Optimum contribution selection conserves genetic diversity better than random selection in small populations with overlapping generations

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Abstract

Small, closed populations are at risk, because of a higher loss of genetic diversity and increased rates of inbreeding. Optimum contribution selection (OCS) limits inbreeding by controlling the increase of average relationship between individuals.
Stochastic computer simulations have been used to investigate how much benefit OCS is giving compared with random selection in different breeding scenarios.
This study showed that OCS results in lower average rates of inbreeding per generation, reduced by 30-85 % depending on the scenario. Generation intervals are about 20% longer. OCS maintains two times more alleles in populations than random selection. Also effective number of founders is higher. OCS is the most advantageous in populations with equal number of breeding males and females in both situations, with one and ten offspring per time step. In scenarios with less breeding males than females OCS gives more benefit in situations with ten offspring per female.

Introduction

From a genetic point of view, conservation programmes have two objectives: first, to reduce the increase in inbreeding and its collateral effects on fitness and other traits that can threaten the survival of the population; second, to maintain the highest level of genetic variability in the population (Eding and Laval, 1999). Two of the most important measures of genetic diversity in animal genetic recourses are heterozygosity and allelic diversity. The loss of heterozygosity is dependent on the rate of inbreeding, which causes increase of homozygosity. The allelic diversity means the average number of alleles in each locus.

The rate of inbreeding is the most important parameter in programmes that maintain genetic diversity (FAO, 2000). The rate of inbreeding per generation is more important than the actual level of inbreeding, because the actual level of inbreeding is relative to the base population, which is assumed to be unrelated and not inbred. The amount of genetic variation, which is maintained in the population in the long-term, is a function of the rate of inbreeding.

The long-term genetic contribution measures the proportion of genes from remote ancestors to the gene pool of the population. Per generation, genetic contributions sum to unity (Woolliams *et al.*, 1999). Inbreeding is minimized when contributions of ancestors to the next generation are equal. The descendant population with unequal representation of founders will contain less genetic variability than population with the same number of founders contributing equally (Lacy, 1989).

The generation interval is a measure of how long it takes to replace parents by their offspring. The generation interval for males/females is the average age of male/female at the birth of their selected offspring (Falconer and Mackay, 1996). In most of the animals populations, which are under the human control, generations are not discrete but overlapping. It means that there are parents at a different age having offspring in the same time. The selected offspring can have progeny at the same time as their parents have a next one. When generations overlap, the generation interval differs from the cohort interval (time step, time unit). Therefore the same coefficient has a different value when expressed per time unit or per generation. Generation interval can be also defined as the time in which genetic contributions sum to unity (Bijma and Woolliams, 1999). Prolongation of generation intervals is advantageous, because it is effective in reducing inbreeding (Wang *et al*., 1994) and the rate of loss of genetic variation (FAO, 2000) per time unit, because they are spread over more time units.

The predictions of loss of genetic variability are relative to the genetic variability in the founder population (Lacy, 1989). Because each generation is a genetic sampling from the previous one, some of the genetic variation present in the founders genotypes will be lost in the next generations. Therefore, to maintain genetic diversity in population, it is important to maximize the retention of founder diversity. From pedigree analysis one can obtain the number of founders represented in the individuals in the latest generation and effective number of founders, which includes the possible differences in founders contributions. The effective number of founders is defined as the number of equally contributing founders that would be expected to produce the same genetic diversity as the analysed population (Lacy, 1989). Effective number of founders reflects the rate of inbreeding, therefore maintaining equal genetic contributions of founders between generations is one important factor in minimizing the rate of inbreeding and conserving genetic variability of the population (Lacy, 1989, Caballero and Toro, 2000). Likewise, equal genetic contributions of non-founder ancestors contributes to minimize the rate of inbreeding.

