Theor Appl Genet (1995) 91:421–431

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Balancing selection response and rate of inbreeding by including genetic relationships in selection decisions

Received: 18 November 1994 / Accepted: 22 November 1994

Abstract An iterative selection strategy, based on estimated breeding values (EBV) and average relationship among selected individuals, is proposed to optimise the balance between genetic response and inbreeding. Stochastic simulation was used to compare rates of inbreeding and genetic gain with those of other strategies. For a range of heritabilities, population sizes and mating ratios, the iterative strategy, denoted ADJEBV, outperforms other strategies, giving the greatest genetic gain at a given rate of inbreeding and the least breeding at a given genetic gain. Where selection is currently by truncation on the EBV, with a restriction on the number of full-sibs selected, it should be possible to maintain similar levels of genetic gain and inbreeding with a reduction in population size of 10–30%, by changing to the iterative strategy. If performance is measured by the reduction in cumulative inbreeding without losing more than a given amount of genetic gain relative to results obtained under truncation selection on the EBV, then with the EBV based on a family index, the performance of ADJEBV is greater at low heritability, and is generally greater than where EBV are based on individual records. When comparisons of genetic response and inbreeding are made for alternative breeding scheme designs, schemes which give higher genetic gain within acceptable inbreeding levels would usually be favoured. If comparisons are made on this basis, then the selection method used should be ADJEBV, which maximises the genetic gain for a given level of inbreeding. The results indicated that all selection strategies used to reduce inbreeding had very small effects on the variance of gain, and so differences in this respect are unlikely to affect choices among selection strategies. Selection criteria are recommended based on maximising a selection objective which specifies the desired balance between genetic gain and inbreeding.

Key words Inbreeding · Selection · Genetic improvement

Introduction

Recent developments in animal breeding strategies designed to increase short-term genetic gain also have the potential to increase rates of inbreeding to levels of concern. These developments include evaluation using the records of all relatives (e.g., best linear unbiased prediction using an animal model), increased female reproductive rates (e.g., in cattle, use of multiple ovulation and embryo transfer or in vitro embryo production), and selection of animals at a younger age, using pedigree rather than progeny information. In the short term increased genetic gain associated with increased inbreeding will in the long term lead to decreased genetic gain due to declines in fitness and genetic variance. In many breeding schemes a balance between genetic gain and inbreeding is sought (Quinton et al. 1992). If inbreeding rates are sufficiently low to be of no concern, the best procedure is to select by truncation on estimated breeding values (EBV) of maximum accuracy. In practice, long-term inbreeding rates are controlled by maintaining large populations and by restricting the number of close relatives allowed to breed. Toro and Perez-Enciso (1990) used linear programming to select parental pairs which maximised the mean EBV but limited the mean inbreeding coefficient of the progeny, which reduced immediate inbreeding of progeny but did not have much effect on the long-term inbreeding rate, because it considered only relationships among mating pairs rather than relationships among all pairs of animals selected (De Boer and van Arendonk 1994).

Communicated by L. D. VanVleck

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Recently, Brisbane and Gibson (1995a), Verrier et al. (1993), and Grundy and Hill (1993) proposed strategies designed to reduce inbreeding while maintaining genetic response, based on reducing the correlation of the EBV of relatives through changes in the methods of genetic evaluation. Such methods are partially effective, but do not explicitly set a goal for selection.

If G_n is the genetic mean after n generations of selection, and F_n is the mean inbreeding coefficient, then a reasonable selection objective is

$$M_1 = G_n + DF_n, \tag{1}$$

where D is the value of unit of inbreeding relative to a unit of genetic gain and is usually negative. The value of D is often difficult to define (see Discussion). Nevertheless, there is in any breeding scheme a balance between G and F that will be optimum for a given n. Given M_1, it seems logical to find a method of selection based explicitly on predictions of G_n and F_n. The objective of this study was to examine a selection strategy based on an unbiased EBV and predictions of inbreeding contributions from relationships among selected animals. Wray and Goddard (1994) have proposed the same objective as (1) and defined an alternative approach (see Discussion).

Theory

To use the mean EBV of selected animals as a measure of the effect of a selection decision in a given generation on G_n seems reasonable. A measure of the effect on F_n is less obvious. In practice, the contribution of a particular animal to long-term inbreeding depends on changes in the frequency of its genes in the gene pool of future generations of descendants, which are dependent upon future selection decisions. Wray and Thompson (1990) noted that, with discrete generations of selection, the frequency of genes from a given ancestor reaches a stable equilibrium in the long term. They showed that if the genetic contribution of an ancestor is defined as the proportion of genes originating from that ancestor, then the asymptotic rate of inbreeding is equal to one-quarter of the sum of squares of stabilised genetic contributions across ancestors. The stabilised genetic contribution of an ancestor is partly dependent on its own genetic merit, and partly on Mendelian sampling and environmental contributions to the EBV of its descendants. The latter two are random events which are unknown when the ancestor is selected. However, it is known that, with Nm sires and Nf dams in each generation, the average stabilised contribution is 1/(2Nm) across sires and 1/(2Nf) across dams. These are also the actual contributions of every sire and dam to their progeny generation prior to selection. The mean relationship among animals in generation t, given by

$$\bar{a}_t = \frac{1}{4}\bar{a}_s + \frac{1}{2}\bar{a}_{sd} + \frac{1}{4}\bar{a}_d \tag{2}$$

(where $\bar{a}_s$, $\bar{a}_d$, $\bar{a}_{sd}$ are the mean additive relationships among sires, among dams, and between sires and dams of generation t animals) is a weighted sum of squares of contributions from all ancestors to parents of animals in generation t. If it is assumed that the contributions of all ancestors have reached their stabilised values, then the mean relationship among animals in generation $n(n > t)$ is equal to $\bar{a}_t$ plus the weighted sum of squared contributions to parents of generation n from animals in generations between t and n. This would be true if within-family selection was practised in the interval between generations t and n. Animals is generations between t and n do not exist at the time of the selection decision in generation t, and so the second term is independent of the first (i.e., $\bar{a}_n$ is equal to $\bar{a}_t$ plus a term independent of the selection decision in generation t). If mean relationship is a good measure of mean inbreeding under random mating, then $\bar{a}_t$ is a good measure of the effect of selection in generation t on F_n, subject to the assumption that contributions of ancestors of generation t remain constant in subsequent generations. An empirical approach to the prediction of the effect of selection on F_n, accounting for the effect of ancestral genetic merit on stabilised contribution, will be presented elsewhere (Brisbane and Gibson 1995b).

