coefficient of $\bar{h} = 0.2 - 0.4$ (see review in [28]). However, the validity of these estimated values has recently been questioned; new experimental studies on *Drosophila melanogaster* and other organisms suggest that the mutation rates are lower and the average effect in fitness higher than that previously predicted [2,5,19].

In this study, we investigated two sets of parameters for deleterious mutations (Tab. II). The mutant effects are assumed to follow a gamma distribution,

$$g(s) = (\beta/\bar{s})^\beta s^{b-1} e^{-s\beta/\bar{s}}/\Gamma(\beta) \tag{11}$$

Table II. Sets of parameters for deleterious mutations.

	U	s	h	β
Model I	1	0.02	0.35	1
Model II	0.1	0.2	0.2	2

with shape parameters $\beta = 1$ (exponential distribution) and $\beta = 2$ for each model respectively, in accordance to the analysis of Keightley [18], García-Dorado and Caballero [15] and García-Dorado *et al.* [16].

To examine the outcome of mutations with various effects, we proceeded as in Wang *et al.* [33]. One mutant with a given selection coefficient, s, was sampled from the distribution defined by equation (11). The genetic load, or mean time to extinction, was then calculated for this mutant under mass and familial selection. This process is repeated for a large number of deleterious mutants (10^4) in order to ensure the convergence of our results. The geometric mean was used to calculate the final output of the expected genetic load (mean time to extinction).

3. RESULTS

3.1. Genetic load in the short term

We first investigated how parameters such as population size, selection and dominance coefficients influence the short-term performances of familial and mass selection.

Whether the effect of familial selection on population fitness is beneficial depends highly on the strength of selection (Fig. 1). For slightly deleterious alleles, familial selection reduced the rate of fitness loss. The reason is that selection was ineffective against these mutants in both cases, and the accumulation of deleterious mutations was governed by the action of genetic drift. Thus, populations under familial selection will show higher fitness due to enhanced effective size that this type of selection implies. Conversely, mass selection was more effective when selection was strong. As long as mutants were not highly recessive, the effect of selection overcame the effect of genetic drift, and therefore our results approached the deterministic expectation under which genetic load is halved with mass selection [7,22].

The relative increase in fitness with familial selection is a decreasing function of the dominance of deleterious alleles (Fig. 1). Familial selection enhanced the effective size of populations. Consequently, the rate of inbreeding was lower and higher levels of heterozygosity were conserved within populations. Hence, highly recessive alleles were masked in the heterozygous form and fitness was higher relative to mass selection. Conversely, for co-dominant alleles, familial selection lowered population fitness for all values of s.
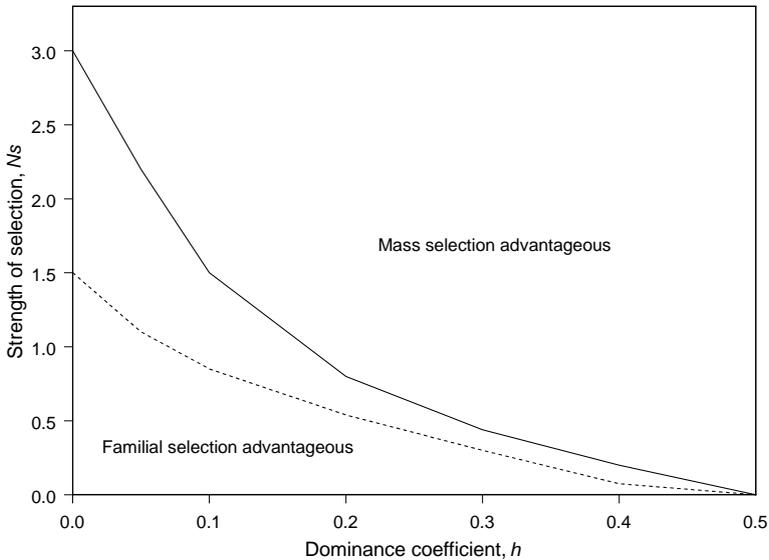
Figure 1. The influence of the dominance coefficient (h) and strength of selection (Ns) of deleterious mutations on the genetic load with mass and familial selection (i) at generation 20 (solid line); (ii) at equilibrium (dashed line). The curves correspond to combinations of h and s for which fitness is equal for both regimes. In the region below the curves, fitness is higher with familial selection, while in the region above the curves fitness is higher with mass selection. Population size is set to $N = 10$, the mutation rate per locus per generation towards the deleterious allele is $u = 10^{-5}$ ($U = 1$) and the rate of reverse mutations $v = 10^{-6}$.