Several authors (Meuwissen, 1997, Caballero and Toro, 2000) have demonstrated, theoretically and by computer simulations, that the most effective method to maintain genetic diversity is to find the optimal contributions of parents to the next generation. Optimum contribution selection (OCS) is the method, which maximizes the genetic gain while controlling the rate of inbreeding by maintaining the sum of squared genetic contributions at a constant value (Grundy *et al.*, 1998). OCS requires only estimated breeding values (EBV) of the selection candidates and relationships between them. The optimal solution is expressed in genetic contributions of selection candidates to the next generation (Meuwissen, 1997), which is proportional to the optimal number of offspring for each candidate (Meuwissen and Sonesson, 1998). OCS algorithm was developed for overlapping generations by Meuwissen and Sonesson (1998) and Grundy *et al.* (2000). In the method proposed by Meuwissen (1997) the genetic merit of the selected group is maximized with a constraint on the average genetic relationship between selected individuals. Additional constraints on the maximum biologically possible contributions, predefined number of selected sires and dams, and equal number of offspring per selected animals can be applied. Meuwissen and Sonesson (1998) extended the method of Meuwissen (1997) to overlapping generations. They also simulated a closed nucleus herd and stated that at the same rate of inbreeding OCS obtained more genetic gain than direct selection for BLUP breeding values. The advantage of OCS over BLUP selection is higher in smaller populations and with more stringent restrictions on inbreeding (Meuwissen and Sonesson, 1998). Sonesson *et al.* (2000) compared the algorithms of Meuwissen and Sonesson (1998) and Grundy *et al.* (2000) to determine the optimum genetic contribution of each animal in the current generation to genetic response and inbreeding in the future generations, and stated that both algorithms gave similar results in a simulation study. OCS can be applied in conservation programs for small and endangered populations with overlapping generations and several reproductive age classes. In this case the rate of inbreeding is minimized with no regards to genetic gain (Sonesson and Meuwissen, 2001).

After selecting individuals to be parents of the next generation, mating system is the next important factor in breeding programs. In the methods mentioned above (Meuwissen, 1997, Meuwissen and Sonesson, 1998, Grundy *et al.*, 1998, Grundy *et al.*, 2000) random mating is assumed. Sonesson and Meuwissen (2001) compared random mating with minimum coancestry mating, in both cases using OCS as the selection method. Minimum coancestry mating resulted in lower levels of inbreeding than random mating, but ΔF was approximately the same or somewhat higher.

In this paper random selection (RS) is compared with optimum contribution selection (OCS) in different scenarios. Different population sizes, sex ratios of mated individuals, number of offspring per female, and age when individuals are available as selection candidates are taken into consideration. On the basis of the literature cited above, it is assumed that optimum contribution selection will result in lower rate of inbreeding, longer generation intervals, less founder alleles lost and higher effective number of founders compared with random selection. The main purpose is to investigate how much benefit OCS is giving compared to random selection in the parameters given above.

Methods

In this paper computer simulations were used to model the selection schemes for random selection (where each candidate has equal chance to be selected and pass its genes to the next generation) and optimum contribution selection. Analysis was done for populations with overlapping generations. It was assumed that there are no mutations and migrations taking place. There was also no directional selection for any trait. The number of breeding males and females and the number of offspring per female were constant in all time steps, therefore, there were no changes in effective population size over time.

In Table 1 different breeding scenarios are presented, which were considered in this paper.

Table 1. Parameters of the breeding scenarios considered in this study.

No.	N_f	N_m:N_f	N_p	Minage	Maxage	N_{ts}	N_{rep}
1	50	1:1	1	4	12	50	10
2	50	1:15	1	4	12	50	10
3	100	1:1	1	4	12	50	10
4	100	1:15	1	4	12	50	10
5	200	1:1	1	4	12	50	10
6	200	1:15	1	4	12	50	9
7	50	1:1	10	2	6	20	10
8	50	1:5	10	2	6	20	10
9	100	1:1	10	2	6	20	3
10	100	1:5	10	2	6	20	5

N_f – number of breeding females;
N_m – number of breeding males;
N_p – number of offspring per female per time step;
Minage – minimal age when individuals can start to reproduce;
Maxage – maximal age when individuals are available as the parents;
N_{ts} – number of time steps of analysis,
N_{rep}- number of replicates for OCS.