In generation t the population selection criterion to be maximised is

$$\begin{aligned} M_2 &= \frac{1}{2}\overline{EBV}_{t,s} + \frac{1}{2}\overline{EBV}_{t,d} - k\left[\frac{1}{2}\bar{a}_t\right] \\ &= \frac{1}{2}\overline{EBV}_{t,s} + \frac{1}{2}\overline{EBV}_{t,d} - k\left[\frac{1}{8}\bar{a}_{t,s} + \frac{1}{4}\bar{a}_{t,sd}\frac{1}{8}\bar{a}_{t,d}\right] \end{aligned} \tag{3}$$

where k is an arbitrary constant and $\overline{EBV}_{t,s}$ and $\overline{EBV}_{t,d}$ are the mean EBV of selected sires and dams. This selection strategy is termed ADJEBV, and its performance will be compared with those of strategies OMIT and SUBOPT described by Brisbane and Gibson (1995a), and the strategy REST, widely used in practice where animals are selected on EBV, but with the maximum number of animals selected from the same full-sib family restricted.

Methodology

General simulation methods and assumptions

Stochastic methods were used to simulate repeated cycles of selection, under the strategies OMIT, SUBOPT, ADJEBV and REST described below. The trait conforms to an additive infinitesimal model (e.g., Bulmer 1971), generations were discrete and selected animals were mated at random in a hierarchical design. Breeding values of base animals were distributed as $N(0,\sigma^2_{A0})$, environmental effects were distributed as $N(0,\sigma^2_e)$ in all generations, and the phenotypic record for each animal was the sum of the breeding value and the uncorrelated environmental effect. In each generation subsequent to the base, progeny breeding values were generated as

$$A_i = \frac{1}{2}A_s + \frac{1}{2}A_d + \Phi_i \tag{4}$$

where A_s and A_d are the breeding values of the sire and dam, and Φ_i is the Mendelian sampling term, distributed as $N[0, 0.5(1-0.5(F_s + F_d)\sigma^2_{A0}]$, where F_s and F_d are the inbreeding coefficients of the sire and dam. Inbreeding coefficients were calculated using the FORTRAN subroutine FINBRD (B. Tier 1986, unpublished). Each of the four selection strategies can produce a range of possible inbreeding and response rates. For each strategy, mean genetic merit was plotted against mean inbreeding after nine generations of selection. The units of genetic merit are initial genetic standard deviations, $\sigma_{A0} = 1$ and $\sigma^2_e = (1-h^2)/h^2$, where h^2 is heritability. In each generation there were Nm sires, Nf dams, $n_w/2$ progeny of each sex per dam, and $N = \mathrm{Nf}.n_w/2$ selection candidates of each sex.

Computing strategy for maximising the population selection criterion of ADJEBV

Nm sires and Nf dams are initially selected by truncation on the EBV based on a family selection index of the individual record, and the records of the full- and half-sibs. For the ith male candidate, the mean relationship with selected sires, $\bar{a}_{s,i}$, is calculated as

$$\bar{a}_{s,i\cdot} = \frac{\sum_{j=1}^{N} a_{s,ij}x_{sj}}{\sum_{j=1}^{N} x_{sj}}, \quad j \neq i \tag{5}$$

where $x_{sj} = 1$ if male j is a selected sire or 0 if male j is unselected, and $a_{s,ij}$ is the relationship of the ith male with the jth male (here, and throughout, the subscript . denotes averaging over the indicated level of the effect). If male i is a selected sire, $\bar{a}_{s,i.}$ involves summation of Nm-1 relationships, because the case where $j = i$ is not included at this stage. If male i is not selected, summation is over Nm relationships. An adjustment is then made to account for the relationship of the animal with itself ($a_{s,ii}$), to yield

$$\bar{a}^*_{s,i.} = \frac{1}{Nm}a_{s,ii} + \left(1 - \frac{1}{Nm}\right)\bar{a}_{s,i.} \tag{6}$$

The mean relationship of the ith male with selected dams, $\bar{a}_{sd,i}$, is calculated as

$$\bar{a}_{sd,i.} = \frac{1}{Nf}\sum_{j=1}^{N} a_{sd,ij}x_{dj} \tag{7}$$

Mean relationships of females with selected dams and with selected sires are obtained similarly. Note that $\bar{a}^*_{s,i.}$ is equal to the mean relationship of the ith male with selected males (including self) if the ith male is in the selected group. If the ith male is not selected then $\bar{a}^*_{s,i.}$ is a weighted combination of the relationship of the ith male with itself, and the mean relationship of the ith male with selected sires, such that the relationship of the animal with itself is given the same weight as it would be given for an animal in the selected group. The same is true of $\bar{a}^*_{s,d,l.}$ for females.

Adjusted EBV are then calculated as

$$EBV_{s,i,adj} = \frac{1}{2}EBV_{s,i.} - k\left(\frac{1}{8}\bar{a}^*_{s,i.} + \frac{1}{4}\bar{a}_{sd,i.}\right) \tag{8}$$

for the ith male, and

$$EBV_{d,l,adj} = \frac{1}{2}EBV_{d,l.} - k\left(\frac{1}{8}\bar{a}^*_{d,l.} + \frac{1}{4}\bar{a}_{ds,l.}\right) \tag{9}$$

for the lth female, where k is the adjustment factor of the mean relationships. The adjusted EBV given by (8) and (9) measure the contribution of each animal to M_2. In the adjusted EBV, relationships with selected animals of the opposite sex are given twice as much weight as relationships with animals of the same sex, because this subsequently happens in M_2. This ensures that the adjusted EBV provide an accurate measure to rank animals on the basis of their effect on M_2 when they are selected.

In most situations the number of possible combinations of selected animals is too large to find the maximum of (3) directly. Thus, the following iterative procedure is used. The unselected animal with the highest adjusted EBV is switched for the selected animal with the lowest adjusted EBV, and adjusted EBV for all animals are recalculated. If this switch results in an increase in the population selection criterion, M_2, it is accepted and the process repeated. Otherwise, it is rejected. When a switch is accepted, the animal switched out of the selected group returns to the unselected group, and is available for re-selection. When switches are accepted, one switch in males is followed by Nf/Nm switches in females. When a switch is rejected, the process shifts to the opposite sex, and if the switch there is rejected, the search is terminated. This iterative procedure has not been proven to maximise the population selection criterion, M_2.

Unadjusted EBV are calculated from a family selection index (Hazel 1943) of the individual record, the mean of n_w full-sib records (including the individual record) and the mean of $d.n_w$ half-sib records (including the individual and full-sib records, so $d = \mathrm{Nf/Nm}$). Index weights are calculated using base-population genetic parameters and remain constant in every generation. The value of k used in the adjusted EBV and in M_2 is varied in order to achieve a range of inbreeding and response rates. The number of times each candidate is selected is recorded to indicate how many cycles of selection are required and the pattern of selection across animals.