We also examined the relationship between genetic load and population size for the two different models proposed by the empirical observations (see section 2).

The results from Model I show that familial selection significantly increased the fitness of small populations ($N < 30$), *e.g.* for a population of 10 individuals, an 8% increase in fitness with familial selection was observed at the 20th generation (Fig. 2). However, for higher population sizes, mass selection performed better although the differences remained low for populations of up to 50 individuals.

Conversely, when more detrimental mutations of lower mutation rates were considered (Model II), familial selection resulted in a 3% decrease in fitness for almost all population sizes (Fig. 2). Notice, however, that with this model the reduction in fitness relative to an infinite population was in any case slight; relative fitnesses with familial selection were always higher than 0.95. If it is revealed that this model better describes the mutational process, previous models would have overestimated the importance of the mutation accumulation
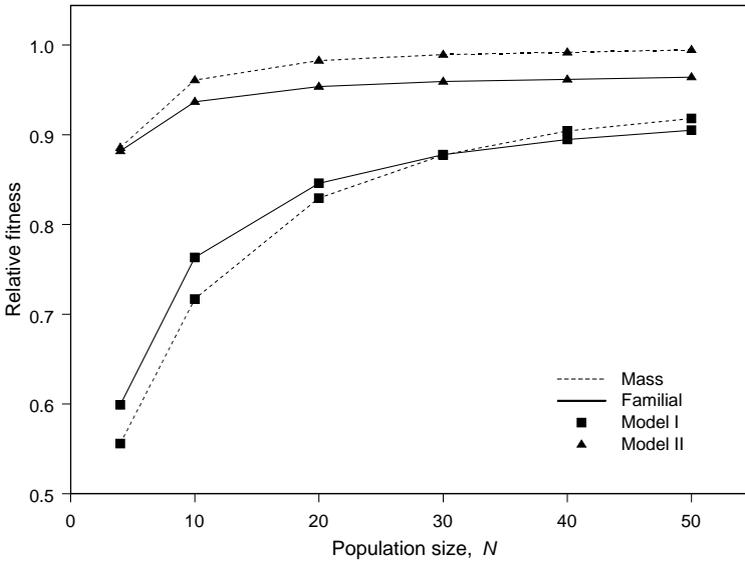
Figure 2. The mean fitness at generation 20 with mass and familial selection in relation to population size for two different sets of mutation parameters (see Tab. II). The fitness values are scaled by the fitness expected in an effectively infinite population at mutation-selection balance.

on the persistence of a small population, *e.g.* Lynch *et al.* [26, 27]. However, in all the experiments that suggest these mutation parameters, the existence of an undetected class of very slightly deleterious alleles, which could alter the predicted distribution of selection coefficients and mutation rates, cannot be ruled out [2, 19].

3.2. Testing diffusion approximations

In terms of genetic load at equilibrium, diffusion approximations and the transition matrix approach gave almost identical results when $Ns < 1$, the deviation of diffusion approximations being less than 1% (Tab. III). For higher deleterious effects, the diffusion approach overestimated genetic load. However, even for such mutants the relative differences between mass and familial selection were independent of the method used.

Moreover, the mean times to extinction predicted by diffusion approximations and the transition matrix approach were identical as long as the reproductive rates were not too low, $R \geq 20$ (results not shown). For lower reproductive rates, the assumption of constant population size during phase 2 does not hold [26] and the estimation of the mean time to extinction with diffusion approximations is invalidated.

Table III. Genetic load per locus calculated by means of transition matrix approach and diffusion approximations for familial and mass selection. The population size is set to $N = 50$.

