

# Mendelian sampling terms as a selective advantage in optimum breeding schemes with restrictions on the rate of inbreeding

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## Summary

Quadratic indices are a general approach for the joint management of genetic gain and inbreeding in artificial selection programmes. They provide the optimal contributions that selection candidates should have to obtain the maximum gain when the rate of inbreeding is constrained to a predefined value. This study shows that, when using quadratic indices, the selective advantage is a function of the Mendelian sampling terms. That is, at all times, contributions of selected candidates are allocated according to the best available information about their Mendelian sampling terms (i.e. about their superiority over their parental average) and not on their breeding values. By contrast, under standard truncation selection, both estimated breeding values and Mendelian sampling terms play a major role in determining contributions. A measure of the effectiveness of using genetic variation to achieve genetic gain is presented and benchmark values of 0.92 for quadratic optimisation and 0.5 for truncation selection are found for a rate of inbreeding of 0.01 and a heritability of 0.25.

## 1. Introduction

Dynamic selection algorithms for simultaneously managing genetic gain and inbreeding have been developed during the past decade (Wray & Goddard, 1994; Brisbane & Gibson, 1995; Meuwissen, 1997; Grundy *et al.*, 1998*b*). The general framework can be described as constrained quadratic optimization of the usage of selection candidates. Although different objective functions have been used, they all had the form  $\mathbf{c}^T \mathbf{g} - \lambda \mathbf{c}^T \mathbf{A} \mathbf{c}$ , where  $\mathbf{c}$  is the vector of mating proportions (usage) of selection candidates,  $\mathbf{g}$  is the vector of estimated breeding values (EBVs) of selection candidates,  $\mathbf{A}$  is the numerator relationship matrix among selection candidates and the factor  $\lambda$  represents a penalty on the increase in inbreeding. A key property of such an objective function is that it keeps the method used for genetic evaluation and the restriction in inbreeding separated. Thus, EBVs can be estimated with the best available technique (i.e. best linear unbiased

predictions (BLUP)) and the selection policy is independently chosen according to risk preference. Simulation studies by Meuwissen (1997) and Grundy *et al.* (1998*b*) showed that optimized selection can potentially achieve at least 20% higher genetic gains than traditional BLUP truncation selection at the same rate of inbreeding ( $\Delta F$ ). Moreover, when applied to real livestock populations of beef cattle and sheep, even higher gains were predicted (Avendaño *et al.*, 2003).

The unified theory of genetic contributions put forward by Woolliams & Thompson (1994) has provided the necessary framework for linking long-term genetic contributions to rates of gain and inbreeding in livestock populations. The long-term genetic contribution ( $r_i$ ) of an individual  $i$  was defined by Wray & Thompson (1990) as the proportion of genes it contributes in the long-term to the population. These authors demonstrated that the rate of inbreeding per generation is proportional to the sum of squares of long-term contributions,  $E(\Delta F) = 0.25 \sum r_i^2$  with the sum taken over all ancestors. Woolliams & Thompson (1994) showed that the rate of genetic gain can be related to the covariance between long-term contributions and the Mendelian sampling terms ( $a_i$ ),

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$E(\Delta G) = \sum r_i a_i$ . This definition of gain makes explicit that genetic gain arises from ‘good’ ancestors contributing more genes and that the process of contribution of genes is multigenerational in nature. Furthermore, it makes explicit that sustained genetic gain relies on the exploitation of the Mendelian sampling variation (i.e. the new genetic variation created each generation) (Woolliams *et al.*, 1999a).

There is no available framework for predicting  $\Delta G$  under constrained  $\Delta F$  in the context of quadratic indices. Grundy *et al.* (1998b) attempted such a prediction but failed to provide deterministic predictions of key parameters such as selection intensities. Under truncation selection, genetic gain can be predicted using simple linear regression theory and the predicted selection differential ( $\hat{S}$ ) expressed as  $\hat{S} = b_{g,i} i \sigma_I$ , where  $b_{g,i}$  is the regression of the true breeding value on the selection index used (e.g. BLUP),  $i$  is the selection intensity and  $\sigma_I$  is the standard deviation of the selection index. Such expressions are lacking for quadratic optimization.

The study of Grundy *et al.* (1998b) showed the link between the optimization problem of maximising  $\Delta G$  at fixed  $\Delta F$  using quadratic indices and the management of long-term genetic contributions. They showed that the optimal solution could be achieved by linearly allocating long-term contributions of selection candidates according with their Mendelian sampling terms. An expression for the potential ideal rate of gain ( $\Delta G_{ideal}$ ) that would be achievable with this ideal outcome was derived but genetic responses from stochastic simulations were always substantially lower than  $\Delta G_{ideal}$ . This was attributed to the lack of knowledge about  $r$  and  $a$  at selection time and that, in a multi-generational process, long-term contributions of individuals cannot be independently managed, as pointed out by Woolliams *et al.* (2002).