Two types of populations with different reproductive parameters were considered. First with individuals reproducing from four to twelve years old (one year is equal to one time step of analysis) and one offspring per female per year (time step). Two different sex ratios among parents were considered: one female per male and fifteen females per one male. These populations were evaluated over fifty time steps.

In the second case individuals were reproducing from two to six years old and there was ten offspring per female per year. Like previously, there were two different sex ratios: one female per male and five females per male. Evaluation here was for twenty time steps. Number of time steps was smaller for this type of population than for scenarios with one offspring per female per time step, because of longer computing time required to run those scenarios.

Three different numbers of breeding females were considered for scenarios with one offspring per female: fifty, hundred and two hundreds. For scenarios with ten offspring per female, scenarios with fifty and hundred breeding females were considered.

Each of ten presented scenarios was applied two times: for random selection and optimum contribution selection algorithms.

In both selection schemes considered in this paper, random mating was assumed, which means that the selected individuals have equal chance of mating with any selected individual of the other sex.

Optimum contribution selection (as described in Grundy *et al.*, 2000) was implemented by Berg (2003) using an evolutionary algorithm (*EVA*). Estimated breeding values (EBV) of the selection candidates and relationships between them are required as the input to the program. *EVA* chooses animals with the highest EBV as the parents of the next generation, and at the same time optimizes their genetic contribution to the next generation using all given parameters and restrictions. *EVA* was also used for the random selection scheme. Estimated breeding values were assigned to the selection candidates randomly every time step. In this way, there was no directional selection. Constraints on the genetic contribution per sex, predefined number of selected sires and dams and number of offspring per selected animals were applied.

To run the simulations a SAS program procedure was used. This program is using three algorithms written in Fortran: *EVA* (Berg, 2003), *Pedig* (Boichard, 2002), and a program for doing the gene drop analysis.

Parameters given in Table 1 were used as input to the program. For OCS the number of initial time steps, for which selection is random, was specified as five for situation with twenty time steps and ten for situations with fifty time steps. Ten replicates were run for all scenarios for RS, for OCS the number of replicates is shown in Table 1. Because of very long computing time required to run the OCS scenarios the number of replicates is smaller for some scenarios.

Pedigrees were obtained for each replicate as output from the program. The program calculated coefficients of inbreeding (as described in Meuwissen and Luo, 1992), the rate of inbreeding and generation intervals from those pedigrees. These parameters are the average values across replicates.

As the next step, the gene dropping procedure (MacCluer *et al.*, 1986) was applied to each pedigree. In this procedure, two unique hypothetical alleles were assigned to each founder in the base population. The genotype of descendants was constructed working down the pedigree using stochastic methods to assign randomly genotype to each descendant based on Mendelian segregation of the parental alleles. The number of founder alleles lost through generations was obtained and calculated as the average over replicates.

To calculate the effective number of founders the *prob_orig.f* program, which is a part of the Pedig program created by Boichard (2002) was used. This program can be freely downloaded from http://www-sgqa.jouy.inra.fr/diffusions.htm. As the input to the program pedigrees created by simulation program were used. As the output from this program the number of founders, whose genes are present in the most recent population, was obtained. In addition, the effective number of founders was obtained. Also in this case average values for replicates were calculated.

Results

The rate of inbreeding

For all scenarios coefficient of inbreeding for optimum contribution selection is lower than for random selection (Table 2). It is also lower in situations with equal number of males and females compared to situations with fewer males than females. The coefficient of inbreeding is different for different population sizes. The bigger the population is, the smaller the coefficient of inbreeding is obtained. OCS is the most advantageous in populations with more offspring per female, and in scenarios with one offspring when there is equal number of breeding males and females.

Table 2. The coefficient of inbreeding in last time step of simulation and the average rate of inbreeding per generation. Averages over replicates are presented. The difference is given in percentage relative to RS.