Ns	h	Mass Load ($\times 10^{-3}$)		Familial Load ($\times 10^{-3}$)	
		Matrix	Diffusion	Matrix	Diffusion
0.2	0	3.4817	3.4801	3.4805	3.481
	0.5	3.4820	3.4811	3.4825	3.4831
0.5	0	7.8690	7.8616	7.8681	7.8730
	0.5	7.8638	7.8658	7.8757	7.8814
1	0	11.507	11.504	11.510	11.555
	0.5	11.513	11.518	11.529	11.583
1.5	0	9.8936	9.9832	9.9120	10.0449
	0.5	9.8970	10.0001	9.9292	10.0880
2	0	6.0191	6.2106	6.0462	6.2286
	0.5	6.0129	6.2312	6.0507	6.2694
3	0	1.3137	1.3941	1.3382	1.4450
	0.5	1.3104	1.4474	1.3408	1.4683
4	0	0.2261	0.2544	0.2427	0.2780
	0.5	0.2316	0.2748	0.2536	0.2941
5	0	0.0436	0.0512	0.0568	0.0670
	0.5	0.0520	0.0622	0.0715	0.0833
10	0	0.0101	0.0115	0.0196	0.0240
	0.5	0.0185	0.0211	0.0346	0.0394

Overall, the influence of the approach on our results was minor and we will thereafter show results obtained only with diffusion approximations.

3.3. Genetic load at equilibrium

We first noticed that the range of selection and dominance coefficients for which familial selection showed lower genetic load at equilibrium relative to mass selection was decreased compared to the case of the short-term load (Fig. 1). This was because familial selection slowed the rate of mutation accumulation but did not effectively change the probability of the ultimate fixation of these mutants.

The differences in genetic load at equilibrium between mass and familial selection were therefore minor for small populations and/or slightly deleterious mutations (Tab. III and Fig. 3). For these cases, deleterious mutations will actually accumulate to high frequencies and genetic load is substantial for both
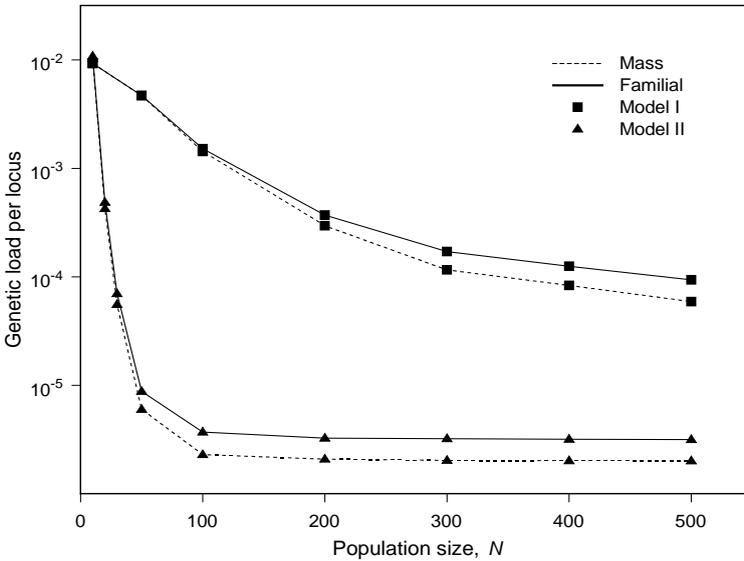
Figure 3. The genetic load per locus at equilibrium with mass and familial selection in relation to population size for two different sets of mutation parameters (see Tab. II). The mutation rate per locus per generation towards the deleterious allele is $u = 10^{-5}$ for the Model I and $u = 10^{-6}$ for Model II; the rate of reverse mutations is $v = 0.1u$.

selective regimes (see also [21]). It was only after a threshold of $Ns \sim 5$ that the higher effectiveness of mass selection reduces genetic load to lower levels relative to familial selection.

In accordance with the results concerning the short-term fitness, when the mutation set corresponded to model II, genetic load was substantially lowered even for small population sizes ($N \sim 50$). Differences between the two selective regimes were therefore of minor importance.

3.4. Mean time to extinction

For both mass and familial selection, the mean time to extinction was minimized for intermediate values of Ns ($Ns \sim 1$, Fig. 4). This was because highly deleterious mutations are kept in low frequencies by selection, whereas nearly neutral alleles accumulate but have lesser effects on fitness [23,24].