The OMIT strategy

Details of assumptions and methods used for simulation of OMIT were described by Brisbane and Gibson (1995a). Animals are selected on an index of their individual record, all half-sib records, and a variable number of full-sib records. Ranges of inbreeding and response rates are obtained across breeding schemes by varying the number of full-sib records used in the index. Within a given simulation, the number of full-sib records used is constant and index weights are calculated which maximise the accuracy of the EBV for the records which are used. In each generation of selection, index weights are re-calculated to maximise accuracy given the effect of selection on the parental variances (Brisbane and Gibson 1994a).

The SUBOPT strategy

Details of assumptions and methods used for simulation of SUBOPT were described by Brisbane and Gibson (1995a). Animals are selected on an index of their individual record, and all records of full and half-sibs. The index weights are found by the following procedure. The optimum index weights are calculated in the usual way (Hazel 1943) using base population genetic parameters, and then the index weight on the individual record is increased by some proportion (e.g., 10%, 20% or 30%). Because of this increase, the regression of true breeding value on the index is no longer unity. The index weight for the full-sib records is then reduced progressively until the regression returns to unity. The index weight on the half-sib records is not changed. Selection proceeds using these index weights in every generation. The size of the increase in the weight on the individual record is varied across simulations, which leads to different index weights and different combinations of inbreeding and genetic gain across breeding schemes.

The REST strategy

The unadjusted EBV is calculated for each animal as for the ADJEBV strategy. Nm sires and Nf dams are selected such that the mean unadjusted EBV is maximised in each sex, given restrictions that no more than S sires and D dams can be selected from any full-sib family. Across breeding schemes, S and D are varied to achieve a range of inbreeding and response rates.

Parameter combinations investigated

Effect of heritability

The four strategies, ADJEBV, REST, OMIT SUBOPT were compared at heritabilities of 0.1, 0.3 and 0.5. Small population sizes were used to save computing time, with Nm = Nf = 5 and $n_w = 12$ for each heritability. The number of replicates was 1000 in each case.

Effect of population size and mating ratio

The selection strategies were studied for the following four population structures: (1)Nm = 8, Nf = 64, (2)Nm = 16, Nf = 128, (3)Nm = 8, Nf = 128, (4)Nm = 16, Nf = 64.

In each case $n_w = 6$, $h^2 = 0.3$, with 800 replicates made for (1) and (3), and 600 replicates for (2) and (4). Comparison of (1) with (2) examines the effect of population size. Comparisons of (1) and (2) with (3) and (4) are designed to show the effect of varying the mating ratio.

Options for reduced population size with ADJEBV

At a given rate of inbreeding, ADJEBV is expected to give more genetic gain than REST. It is of interest to ask how much larger the population would have to be using REST to obtain the same response and inbreeding as with ADJEBV. The ADJEBV strategy was simulated for Nm = 8, Nf = 64, $n_w = 6$ and $h^2 = 0.3$. With REST three different population sizes were used, each with $n_w = 6$, $h^2 = 0.3$ and 800 replicates: (1)Nm = 9, Nf = 72, (2)Nm = 10, Nf = 80, (3)Nm = 11, Nf = 88.

ADJEBV and REST with EBV based on individual performance

ADJEBV and REST were examined for EBV based only on the individual record, as opposed to an index of relatives. All simulations had Nm = 8, Nf = 64, $n_w = 6$ and $h^2 = 0.3$. Number of replicates was 800 for REST and 600 for ADJEBV.

Results

The results are presented as plots of genetic gain versus inbreeding after nine generations of selection, in Figs. 1 to 9. Moving to the left, points on (1) the ADJEBV line represent increasing values of k, (2) those on the OMIT line represent decreasing numbers of relatives included in the index, (3) those on the SUBOPT line represent increasing weight on the individual record, and (4) those on REST line represent increasing the restrictions (i.e., decreasing the number) of full sibs allowed to breed. The values of k used to obtain each point for the ADJEBV strategy are given in the legend for each figure. Lines for ADJEBV, SUBOPT, and REST converge to the same point on the right of each plot, representing truncation selection on the EBV based on the optimum index calculated using base-population parameters, with no subsequent re-optimisation of the index weights. The line for OMIT does not end at the right-hand side at the same point as the other strategies, because index weights are re-optimised in each generation of selection. Moving to the left on any graph, the lines diverge as selection strategies differ increasingly. In all figures, one strategy is deemed to give a better performance than another if the combination of response and inbreeding achieved by the first strategy lies above and to the left of the combination acheived by the second. The first strategy then gives a better response at a given inbreeding, or lower inbreeding at a given response. Standard errors ranged from 0.01 to 0.025 for genetic gain, and from 0.0002 to 0.002 for cumulative inbreeding. ADJEBV and SUBOPT tended to give similar results, especially for higher inbreeding rates and in earlier generations.

The comparisons of SUBOPT with OMIT are given in more detail by Brisbane and Gibson (1994a), and are included here for comparison with the other methods. From Figs. 1 to 9 the strategies generally rank ADJEBV > SUBOPT > REST > OMIT in terms of the genetic gain achieved at any rate of inbreeding. For no instance shown in Figs. 1 to 9 did any strategy significantly outperform ADJEBV in terms of genetic gain at a given level of inbreeding. When the mating ratio is 1:1 (Figs. 1, 2 and 3) strategy REST becomes inferior in performance to OMIT at lower levels of inbreeding where more severe restrictions are placed on the number of full sibs selected. Figures 1, 2 and 3 are for six progeny