Scenario	Inbreeding in last time step			Average rate of inbreeding per generation		
	RS	OCS	Diff. (%)	RS	OCS	Diff. (%)
1	0.0266	0.0037	-86	0.0039	0.0007	-83
2	0.2066	0.0698	-66	0.0334	0.0119	-64
3	0.0128	0.0017	-87	0.0019	0.0003	-84
4	0.0981	0.0592	-40	0.0152	0.0106	-30
5	0.0066	0.0009	-86	0.0010	0.0002	-83
6	0.0499	0.0273	-45	0.0076	0.0048	-37
7	0.0242	0.0040	-83	0.0042	0.0009	-79
8	0.0757	0.0158	-79	0.0135	0.0032	-76
9	0.0123	0.0016	-87	0.0022	0.0004	-84
10	0.0387	0.0089	-77	0.0069	0.0019	-73

Similarly to the coefficient of inbreeding, the rate of inbreeding is always lower for optimum contribution selection (lower than one percent, only in scenarios number 2 and 4 is slightly above) compared with random selection (Table 2). OCS gives more benefit in scenarios with ten offspring, and in scenarios with one offspring when there is equal number of breeding males and females.

Generation interval

Optimum contribution selection results in longer generation intervals than random selection (Table 3). OCS gives more benefit in scenarios with equal number of breeding males than females compared with situations with less males. In general, OCS is more beneficial in scenarios with ten offspring per female.

Table 3. Average generation interval. Averages over replicates are presented. The difference is given in percentage relative to RS.

Scenario	RS	OCS	Diff. (%)
1	7.41	9.12	23
2	7.36	8.65	18
3	7.41	9.15	24
4	7.45	8.81	18
5	7.43	9.10	22
6	7.49	8.74	17
7	3.54	4.51	28
8	3.47	4.23	22
9	3.55	4.55	28
10	3.55	4.30	21

Loss of founders alleles

Optimum contribution selection maintains more founders alleles in a population than random selection (Table 4). In scenarios with one offspring per female and equal number of males and females (scenarios number 1, 3 and 5) 26% less alleles are lost by last time step. When there are fifteen females per male (scenarios number 2, 4 and 6) OCS results in 3,5% less alleles lost. In scenarios with ten offspring per female the difference between optimum contribution selection and random selection is bigger. In situations where there is equal number of males and females (scenarios number 7 and 9), OCS results in average in 46% less alleles lost and 6% when there are five females per male (scenarios number 8 and 10). Generally, in all cases less alleles are lost when there is equal number of breeding males and females in populations.

In all situations OCS gives better results than RS. In scenarios with equal number of breeding males and females OCS results in two times more alleles left than random selection. In scenarios with less breeding males than females OCS maintains in average 50% more alleles than RS. More alleles are left in populations with ten offspring per female for both, optimum contribution and random selection.

Table 4. Number of alleles left in the populations of animals born in last time step. Averages over replicates are presented. The difference is given in percentage relative to RS.

Scenario	RS	OCS	Diff. (%)
1	43	84	96
2	9	19	109
3	83	170	105
4	20	29	47
5	169	332	96
6	41	61	49
7	53	122	130
8	24	34	43
9	103	238	132
10	45	69	53

Effective number of founders

Optimum contribution selection gives more benefit in number of founders scenarios with one offspring per female, especially in situations with equal number of breeding males and females (scenarios number 1, 3 and 5), where the difference between OCS and RS is on average 240% (Table 5).

Optimum contribution selection results also in a higher effective number of founders compared with random selection (Table 5). OCS has the biggest advantage in scenarios with equal number of breeding males and females, especially in scenarios with one offspring per female, 365% in average.

Table 5. Number of founders and effective number of founders. Averages over replicates are presented. The difference is given in percentage relative to RS.