For values of Ns for which time to extinction was low, the effect of familial selection was low but increased with Ns. It had a minor effect for slightly deleterious mutations, while it significantly decreased the mean time to extinction for higher values of Ns e.g. for $Ns = 2$ and $R = 20$, the average numbers of generations until extinction were 465 and 348 for mass and familial selection respectively, which represents a reduction of 25%.
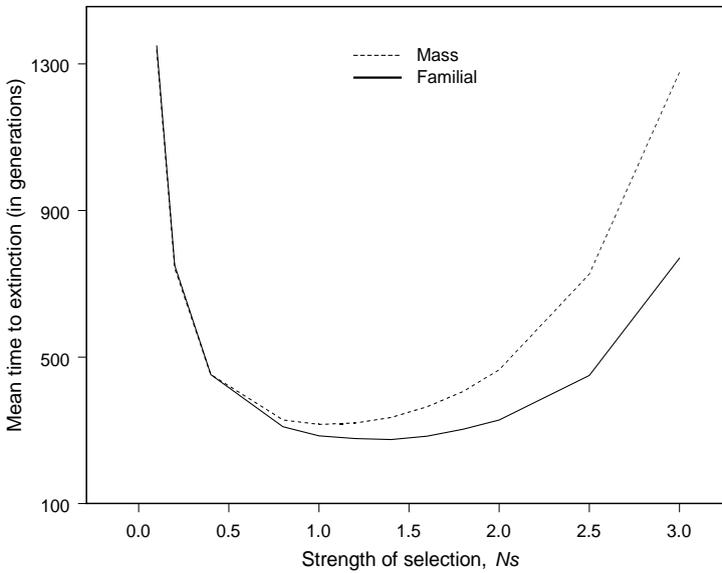
Figure 4. Mean time to extinction with mass and familial selection in relation to the strength of selection (Ns). The population size is set to $N = 20$, the net reproductive rate to $R = 20$, the total mutation rate per genome to $U = 1$ and the dominance coefficient to $h = 0.35$.
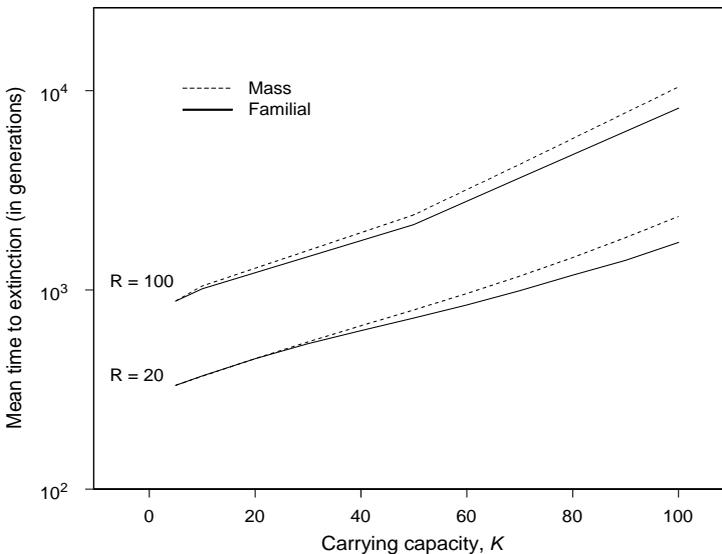

Figure 5. Mean time to extinction with mass and familial selection in relation to population size and the net reproductive rate. The initial size of populations coincides with the carrying capacity. The set of mutation parameters corresponds to Model I (see Tab. II).

Figure 5 shows the relationship between population size and mean time to extinction. We show results corresponding only to the mutation set of Model I. The mean time to extinction predicted by Model II is several orders higher than that by Model I and should not concern conservation programs. If we take for instance $N = 10$, $R = 20$, the mean time to extinction for both selective regimes was of the order of 10^4 generations.

Our findings suggest that familial selection would not have any negative effect on the persistence of small populations ($N \leq 50$). However, for larger populations, familial selection results in a decrease in mean time to extinction.

In our analysis, we considered a relatively large net reproductive rate ($R = 20 - 100$). This was because for lower values of the net reproductive rate, diffusion approximations are inaccurate (see also [26]). With lower reproductive rates, mean time to extinction will be substantially decreased. We expected, however, that our main conclusion, *i.e.* times to extinction are similar under both familial and mass selection for $N \leq 50$, would hold. Evidence supporting this statement comes from the work of Fernández and Caballero [11] according to which the differences in fitness between mass and familial selection decrease for low reproductive rates ($R = 5$).

