SELECTION CRITERIA TO PURGE DELETERIOUS ALLELES

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INTRODUCTION

An optimal conservation program should aim at minimizing both genetic drift and the rate of accumulation of deleterious alleles. However, it was shown that methods used to minimize genetic drift (e.g. minimization of kinship, equalization of parental contribution) are suboptimal with respect to minimal accumulation of deleterious alleles (Schoen *et al.*, 1998; Fernández and Caballero, 2001a, b). Unfortunately, little is known about selection strategies for purging deleterious alleles. The objective of this computer simulation was therefore to evaluate different selection criteria (random, viability, kinship, inbreeding, ancestral inbreeding, and inbreeding index) with respect to their effectiveness to purge various types of alleles (lethal to mildly deleterious).

MATERIAL AND METHODS

Genetic model and mating scheme. We considered a genome with 500 biallelic fitness loci, each with alleles A and a. All loci were assumed to be unlinked and to segregate independently. An overview of the genetic models is given in Table 1. The initial frequency of allele a was set to 0.001 for all six models.

Genetic model ^A		Relative viability			
		AA	Aa	aa	
S	h	1	1 - <i>hs</i>	1 - <i>s</i>	
0.150	0.000	1.000	1.000	0.850	
	0.500	1.000	0.925	0.850	
	0.700	1.000	0.895	0.850	
1.000	0.000	1.000	1.000	0.000	
	0.020	1.000	0.980	0.000	
	0.500	1.000	0.500	0.000	

Table 1. Genetic models used in simulation

^As is the coefficient of selection against *aa* and *h* is the dominance coefficient of *a*

The breeding population consisted of 30 individuals with a sex ratio of 1:2. Potential parents were drawn randomly from a base population of unrelated animals for the first parental generation. Each selected dam was mated randomly to one of the potential sires and gave birth to six offspring. Potential parents for the next generation were chosen from the produced offspring according to six different selection criteria and mated randomly. We assumed that selection occurs at the diploid stage of the life cycle and that the loci act multiplicatively in determining viability. Therefore, the viability of an individual is the product of its 500 relative viability values. Survival of an individual was determined by comparing its viability with a number randomly drawn from a uniform distribution. The individual survived if the random number was smaller than its individual viability or died otherwise. One hundred repetitions were carried out for each selection criterion and genetic model (scenarios: see below). A total of 36 scenarios over 40 discrete generations of constant population size was evaluated. The effectiveness of purging was assessed by two means, the reduction of the number of

deleterious alleles per generation and the average viability per generation. In addition, the rate of inbreeding and effective population size per generation were calculated (Falconer and Mackay, 1997).

Selection criteria. Six different selection criteria were investigated. (i) Random selection (RS): Parents of the next generation were chosen and mated randomly, used as the reference scheme. (ii) High viability (HV): Parents with high viability were selected. (iii) Low kinship (LK): The kinship coefficient is defined as the probability that two alleles randomly sampled from the same locus in two individuals are identical by descent (Malécot, 1948). For each individual its mean kinship to living animals of the opposite sex was calculated. Animals with low mean kinship were selected and full-sibs mating was prohibited to mirror a situation comparable to a practical conservation breeding program. (iv) High inbreeding (HF): Selection based on high inbreeding coefficients was performed. Inbreeding coefficients (f) were calculated using the tabular method (Tier, 1997). (v) High ancestral inbreeding (HFA): Selection was based on high ancestral inbreeding. Ballou (1997) defined the ancestral inbreeding coefficient (f_a) as the cumulative proportion of an individual's genome that has previously been exposed to inbreeding in its ancestors. If deleterious alleles that contribute to inbreeding depression are effectively removed by selection when in the homozygous state in ancestors, then the effect of inbreeding in the current generation would decline as fa increases. In this study we used the true value of *fa* calculated as the proportion of alleles of an individual that has undergone identity by descent (IBD) in the past at least once. (vi) Inbreeding index (FX): Selection was based on an index combining the individual's f and fa by giving equal weightings on f and fa. The index was built as sum of f + (1 - fa). Animals with low index value were selected to favor a combination of low inbreeding and high ancestral inbreeding.

RESULTS AND DISCUSSION

Number of deleterious alleles and viability. An overview of selection results is given in Table 2. Any selection criterion became more effective for purging with increasing *s* resulting in a viability rebound. In cases where the genetic load resulted from deleterious alleles of large effect (s = 1), the deleterious alleles remaining in each generation decreased fastest under selection on HV followed by HF, HFA, RS, FX and LK when h > 0. However, when h = 0 (complete dominance of *A*) the deleterious allele could not be purged efficiently by selection on HV because viability did not allow distinguishing between heterozygote and the favorable homozygote genotypes. Therefore, selection on HFA or HF provided better results. No deleterious allele was present in any of the 100 repetitions after generation 2, 8, 9, 11, 18 and 19 for h = 0.5 under selection on HV, HF, HFA, FX, RS and LK, respectively.