Scenario	Number of founders			Effective number of founders		
	RS	OCS	Diff. (%)	RS	OCS	Diff. (%)
1	100	337	237	65	293	348
2	30	88	198	10	21	104
3	201	681	239	125	595	375
4	60	158	161	16	23	48
5	391	1343	244	248	1170	372
6	121	280	131	30	44	44
7	95	199	108	59	171	187
8	41	65	58	21	38	85
9	187	399	113	107	334	212
10	86	129	50	39	80	105

Discussion

In breeding programmes, whose main purpose is to maintain genetic diversity, one of the main goals is to keep the rate of inbreeding as small as possible (FAO, 2000). Optimum contribution selection is a good way to achieve that. In this study, both the coefficient of inbreeding and the rate of inbreeding per generation are smaller for OCS compared with random selection. Optimum contribution selection gives the rate of inbreeding per generation below or slightly above one percent in all scenarios. This is consistent with the recommendations of the FAO.

The rate of inbreeding in smaller populations is higher. It occurs for both optimum contribution and random selection. OCS is controlling the increase of average relationship, and therefore also future inbreeding, by reducing probabilities of selecting closely related individuals. OCS is more advantageous when there is an equal number of breeding males and females in the population. When individuals are selected randomly, the probability of mating parents with their offspring is higher with more males being selected, and OCS is avoiding co-selection of parents and their offspring.

Optimum contribution selection results in about 22% longer average generation intervals than random selection. Longer generation intervals are advantageous, because they reduce the rate of inbreeding, and thus the loss of genetic variation per time unit. The number of breeding individuals does not have any impact on the length of generation interval.

In general, as it was expected, optimum contribution selection results in less alleles lost. It occurs due to equalling of long-term contributions. Individuals that are less related, carrying different alleles are selected, thus more different alleles are passed on to the offspring. Most alleles are lost in scenarios with fewer males than females with both random and optimum contribution selection. Also less alleles are lost in scenarios with ten offspring per female, because it is more probable to maintain both alleles of a female when there is ten offspring per female.

For maintaining genetic diversity in a population, maximization of founder diversity retention is also an important factor. In this paper, the number of founders and effective number of founders were estimated to investigate this problem. It is important to maximize the effective number of founders, because it contributes to the rate of inbreeding. Optimum contribution selection by optimisation of ancestor contributions in descendants generation is able to maximize this coefficient.

The number of founders represented in the youngest, not yet selected individuals was calculated. The values obtained for OCS are always higher than for RS. The number of founders is higher in scenarios with an equal number of breeding males and females compared with fewer males than females. The effective number of founders is also higher for optimum contribution selection than for random selection in all cases. In scenarios with equal number of breeding males and females OCS is more advantageous in effective number of founders. It occurs, because random selection results in lower effective number of founders, like in all other scenarios, but in this case OCS gives effective number of founders only slightly lower than number of founders. This means that in this case optimum contribution selection results in almost maximal possible values.

Loss of genetic variation is inversely proportional to the effective population size. Effective population size can be maximized by equal number of breeding males and females in population. In this study, in scenarios with an equal number of males and females, a lower rate of inbreeding was obtained and also higher number of founders, and effective number founders and less alleles were lost than in scenarios with unequal numbers of males and females.

The optimum contribution selection procedure was developed to maximize the response to selection while controlling the rate of inbreeding and it is especially advantageous in small populations (Meuwissen and Sonesson, 1998, Grundy *et al.*, 1998). The majority of authors considering optimum contribution selection in unselected populations are assuming discrete generations (Sonesson and Meuwissen, 2000, Fernández, *et al.*, 2003). Results obtained in their studies show that OCS is effective in reducing the rate of inbreeding. Fernández *et al.* (2003) proposed several hierarchical designs to control inbreeding for situations with different numbers of breeding males and females. Sonesson and Meuwissen (2001) show advantages of optimum contribution selection in populations with different numbers of selection candidates, rates of individuals survival and number of newborn animals per time step for random and minimum coancestry mating. In most animal populations, generations are not discrete but overlapping. Replacement of the parents by their offspring is a continuous process and the generation interval differs from the cohort interval (year, time step). In this paper overlapping generations are assumed. The obtained rate of inbreeding seems to be smaller or equal than in similar simulations results found in the literature (Sonesson and Meuwissen, 2001). However, there are differences in number of time steps of simulations, number of replicates and number of selection candidates in each time step. Therefore, precise comparison of these results is not possible.