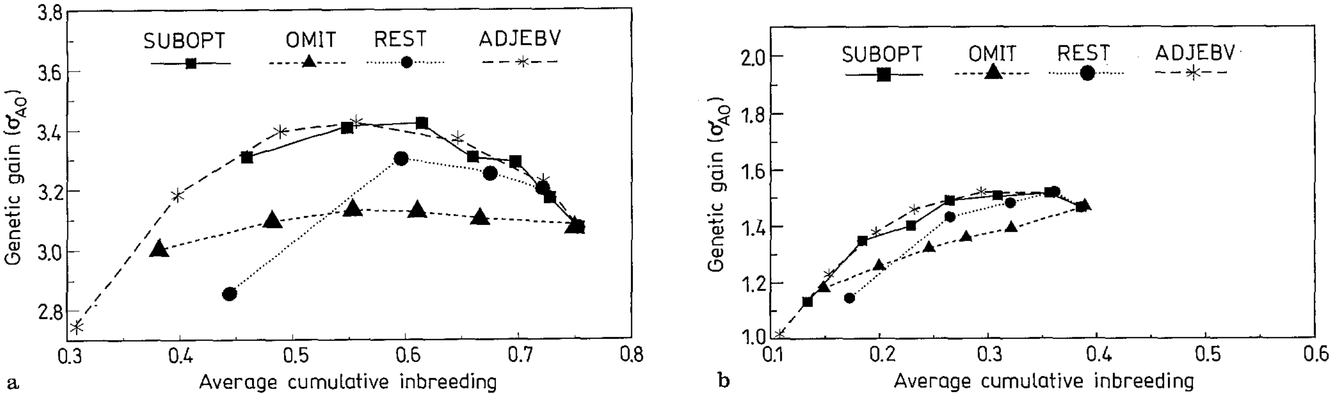

Fig. 1a,b Genetic gain plotted against inbreeding for four selection strategies with five parents of each sex in each generation and $h^2 = 0.1$. **a** Nine generations of selection; $n_w = 12$; $k = 0.3, 1, 2, 3, 5$, and 10. **b** Three generations of selection; $n_w = 12$; $k = 0.3, 1, 2, 3, 5$ and 10

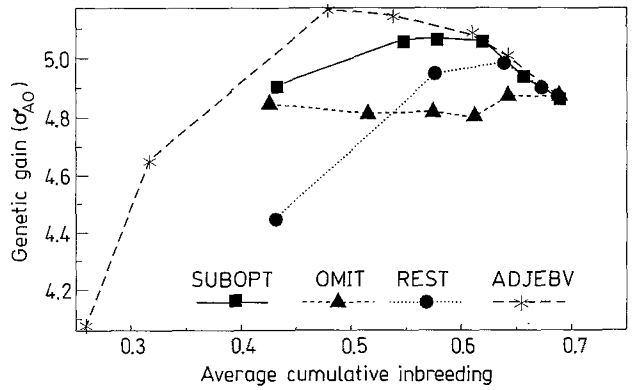

Fig. 2 Genetic gain plotted against inbreeding for four selection strategies after nine generations, with five parents of each sex in each generation and $h^2 = 0.3$; $n_w = 12$; $k = 0.5, 1, 2, 3, 10$ and 20

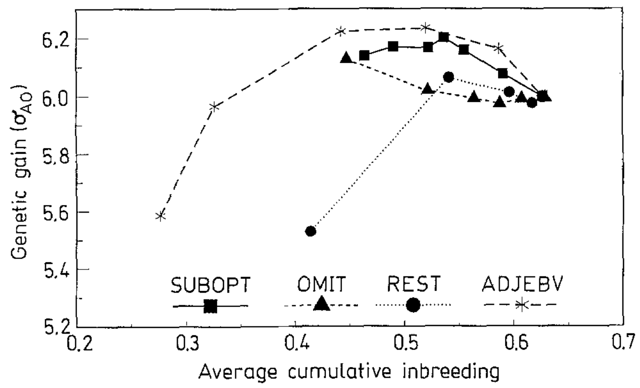

Fig. 3 Genetic gain plotted against inbreeding for four selection strategies after nine generations, with five parents of each sex in each generation and $h^2 = 0.5$; $n_w = 12$; $k = 0.5, 1.5, 3, 8$, and 15

of each sex per dam, and the four points for REST represent maximum of four, three, two and one males selected from a full-sib family. At generation 9, as the maximum number of full sibs selected decreased from four to two, response generally increased while inbreeding decreased, but when the maximum was further decreased to one, there was a sharp drop in response, presumably due to loss in selection intensity. For Nm = 5, Nf = 15, $n_w = 12$ and $h^2 = 0.1$, 0.3 or 0.5, and with the larger number of full-sib families, even the most stringent restriction had little effect on selection intensity, and REST outperformed OMIT in all cases (data not shown). Also ADJEBV had greater superiority over SUBOPT in this situation. The performance of SUBOPT might, however, be improved if the index weight on half-sib information were reduced in addition to that on full-sib information. Figures 1a, b show genetic gain and inbreeding at generations 9 and 3 for the same simulations (Nm = Nf = 5, $h^2 = 0.1$, $n_w = 12$), illustrating greater curvature of lines in later generations. After three generations, maximum genetic gain was achieved at close to the highest level of inbreeding, whereas after nine generations, maximum genetic gain occurred at much less than the highest level of inbreeding, due to the cumulative effect of inbreeding reducing genetic variance and hence selection response. Similar differences at generations 3 and 9 were observed for other parameter combinations (data not shown), although the effect was smaller for larger population sizes.

Effect of heritability

Figures 1a, b, 2 and 3 show results for four selection strategies with $h^2 = 0.1$, 0.3 and 0.5, at Nm = Nf = 5, with all figures drawn to the same scale. There was much less genetic gain, more inbreeding, and better performance of strategies ADJEBV, SUBOPT and REST at lower heritability. As inbreeding was reduced using ADJEBV, the loss of genetic variance due to inbreeding decreased, which increased response, while the selection intensity was reduced, which decreased response. The shape of the line observed on each graph is the net result of these two opposing actions. After nine generations of selection with $h^2 = 0.1$ (Fig. 1a), genetic gain was increased by about 0.36 units using ADJEBV, compared to truncation selection on the optimum index (equivalent to ADJEBV with $k = 0$). Inbreeding was reduced from 0.75 to 0.60. With $h^2 = 0.5$, the increase in response was about 0.24 units (Fig. 3) and inbreeding was reduced from 0.65 to 0.46. The proportionate increase in response was 12% at $h^2 = 0.1$ but only 4% at $h^2 = 0.5$. In the simulation model, genetic variance is close to a linear function of average inbreeding level [the variance of Mendelian sampling is $0.5(1-0.5(F_s+F_d)\sigma^2_{A0})$, as mentioned earlier, and the genetic variance is the sum of this and a linear function of the parental genetic variance]. The proportionate increase in variance retained is $(1-0.6)/(1-0.75)-1=0.6$ at $h^2 = 0.1$, and $(1-0.46)/(1-0.65)-1=0.54$ at $h^2 = 0.5$. With truncation selection on the EBV derived from family indexes, genetic gain should be roughly proportional to genetic variance. With ADJEBV the results were a 12% increase in gain with 60% more variance retained at low heritability and a 4% increase in gain with 54% more variance retained at high heritability. The fact that the increase in gain achieved in relation to the increase in variance retained was almost three-fold greater at low heritability suggests that loss in selection intensity is less at low heritability. When heritability is lower, so that EBV are more highly correlated and the effect of selection on inbreeding is greater, the ADJEBV procedure may find animals in families less related to the initially selected group which are of better additive genetic merit. At $h^2 = 0.1$ using ADJEBV, cumulative inbreeding can be reduced from 0.75 to 0.35 with no loss of genetic response (Fig. 1). At $h^2 = 0.5$ cumulative inbreeding can be reduced from 0.63 to 0.33 with no loss of genetic response (Fig. 3).