4. DISCUSSION

The goal of this study was to examine the effect of familial selection on population viability (i) in the first generations after implementation of this selective regime and (ii) in the long term. The outcome of familial selection was compared with that of a random mating population under mass selection.

4.1. Short-term viability

Familial selection doubled the effective size of populations and therefore decreased the rate of inbreeding. This was reflected by a larger number of heterozygous loci and a smaller number of homozygous loci in a population under familial selection (results not shown). Hence, in small populations – where selection is ineffective against mildly deleterious mutations – highly recessive alleles were masked in the heterozygous form and fitness was higher relative to the case of mass selection.

Conversely, for higher population sizes and/or strongly detrimental mutants, the frequency of mutant genes was mainly determined by selection. A population under mass selection will have a greater opportunity to purge these mutants due to a more effective selection and will exhibit therefore higher fitness in relation to familial selection.

In conclusion, familial selection is expected to decrease the rate of fitness loss of small populations ($N \leq 30$) when slightly deleterious alleles of high mutation

rates are assumed (Model I), while the slight decrease of fitness relative to mass selection with a mutation set of more detrimental genes (Model II) is not of any concern in conservation management.

These findings were, in general, consistent with experimental findings, which suggest that familial selection would have a positive effect on the viability of small populations ($N = 8$) [3]. A recent experimental study has suggested that familial selection has no significant effect on fitness for intermediate population sizes [13]. However, the authors compared familial and mass selection for the same effective size (25 and 50 couples for familial and mass selection respectively). It is therefore unclear what would be the net effect of familial selection on the viability of a given population. Finally, Shabalina *et al.* [30], found that familial selection decreases substantially the fitness of large populations ($N_e = 400$).

The equalization of family sizes could also be combined with more sophisticated management methods that include the choice of the couples to be formed according to a given rule, *e.g.* the minimum coancestry method [12]. However, a comparison of our results with those of Fernández and Caballero [12] showed that such methods lead in most cases to an only slight improvement of population fitness with regards to familial selection. In any case, the general guideline of our study holds: conservation efforts should focus on measures that increase the effective size of the population, since such methods enhance both the genetic variability and population fitness. From this view-point, circular mating – for which the rate of loss of heterozygosity is of the order of $1/N^2$ – might be interesting to consider, although linkage between loci, associated to consanguineous matings, might impair the advantage expected when the single locus case is considered.

4.2. Long-term viability

To evaluate the long-term consequences of familial selection two different approaches were used. Using the single locus theory, we first calculated the effect of familial selection on the genetic load of populations at a mutation-drift-selection balance. Moreover, we estimated the mean time to extinction due to deleterious mutations for mass and familial selection.

In terms of genetic load per locus, familial selection was slightly advantageous for a narrow range of values of mutation parameters, *i.e.* for slightly deleterious and highly recessive alleles. However, for most of the values of dominance and selection coefficients, genetic load was almost identical with both familial and mass selection. Mass selection showed lower genetic load only for strongly deleterious mutants and/or large populations.

In terms of mean time to extinction, familial selection should not have any negative effect on small populations and/or slightly deleterious alleles ($Ns \leq 1$).

Our model predicted that the mean time to extinction should be identical for both mass and familial selection for populations of 50 individuals. Conversely, for higher population sizes, a decrease in mean time to extinction was observed with familial selection. For instance, for populations of 100 individuals and exponentially distributed mutation effects, familial selection resulted in a 20% reduction in mean time to extinction relative to mass selection. It is noteworthy that the reduction of the mean time to extinction with familial selection was due to genetic load caused by mutations that segregate in intermediate frequencies and not to a higher probability of fixation, which was identical for both selective regimes.

However, there are some factors that could modify the relative outcome of mass and familial selection.

The analysis concerning mean time to extinction considered multiplicative fitness across loci. If synergistic interactions are allowed, both genetic load and differences in population viability between mass and familial selection are expected to decrease [7].