Conclusion

All coefficients discussed in this paper can be optimised using optimum contribution selection. It is effective in reducing the rate of inbreeding and prolonging generation intervals. It also results in less founders alleles lost through generations and a higher effective number of founders maintained in population. Optimum contribution selection is most effective in populations, which by their constitution (small overall and effective population size, smaller number of breeding males than females, bigger litters) are especially exposed to all those negative factors. It can be recommended as the best method to conserve rare, endangered breeds and their genetic diversity.

References

Berg, P. (2003). EVA version 1.4. Evolutionary algorithm for mate selection; User's Guide.

Bijma, P. and Woolliams, J. A. (1999). Prediction of genetic contributions and generation intervals in populations with overlapping generations under selection. *Genetics* **151**, 1197-1210.

Boichard, D. (2002). PEDIG: a fortran package for pedigree analysis suited for large populations. *7th World Congress on Genetics Applied to Livestock Production, August 19-23, Montpellier, France.*

Caballero, A. and Toro, M. A. (2000). Interrelations between effective population size and other tools for management of conserved populations. *Genetical Research* **75**, 331-343.

Eding, J. H. and Laval, G. (1999). Measuring genetic uniqueness in livestock. In: J.K. Oldenbroek (ed.) *Genebanks and the conservation of farm animal genetic resources*. ID-DLO, Lelystad, The Netherlands.

Falconer, D. S. and Mackay, T. F. C. (1996). *Introduction to quantitative genetics.* Fourth edition. Longman, Harlow.

FAO. (2000). *Secondary guidelines for development of farm animal genetic resources management plans; Management of small populations at risk.* FAO, Rome.

Fernández, J., Toro, M. A. and Caballero, A. (2003). Fixed contributions design vs. global coancestry to control inbreeding in small populations. *Genetics* **165**, 885-894.

Grundy, B., Villanueva, B. and Woolliams, J. A. (1998). Dynamic selection procedures for constrained inbreeding and their consequences for pedigree development. *Genetical Research* **72**, 159-168.

Grundy, B., Villanueva, B. and Woolliams, J. A. (2000). Dynamic selection for maximizing response with constrained inbreeding in schemes with overlapping generations. *Animal Science* **70**, 373-382.

Lacy, R. C. (1989). Analysis of founder representation in pedigrees: founder equivalents and founder genome equivalents. *Zoo Biology* **8**, 111-123.

MacCluer, J. W., VandeBerg, J. L., Rean, B. and Ryder, A. (1986). Pedigree analysis by computer simulation. *Zoo Biology* **5**, 147-160.

Meuwissen, T. H. E. (1997). Maximizing the response to selection with predefined rate of inbreeding. *Journal of Animal Science* **75**, 934-940.

Meuwissen, T. H. E. and Luo, Z. (1992). Computing inbreeding coefficients in large populations. *Genetics Selection Evolution* **24**, 305-313.

Meuwissen, T. H. E. and Sonesson, A. K. (1998). Maximizing the response of selection with a predefined rate of inbreeding: overlapping generations. *Journal of Animal Science* **76**, 2575-2583.

Sonesson, A. K., Grundy, B., Woolliams, J. A. and Meuwissen, T. H. E. (2000). Selection with control of inbreeding in populations with overlapping generations: a comparison of methods. *Animal Science* **70**, 1-8.

Sonesson, A. K. and Meuwissen, T. H. E. (2001). Minimization of rate of inbreeding for small populations with overlapping generations. *Genetical Research* **77**, 285-292.

Wang, J. L., Xu, J. C., Song, J. Z. and Tang, W. S. (1994). Study on mating systems for controlling inbreeding levels in domestic animal populations with overlapping generations. In *Proceedings of the Fifth World Congress on Genetics Applied to Livestock Population* **21**, 536-539.

Woolliams, J. A., Bijma, P. and Villanueva, B. (1999). Expected genetic contributions and their impact on gene flow and genetic gain. *Genetics* **153**, 1009-1020.