Effects of population size and mating ratio

Figures 4 to 7 show results for the four selection strategies for four population sizes with $h^2 = 0.3$. All figures

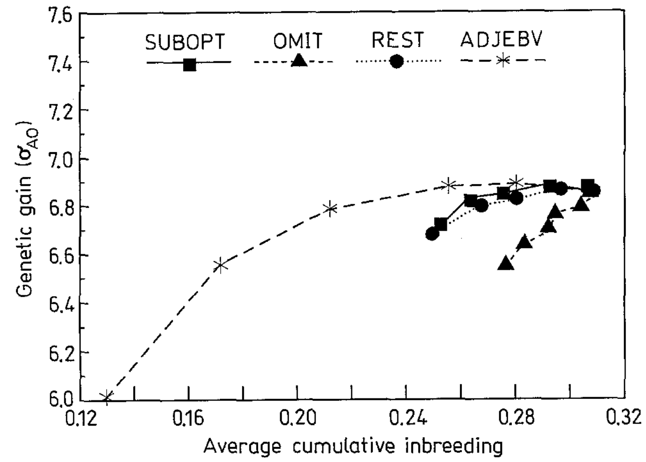

Fig. 4 Genetic gain plotted against inbreeding after nine generations of selection with eight sires and 64 dams in each generation; $h^2 = 0.3$; $k = 1, 2, 5, 10$ and 25

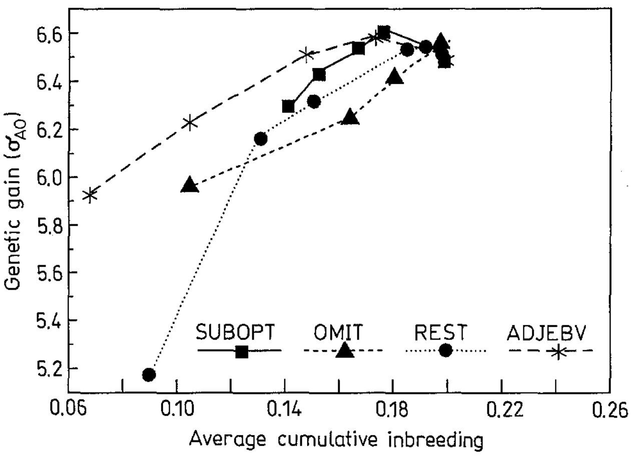

Fig. 7 Genetic gain plotted against inbreeding after nine generations of selection with 16 sires and 64 dams in each generation; $n_w = 6$, $h^2 = 0.3$; $k = 2, 5, 15$ and 25

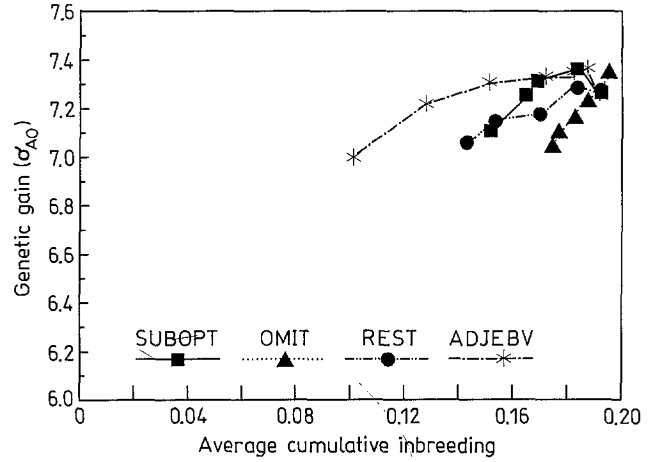

Fig. 5 Genetic gain plotted against inbreeding after nine generations of selection with 16 sires and 128 dams in each generation; $n_w = 6$, $h^2 = 0.3$; $k = 0.5, 1, 2, 5, 10$, and 20

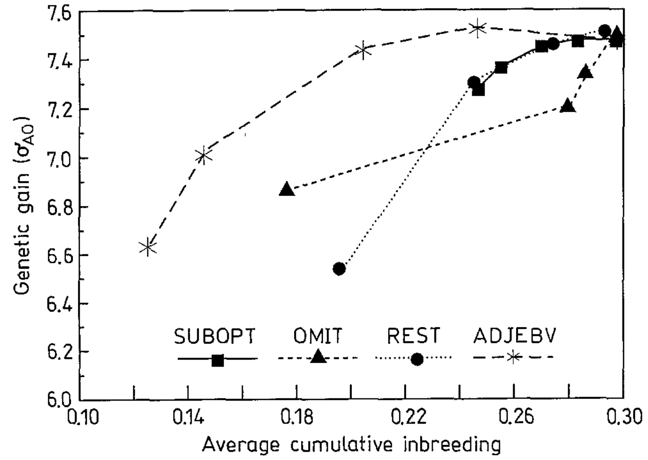

Fig. 6 Genetic gain plotted against inbreeding after nine generations of selection with eight sires and 128 dams in each generation; $n_w = 6$, $h^2 = 0.3$; $k = 2, 5, 15$ and 25

are drawn to the same scale. In these larger populations, rates of inbreeding ranged from 1.1% to 3.5% per generation, and are representative of some rates which occur in the animal breeding industry.

ADJEBV performs better at the smaller population size. At the small population size (Fig. 4) inbreeding was reduced from 0.31 to 0.23 with no loss of genetic response, and at the large population size (Fig. 5) inbreeding was reduced from 0.19 to 0.14 with no loss of response. The proportional reduction was, however, 26% in both cases. The k values from right to left are 0, 1, 2, 5, 10 and 25 in Fig. 4 and 0, 0.5, 1, 2, 5, 10 and 20 in Fig. 5. Thus a given value of k had similar proportional effects in the two populations. Strategies SUBOPT, OMIT, and REST also gave slightly better absolute, but not proportional, performance at the lower population size (Fig. 4 vs 5).

In Fig. 6 the mating ratio is 16:1, with the same number of sires as in the small population size (Fig. 4), but with the same number of dams as in the large population size (Fig. 5). Because the increased number of dams has little effect on effective population size, inbreeding levels were similar to those in the small population (Fig. 4). The performance of ADJEBV for reducing inbreeding, while maintaining selection response, was almost the same for the two mating ratios (Fig. 4 vs 6). In Fig. 7, the mating ratio is 4:1, with the same number of sires as in the large population size (Fig. 5), and the same number of dams as in the small population size (Fig. 4). As expected, given effective population sizes, inbreeding levels were similar to those in Fig. 5, though responses were less due to reduced selection intensity in males. The performance of ADJEBV was almost idential to that in Fig. 5. Thus, performance of ADJEBV appears not to be affected by the mating ratio and selection intensity in males.