On the contrary, if higher selection coefficients are considered, familial selection will be more disadvantageous. If, for instance an average selective effect of 5% is assumed, for a population of $N = 50$, a 30% decrease in mean time to extinction with familial relative to mass selection is expected. However, there is a narrow range of values of selection coefficient for which this advantage is of practical importance. For highly detrimental mutants ($Ns > 2$), the time to extinction is several orders higher than for slightly deleterious alleles and would not be a matter of concern for conservation programs.

Overall, when endangered populations of small sizes are concerned, familial selection has two beneficial consequences: (1) it maintains high levels of genetic variability, which is important for future adaptations; and (2) it may be advantageous on the short-term viability of small populations without affecting the overall persistence time. It could, therefore, be a good candidate for use in the genetic management of such populations.

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APPENDIX

Familial selection

We consider a population of N individuals that form $N/2$ families. Selection operates within families leaving in the next generation two offspring per family. The expected frequencies of the different crosses and of progeny within each cross are given in Table I.

To calculate the elements of the transition matrix in the case of familial selection we proceeded as follows. The element $p_{i,j;k,l}$ of the transition matrix is given by the probability of having $R_{t+1} = j$ and $H_{t+1} = i$, $D_{t+1} = N - i - j$ individuals of the aa, Aa and AA genotypes respectively in generation $t + 1$ given that we have $R_t = l$, $H_t = k$, $D_t = N - k - l$ in generation t. This probability can be expressed as the product of the probability of having $i_1 AA \times AA$ crosses, . . . , $i_6 aa \times aa$ crosses (see Tab. I) given that there are $R_t = l$, $H_t = k$, $D_t = N - k - l$ genotypes in generation t, and the probability of having $R_{t+1} = j$ and $H_{t+1} = i$, $D_{t+1} = N - i - j$ genotypes in generation $t + 1$ given $i_1 AA \times AA$ crosses, . . . , $i_6 aa \times aa$ crosses. In other words:

$$p_{ij,kl} = \text{Prob}[(i_1, \ldots, i_6)/(D_t = N - k - l, H_t = k, R_t = l)]$$
$$\times \text{Prob}[(D_{t+1} = N - i - j, H_{t+1} = i, R_{t+1} = j)/(i_1, \ldots, i_6)]. \quad \text{(A.1)}$$

The first term of the product was calculated as follows. Let A denote the event that $i_1 AA \times AA$ crosses, . . . , $i_6 aa \times aa$ crosses are formed and B denote

the event that $R_t = l$, $H_t = k$, $D_t = N - k - l$ genotypes occur in generation t. The first term of the product can therefore be expressed by the conditional probability $\text{Prob}(A/B)$.

$$\text{Prob}(A/B) = \frac{\text{Prob}(A \cap B)}{\text{Prob}(B)} \tag{A.2}$$

where

$$\text{Prob}(B) = \frac{N!}{k!l!(N - k - l)!} D_t^{N-k-l} H_t^k R_t^l \tag{A.2a}$$

and

$$\text{Prob}(A \cap B) = \frac{\left(\dfrac{N}{2}\right)!}{i_1! i_2! i_3! i_4! i_5! i_6!} (D_t^2)^{i_1} (2D_t H_t)^{i_2} (2D_t R_t)^{i_3} (H_t^2)^{i_4} (2H_t R_t)^{i_5} (R_t^2)^{i_6}. \tag{A.2b}$$

The possible number of i_2 crosses varies between 0 and the minimum of AA and Aa genotypes: $i_2 = 0, \ldots, \min(N - k - l, k)$. Knowing that we have $i_2 AA \times Aa$ crosses, $i_3 = 0, \ldots, \min(N - k - l - i_2, l)$. Similarly, $i_5 = 0, \ldots, \min(k - i_2, l - i_3)$. Notice that given the number of crosses, i_2, i_3, i_5 we know i_1, i_4, i_6, that is, $i_1 = (N - k - l - i_2 - i_3)/2$, $i_4 = (k - i_2 - i_5)/2$, $i_6 = (l - i_3 - i_5)/2$. Substituting the above expressions for i_1, i_4 and i_6 in equation (A.2b), equation (A.1) becomes:

$$p_{i,j;k,l} = \left[\frac{N!}{k!l!(N - k - l)!}\right]^{-1} \sum_{i_2, i_3, i_5} \frac{\left(\dfrac{N}{2}\right)!}{i_1! i_2! i_3! i_4! i_5! i_6!}$$
$$\times 2^{i_2 + i_3 + i_5} \times \text{Prob}(i, j/i_1, \ldots, i_6). \tag{A1$'$}$$

The probability of having $R_{t+1} = j$ and $H_{t+1} = i$, $D_{t+1} = N - i - j$ genotypes in generation $t + 1$ given $i_1 AA \times AA$ crosses, $\ldots$, $i_6 aa \times aa$ crosses, $\text{Prob}(i, j/i_1, \ldots, i_6)$, was calculated as follows.