If the genetic load resulted from deleterious alleles of small effect (s = 0.15) and h > 0, the arithmetic means over 100 repetitions for the number of deleterious alleles per animal stayed equal or higher under selection on HFA compared to RS, but the variation over the repetitions was clearly higher under HFA. The median (results not shown) for the number of deleterious alleles dropped faster over generations by selection on HFA, only selection on HV and HF were more efficient in purging 50% of repetitions (when h = 0.5, a median of 0.00 is reached in generation 1, 7 and 13, 24 and 31 for HV, HF, HFA, FX and RS, respectively. However, the median for LK was still 0.21 at generation 40). The mean of population viability increased as the number of deleterious alleles decreased for all scenarios (data not shown).

G	s ^A	h	Selection criteria						
			RS	HV	LK	HF	HFA	FX	
0	0.15	0.00	1.00 0.09	0.99 0.08	1.00 0.09	1.01 0.09	0.99 0.08	1.00 0.09	
		0.50	1.00 0.08	1.01 0.09	1.00 0.10	1.00 0.09	0.98 0.09	1.01 0.10	
		0.70	1.00 0.10	1.02 0.09	0.99 0.09	1.01 0.10	1.00 0.09	1.01 0.09	
	1.00	0.00	1.00 0.09	1.01 0.08	1.02 0.10	0.99 0.09	1.01 0.08	1.01 0.11	
		0.02	1.02 0.09	1.00 0.10	1.00 0.09	1.00 0.11	1.01 0.09	1.00 0.08	
		0.50	0.98 0.09	1.00 0.08	1.00 0.09	1.01 0.10	1.01 0.09	0.99 0.09	
10	0.15	0.00	0.89 0.48	0.37 0.37	1.01 0.49	0.76 0.91	0.71 0.87	0.98 0.76	
		0.50	0.43 0.30	0.00 0.00	0.71 0.43	0.23 0.45	0.48 0.69	0.53 0.47	
		0.70	0.31 0.25	0.00 0.00	0.62 0.37	0.24 0.53	0.31 0.56	0.39 0.36	
	1.00	0.00	0.67 0.40	0.37 0.44	0.83 0.38	0.10 0.19	0.17 0.23	0.58 0.44	
		0.02	0.50 0.30	0.00 0.00	0.74 0.34	0.09 0.18	0.15 0.19	0.58 0.49	
		0.50	0.00 0.01	0.00 0.00	0.02 0.04	0.00 0.00	0.00 0.00	0.00 0.01	
20	0.15	0.00	0.75 0.58	0.10 0.19	0.98 0.65	0.53 0.91	0.53 0.80	0.81 0.78	
		0.50	0.25 0.25	0.00 0.00	0.60 0.54	0.09 0.39	0.31 0.61	0.32 0.45	
		0.70	0.11 0.16	0.00 0.00	0.54 0.45	0.15 0.52	0.20 0.51	0.20 0.34	
	1.00	0.00	0.29 0.22	0.12 0.21	0.48 0.29	0.01 0.06	0.00 0.01	0.23 0.27	
		0.02	0.19 0.20	0.00 0.00	0.50 0.32	0.01 0.04	0.00 0.00	0.22 0.25	
		0.50	0.00 0.00	0.00 0.00	0.00 0.00	0.00 0.00	0.00 0.00	0.00 0.00	

Table 2. Mean and standard deviation (italic) of the average number of deleterious alleles *a* per generation (G) and animal over 100 repetitions under six different selection criteria

^As is the coefficient of selection against *aa* and *h* is the dominance coefficient of *a*

Rate of inbreeding and effective population size (N_e). As expected, the rate of inbreeding was lowest under LK and RS and highest under HF. However, the absolute level of inbreeding stayed lower with LK compared to RS over 40 generations. Figure 1 shows a representative pattern of N_e for all scenarios. The effective population size even increased after 5 generations of selection on HFA. N_e reached similar values after 20 generations of FX and HFA. Selections on HF led to a rapid decrease of N_e while under other selection criteria, N_e stayed relatively constant.



Figure 1. Effect of six selection criteria on the effective population size (N_e) when s = 0.15 and h = 0.5

8th World Congress on Genetics Applied to Livestock Production, August 13-18, 2006, Belo Horizonte, MG, Brasil

CONCLUSIONS

Purging is more effective when the recessive genotype is lethal and/or heterozygotes are less viable than homozygotes carrying the positive allele. Selection of individuals with high inbreeding coefficients was more efficient in purging than selection on high ancestral inbreeding coefficients. Nonetheless, in small populations where loss of genetic variability is an important issue, selection for high ancestral inbreeding coefficients is favorable. Effective population size of selection based on high inbreeding coefficient was lower than that of the other selection criteria.

ACKNOWLEDGEMENTS

This research project was financially supported by The Royal Thai government.

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