SUBOPT and REST gave a similar performance at low effective population size (Figs. 4 and 6), but SUBOPT was superior for performance at high effective

Table 1 Number of changes made to the initially selected group and proportion of initially selected parents remaining in the finally selected group with eight sires and 64 dams in each generation[a]

Generation	Number of changes		Proportion remaining			
	$k = 10$	$k = 2$	$k = 10$		$k = 2$	
			Sires	Dams	Sires	Dams
1	16.87 ± 0.14	6.04 ± 0.07	0.773	0.830	0.901	0.961
2	19.13 ± 0.17	7.73 ± 0.09	0.724	0.805	0.870	0.942
3	19.43 ± 0.18	7.86 ± 0.09	0.718	0.802	0.868	0.938
4	19.15 ± 0.17	7.77 ± 0.09	0.724	0.804	0.876	0.940
5	19.23 ± 0.17	7.68 ± 0.08	0.718	0.805	0.878	0.938
6	19.21 ± 0.17	7.48 ± 0.08	0.722	0.805	0.878	0.942
7	18.91 ± 0.17	7.37 ± 0.08	0.723	0.809	0.886	0.945
8	18.60 ± 0.17	7.30 ± 0.07	0.726	0.812	0.884	0.944
9	18.54 ± 0.17	7.23 ± 0.08	0.731	0.812	0.886	0.946
10	18.46 ± 0.17	7.21 ± 0.08	0.728	0.814	0.884	0.947

[a] $n_w = 6$, $h^2 = 0.3$

population size (Figs. 5 and 7). At very low effective population sizes and mating ratios of 1:1 (Figs. 1–3), however, SUBOPT performed better than REST, probably because imposition of even mild restrictions in REST limits opportunities to select high-EBV males. Apart from these differences, comparisons between strategies do not appear to be affected by population size and selection intensity. As mating ratios increase and numbers of progeny per dam decrease, an increasing amount of inbreeding will arise from selection of half sibs. REST and OMIT should be less effective in reducing inbreeding in these situations, as was observed (compare Fig. 4 with Fig. 6 and Fig. 5 with Fig. 7; the point with the lowest inbreeding on the OMIT lines in Figs. 6, and 7 can be ignored for this comparison, as it applies to mass selection), because they are designed to reduce the selection of full sibs.

Efficiency of iteration in ADJEBV selection

The number of changes made to the group selected initially by truncation on the EBV is illustrated for two k values in Table 1 for Nm = 8, Nf = 64, $n_w = 6$ and $h^2 = 0.3$. The number of changes to the selected group was slightly less in the first generation than in later generations. This difference is most likely a result of a reduction in the variance of the unadjusted EBV across selection candidates after the first generation, due to previous generations of selection. A higher variance of the EBV means that at fixed k, M_2 places more emphasis on high-EBV animals, which are those selected initially. As the number of changes increases, the proportion of initially selected parents which remain in the selected group decreases. The number of changes was higher for $k = 10$ than for $k = 2$, as expected given the larger negative weight attached to average relationship.

Table 2 shows the increases in M_2 by generation for $k = 10$. When k was reduced from 10 to 2 (last row of Table 2), the average increases in M_2 were reduced substantially, because there was less to gain by altering the selection from truncation on the unadjusted EBV.

Table 2 Increases in the population selection criterion with eight sires and 64 dams in each generation[a]

Generation	Initial value	Increase
1	0.433	0.109
2	1.040	0.155
3	1.592	0.159
4	2.137	0.154
5	2.663	0.151
6	3.184	0.151
7	3.700	0.146
8	4.207	0.140
9	4.714	0.134
10	5.210	0.134
Average (2–10)		0.147
Average (2–10)	when $k = 2$	0.010

[a] Tabulated values are for $k = 10$. Standard errors of increases in the population selection criterion are about 0.003

Options for reduced population size with ADJEBV

Mean genetic gain is plotted against mean inbreeding after nine generations of selection in Fig. 8, for ADJEBV at one population size, and REST at four population sizes. For ADJEBV, Nm = 8, Nf = 64 and for REST, Nm = 8 and Nf = 64(RP1), or Nm = 9 and Nf = 72 (RP2), or Nm = 10 and Nf = 80 (RP3), or Nm = 11 and Nf = 88 (RP4). In each case $n_w = 6$ (three males, three females). Restrictions used for RP1 were maxima of two males (no restriction on females), two males and two females, one male (no restriction on females) and one male and two females selected from a full-sib family. For RP2, RP3 and RP4, restrictions were maxima of two males (no restriction on females), one male (no restriction on females), one male and two females, and one male and one female selected from a full-sib family. The objective was to determine by how much population size could be reduced if ADJEBV were used to achieve a certain balance of response and inbreeding compared to the use of REST. Figure 8 indicates that the answer is highly dependent on the initial goal. If the initial popula-

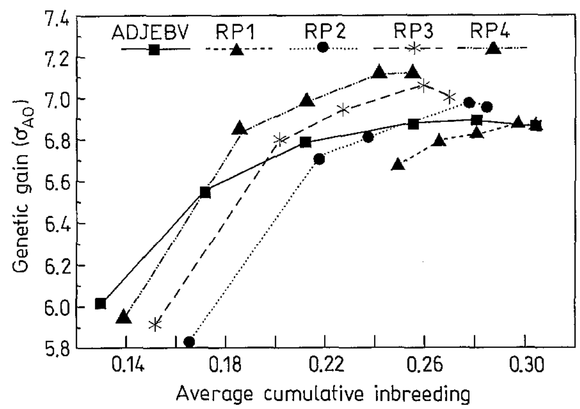

Fig. 8 The benefits of ADJEBV in terms of population size: genetic gain plotted against inbreeding after nine generations of selection. $n_w = 6$, $h^2 = 0.3$; $k = 1, 2, 5, 10$ and 25

tion is defined by RP4 (i.e., Nm = 11, Nf = 88) and the goal is to keep inbreeding below 0.15, ADJEBV would achieve that goal and would give a better response than RP4. Thus population size could be reduced by about 27%. For a higher acceptable inbreeding of 0.2, ADJEBV (with Nm = 8 and Nf = 64) gave a lower response than the optimum RP4, and population size with ADJEBV could be reduced by less than in the previous example. In general, the lower the inbreeding rate desired, the greater the reduction in population size possible in moving from strategy REST to ADJEBV. Although difficult to generalise from the limited situations examined here, reductions of the order of 10–30% should be possible in many situations. Although not shown here, similar conclusions were obtained from results after three and six generations of selection.