Considering that the outcome of selection and drift within each cross is independent of the outcome in the rest of the crosses, the probability of taking $i, j, N - i - j$ genotypes given $i_1 AA \times AA$ crosses, $\ldots$, $i_6 aa \times aa$ crosses is:

$$\text{Prob}(i, j/i_1, \ldots, i_6) = \sum_{j_{ak}, j_{bk}=0,\ldots,2i_k}^{j_{bk}+j_{ak} \leq 2i_k} \prod_{k=2,4,5} \text{Prob}(j_{ak}, j_{bk}/i_k). \tag{A.3}$$

where j_{ak}, j_{bk} is the number of Aa and aa offspring produced by the cross k. Notice that the i_3 (i_6) crosses $AA \times aa$ ($aa \times aa$) give $2i_3$ ($2i_6$) offspring Aa

(*aa*) with probability 1. The number i, j of *Aa* and *aa* genotypes in the next generation is therefore $i = 2i_3 + j_{a2} + j_{a4} + j_{a5}, j = 2i_6 + j_{b2} + j_{b4} + j_{b5}$.

Finally, the probability of taking j_{ak}, j_{bk} individuals of genotype *Aa* and *aa* respectively within the cross k ($k = 2, 4, 5$) is given by the trinomial distribution

$$\text{Prob}(j_{ak}, j_{bk}/i_k) = \frac{(2i_k)!}{j_{ak}!j_{bk}!(2i_k - j_{ak} - j_{bk})} \times f_{k1}^{2i_k - j_{ak} - j_{bk}} \times f_{k2}^{j_{ak}} \times f_{k3}^{j_{bk}}. \quad \text{(A.4)}$$

For the values of f_{ki}, see Table I.

Genetic load at equilibrium

To examine the equilibrium frequencies $\mathbf{Q_{eq}}$, numerical methods were used (the procedures used are those described in Press *et al.* [29]). The mean genetic load of a population at a given locus was computed as follows [26, 31]:

$$l = hsH + sR \quad \text{(A.5)}$$

where

$$H = \sum_{i,j=0}^{N} \frac{i}{N} q_{ij} \quad \text{(A.5a)}$$

$$R = \sum_{i,j=0}^{N} \frac{j}{N} q_{ij} \quad \text{(A.5b)}$$

where q_{ij} is the probability of having i heterozygotes and j homozygotes for the mutant allele at equilibrium, and is calculated by the transition-matrix approach, described above.

Initial conditions

We have considered populations issued from an infinite population under mutation-(mass) selection balance. The equilibrium frequency (q_{eq}) at a given locus of the mutant allele in the ancestral population is obtained from the equation [9]:

$$s(1 - 2h)q_{eq}^2 + sh(1 + u)q_{eq} - u = 0.$$

To find the distribution of genotype frequencies in generation 0, $\mathbf{Q_0}$, the multinomial distribution of equation (6) was used with $D = (1 - q_{eq})^2$, $H = 2q_{eq}(1 - q_{eq})$ and $R = q_{eq}^2$.

In the case of simulations, the interval [0,1] was divided into three regions [0,D], [D, D+H], [D+H, 1], where D and H were calculated as above. To find the genotype at each locus of an individual a random number was generated.

The genotype will be *AA*, *Aa* or *aa* if the number falls in the first, second or third region respectively.

The assumption that the initial population is formed from a large ancestral population at the mutation-selection balance corresponds to an abrupt reduction in population size, which may not be realistic in natural populations. If the decrease is more gradual, the rate of fitness loss will be slower. However, we checked our model for several values of the initial allele frequency and found that the relative outcome of mass and familial selection was independent of the initial frequency.

Distribution of mutational effects

To examine the effect of variable mutational effects we proceeded as in [6].