If a breeding scheme operates at a fixed population size, governed by costs and returns, and within a certain tolerable rate of inbreeding, then ADJEBV would not be used to change population size, but would be used to increase genetic gain slightly at the desired maximum rate of inbreeding.

Performance of ADJEBV and REST with EBV based on individual performance

Mean genetic gain is plotted against mean inbreeding after three, six and nine generations of selection in Fig. 9, for ADJEBV and REST when Nm = 8, Nf = 64, $n_w = 6$, and $h^2 = 0.3$ with the EBV based on individual records. ADJEBV gave a significantly better performance than REST. Genetic gain and inbreeding were both much lower than with a family index (Fig. 9 vs 4). For ADJEBV with a family index (Fig. 4) and with individual records (Fig. 9) compared at the same level of inbreeding, the index gave greater genetic gain. When inbreeding was reduced from 0.18 to 0.13 using ADJEBV with individual records (Fig. 9), genetic gain decreased from 6.3 to 5.9 while the same absolute decrease in inbreeding with the family index (Fig. 4) decreased genetic gain from 6.6 to 6.0. Starting at their initial levels of inbreeding, ADJEBV with the index (Fig. 4) would reduce inbreeding by one-half with about a 10% reduction in response, while a similar reduction with individual records (Fig. 9) would reduce response by more than 20%. The rapid reduction in response with ADJEBV and individual records occurs because inbreeding is at a lower level and is closer to the lower limit imposed by the population size. For Nm = 8, Nf = 64 the lowest possible rate of inbreeding is 8.79×10^{-3}, with within-family selection (Dempfle 1975), giving $F = 0.0764$ after nine generations of selection.

Table 3 shows the ratio of the difference in mean EBV between initially selected sires and finally selected sires divided by the difference in mean relationship among initially selected sires and dams and among finally selected sires and dams. Smaller values of the ratio correspond to greater efficiency in reducing relationships while maintaining genetic gain. For both individual records and EBV based on a family index, the ratio increases as k increases, which is consistent with the

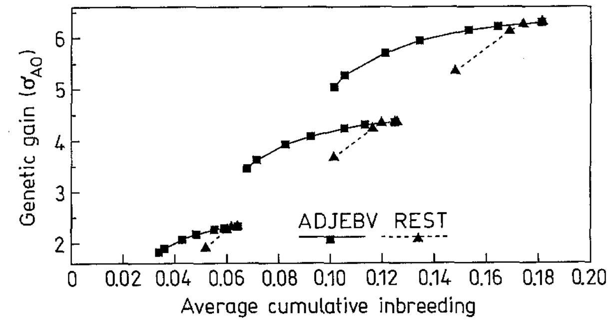

Fig. 9 ADJEBV and REST with EBV based on individual records: genetic gain plotted against inbreeding after three (lower left), six (middle) and nine (upper right) generations of selection. Nm = 8, Nf = 64, $n_w = 6$, $h^2 = 0.3$; $k = 1, 2, 5, 10, 30$ and 50

Table 3 Ratio of loss in selection intensity to reduction in relationship for different selection methods

Selection	Mean EBV of initially selected sires (1)	Mean EBV of finally selected sires (2)	Mean initial sire-dam relationship (3)	Mean final sire-dam relationship (4)	Ratio [(1)–(2)]/[(3)–(4)]
Index $k = 2$	4.505 ± 0.017	4.495 ± 0.017	0.1601 ± 0.0009	0.1517 ± 0.0008	1.190
Index $k = 10$	4.337 ± 0.016	4.265 ± 0.016	0.1222 ± 0.0006	0.1007 ± 0.0004	3.349
Mass $k = 2$	4.048 ± 0.017	4.044 ± 0.017	0.0927 ± 0.0004	0.0889 ± 0.0004	1.053
Mass $k = 10$	3.817 ± 0.015	3.794 ± 0.015	0.0774 ± 0.0002	0.0694 ± 0.0001	2.875

curvilinear plots of genetic gain against inbreeding. At a given k, the ratio is smaller for individual records than for EBV based on a family index, even though overall performance is less for individual records. The behaviour of the ratio should be dependent on the correlation of EBV within families and the difference between mean relationship within families and mean relationship between families, for the following reasons. If families were ranked on mean EBV, the expectation of the difference in EBV between an animal in the nth ranking family and an animal in family $n+1$ would increase with the correlation between EBV. The numerator of the ratio should therefore increase with the correlation between EBV. There would be more animals from family n in the intially selected group than from family $n+1$, and so an animal in family $n+1$ would have a lower mean relationship with the initially selected group. The difference in mean relationship between the two animals would increase with the difference between mean relationship within families and mean relationship between families, and also with the correlation between EBV, because proportionately more animals would be initially selected from family n at higher EBV correlations. The denominator of the ratio should therefore increase with the EBV correlation. The fact that the ratio is smaller for individual records when correlations between EBV are low, than for EBV based on a family index, suggests that the main effect of the EBV correlation is through the numerator, although this may not be true at other selection intensities. The ratio has some similarity to solutions for the optimal selected proportions from families derived deterministically by Lindgren et al. (1993) using order statistics under simplified circumstances.

Discussion

Drift variance between randomly selected lines is $2\mathrm{F}\sigma^2_{A0}$ (Wright 1952). If, as suggested by Hill (1980), this is a good approximation to the variance of genetic change in a selected line, the standard deviation of response should be $\sqrt{(2\mathrm{F})}$, because $\sigma^2_{A0}=1$ for these simulations. Achieved standard deviations of 0.4 to 0.6 (data not shown) were in this general area, although they were not obviously related to inbreeding rates, and were not affected by the selection methods studied. All methods used to reduce inbreeding had very small effects on the variance of gain, and so differences in this respect are unlikely to affect choices among them.

Selection methods to maximise the mean EBV of selected parents, adjusted by a factor of its prediction error variance to account for risk, have been shown to be effective in reducing the variance of genetic gain (Woolliams and Meuwissen 1993). The population selection criterion of Woolliams and Meuwissen (1993) can be written as

$$M^*_2=\boldsymbol{v}'\hat{\boldsymbol{g}}-k_1\boldsymbol{v}'\boldsymbol{C}\boldsymbol{v}$$

while the criterion used here is

$$M=\boldsymbol{v}'\hat{\boldsymbol{g}}-k_2\boldsymbol{v}'\boldsymbol{A}\boldsymbol{v}$$

where $\boldsymbol{v}$ is the vector of genetic contributions of parents, $\boldsymbol{g}$ is the vector of the EBV, $\boldsymbol{C}$ is the prediction error variance-covariance matrix of EBV and $\boldsymbol{A}$ is the additive relationship matrix among parents. Clearly the similarity between the two methods will depend on how similar are $\boldsymbol{C}$ and $\boldsymbol{A}$. In the situation described by Woolliams and Meuwissen (1993) there were large differences in accuracies of evaluations among individuals so that $\boldsymbol{C}$ and $\boldsymbol{A}$ would have very different structures. If all individuals have the same accuracy, as here, the structure of $\boldsymbol{C}$ and $\boldsymbol{A}$ may be quite similar so that the two methods would give similar results. In principle, both risk and inbreeding could be included in the breeding objective, a possibility that is being studied.

A series of iso-objective lines can be drawn on graphs of genetic response versus inbreeding, where each iso-objective line connects points with equal values of the selection objective, M_1. The strategy that maximises the objective is found at the point on the line that just touches (is tangential to) the iso-objective line with the highest objective value. For example, if the value of inbreeding is considered only in terms of inbreeding depression of growth and the inbreeding depression rate is 0.5% per 1% inbreeding, then for $\sigma_a=5\%$ of the mean, complete inbreeding depression would be $10\sigma_a$, and the slope of the iso-objective line would be $D=10$. Over the region of the curve where a small loss in response is traded for a large loss in inbreeding, the k value maximising the selection objective is observed to be around 1.2 to 2 times D. The k value used in selection is greater than D because of the increased response due to the increased genetic variance caused by reduced inbreeding. However, errors in the k value used will not result in a large loss in the value of the objective realised, because the slope of the curve changes quite slowly. The k value required increases with the time horizon, because the effect of loss of variance is cumulative over time.

Wray and Goddard (1994) used $k=\delta G_L(t-1)/2+D$, where t is the time horizon and δG_L is the rate of genetic gain assuming truncation selection with no loss in variance due to inbreeding, but accounting for the reduction in variance due to selection. The predictor of k had a relative error of about $\pm 10\%$ in the limited number of situations studied. The selection procedure was slightly different from that considered here in that EBV and relationships were considered only among sires, with selection of dams completely at random. In attempting to maximise the objective, they investigated the effect of allowing the number of sires selected and the number of matings per sire to vary, while a fixed number of dams was selected randomly. The procedure used to maximise the objective involved selecting one sire initially, and then other sires one at a time based on maximum improvement in the objective at each stage.

Allowing variation in the number of sires and the number of matings per sire improved performance. Allowing the replacement of selected sires with sires outside the selected group, as in the ADJEBV procedure, might also give improved performance. Results obtained by Brisbane and Gibson (1995c) also show that when dams are genetically selected, Wray and Goddard's method over-predicts k if relationships among and between both sexes are used, as was done here. Brisbane and Gibson (1995c) showed that Wray and Goddard's method should under-predict k if only relationships among sires are used, and dams are genetically selected.

When EBV are based only on individual performance, inbreeding is less and closer to the lower limit imposed by population size, and the slope of the plot of response against inbreeding is steeper than if a family index is used. The k value used in selection is actually less than D (Fig. 9), which is not expected from the prediction of k given by Wray and Goddard (1994). However, this situation may be less important than where EBV use information from relatives, because inbreeding is less of a problem.

In the absence of inbreeding depression, the objective of the breeder might be to obtain maximum genetic gain at some time horizon, or perhaps to obtain the most desirable trend in genetic gain over a range of time which would depend on factors such as competition from rival schemes. In many cases, the genetic gain versus inbreeding curve is quite flat near the maximum, so that k could be as large as possible to reduce inbreeding while maintaining gain close to its maximum. In Fig. 4, the expected genetic gain is maximised at 6.889 when $k = 1$. However using $k = 2$, with a loss of 0.01 in expected gain, leads to little change in the probability that genetic gain exceeds any given value, because the standard deviation of gain, of about 0.5, is large in comparison to the change in expectation.

A limitation of the current work is that discrete generations were assumed, whereas most practical breeding schemes involve overlapping generations. When generations overlap, individuals have already produced different numbers of progeny at a given round of selection, and will contribute different numbers of progeny from future breedings, so that accounting for an animal's contribution to long-term inbreeding is a non-trivial problem. Work is underway to investigate the use of ADJEBV with overlapping generations.

Use of ADJEBV may cause changes in the ranking of schemes for genetic gain achieved within tolerable inbreeding levels. For example, in selection nuclei for dairy cattle using MOET (e.g., Nicholas and Smith 1983), genetic gain is reduced more than in a progeny test scheme by restrictions required to control inbreeding. Because ADJEBV allows higher response and lower inbreeding than REST, MOET schemes may perform relatively better with ADJEBV than REST.

When determining the value of D in the selection objective there are three deterimental effects of inbreeding to account for: (1) reduction of additive genetic variance, which limits gain from future selection; (2) inbreeding depression in the trait under selection and (3) inbreeding depression in fitness (ability to survive and reproduce). With competition between rival breeding schemes, the continued profitability of an individual scheme requires the economic performance of its genetic stocks to be consistently high relative to that of other stocks over time, such that a range of time horizons are of interest. With a purebred commerical population, inbreeding depression in the trait under selection may be the most important effect. Consider a breeding program with a rate of gain of $0.2\sigma_A$ per generation, and a rate of inbreeding of 1% per generation. Using these realistic parameters, a rough prediction of genetic gain, neglecting inbreeding, over three generations, is $0.6\sigma_A$. If the genetic selection differential varies directly with σ_A^2 then, after accounting for loss of genetic variance, the response is $0.2 + 0.2(0.99) + 0.2(0.98) = 0.594\sigma_A$, and if the differential varies directly with σ_A, the response is $0.2 + 0.2\sqrt{(0.99)} + 0.2\sqrt{(0.98)} = 0.597\sigma_A$. Depending on the assumption used, the loss of response is $0.003\sigma_A$ to $0.006\sigma_A$. For inbreeding depression to have the same effect, it would need to be only $0.001\sigma_A$ to $0.002\sigma_A$ per 1% inbreeding. For milk yield in dairy cows as an example, σ_A is about 10% of the population mean, so that the rate of inbreeding depression would be only 0.1% to 0.02% of the population mean per 1% inbreeding. Estimates for the rate of inbreeding depression in milk yield in dairy cattle are around 20-times higher than this, at 0.20–0.40% of the population mean per 1% inbreeding (Hodges et al. 1979; Hermas et al. 1987; Miglior et al. 1992). Thus, inbreeding depression in the trait selected is likely to be a much more serious problem than loss of genetic variance due to inbreeding in a purebred population. Loss of genetic variance, however, reduces genetic response in all future generations of selection, and would therefore be expected to become more important in the long term.

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