As a step towards understanding the important elements in the predictive models, the objective of this study was to demonstrate that quadratic optimization manages individual contributions in relation to the best available information on Mendelian sampling terms rather than breeding values. This step is required for the development of usable and tractable predictions of genetic gain for selection tools that maximizes progress with constrained rates of inbreeding. An empirical route was followed through the use of stochastic simulations and comparisons with traditional truncation selection.

## 2. Methods

### (i) Genetic model and simulation procedure

Selection over multiple generations was modelled using stochastic computer simulations. An additive infinitesimal model (Bulmer, 1971) was considered for

the trait under selection. The true breeding values for animals in the base population were obtained from a normal distribution with mean zero and variance equal to the heritability ( $h^2$ ) of the trait. Thus, the phenotypic variance ( $\sigma_p^2$ ) was assumed to be equal to one. In subsequent generations, the true breeding value of the progeny was obtained as half the sum of the true breeding values of their parents plus a random Mendelian sampling term. The Mendelian sampling term of an individual was sampled from a normal distribution with mean zero and variance  $\sigma_a^2 = 0.5[1 - 0.5(F_S + F_D)]h^2$ , where  $F_S$  and  $F_D$  are the inbreeding coefficients of the sire and dam, respectively. The phenotypic value was obtained by adding to the true breeding value an environmental component sampled from a normal distribution with mean zero and variance  $1 - h^2$ . A BLUP animal model was used to obtain estimated breeding values. Populations with discrete generations were evaluated over ten generations of selection. In the base generation ( $t=0$ ),  $N$  (100 or 200) individuals ( $N/2$  males and  $N/2$  females) with full-sib family structure were generated. The first generation of selection was obtained from mating of animals selected at  $t=0$ . Mating amongst selected candidates was at random. A total of 100 replicates were performed.

### (ii) Selection methods

#### (a) Optimized selection

The optimization algorithm described by Meuwissen (1997) for obtaining maximum genetic gain while constraining the inbreeding rate to a specific value was used. This algorithm gives the optimal number of selected candidates and their optimal mating proportions or contributions to the next generation. The constant rate of inbreeding in the long term was achieved by setting the constraint on the average coancestry of selected candidates ( $\mathbf{c}^T \mathbf{A} \mathbf{c} / 2$ ) to  $1 - (1 - \Delta F)^t$ , where  $t$  is the generation number (Grundy *et al.*, 1998b). The output of this optimization procedure is the vector,  $\mathbf{c}$ , of contributions to the next generation for candidates at any particular generation (i.e. mating proportions). The optimal number of offspring for an individual  $i$  is  $2Nc_i$  (a real number), and the actual (integer) number of offspring per parent was obtained following Grundy *et al.* (1998b). The term ‘selected candidates’ in the text refers to those individuals with  $c_i > 0$ .

#### (b) Truncation selection

In standard truncation selection, a fixed number of candidates from each sex (those with the highest EBVs) were selected each generation. The population structure was chosen to enable comparisons with optimized selection at the same  $\Delta F$ . An optimized scheme with a restriction of  $\Delta F = 0.01$  per generation was first run and then a truncation scheme with

numbers of sires and dams giving the same  $\Delta F$  was chosen. Only schemes with a mating ratio of 1 were considered because this was the typical optimal value found by Villanueva & Woolliams (1997) for small schemes. For  $N=100$ , the desired  $\Delta F$  under truncation selection was achieved after selecting 25 males and 25 females. Mating pairs were randomly allocated and every female had two offspring of each sex. Thus, in contrast to optimized selection, a fixed contribution to the next generation of 0.02 was allocated to each selected candidate.

(iii) *Long-term genetic contributions and estimated Mendelian sampling terms at selection time and at convergence*

The relationships between long-term genetic contributions ( $r$ ), estimated Mendelian sampling terms ( $\hat{a}$ ) and EBVs were studied for different values of  $h^2$  (0.01, 0.25, 0.50 and 0.99) and three levels of constraint on  $\Delta F$  (0.005, 0.01 and 0.02). The long-term contribution of an ancestor  $i$  to a descendent  $j$  is defined as the proportion of genes of  $j$  that are expected to derive by descend from the ancestor  $i$  (Wray & Thompson, 1990; Woolliams *et al.*, 1999a). The contributions converge over several generations to be the same for all descendants in the population. The long-term genetic contributions of ancestors born in generation 3 to descendants born in generation 8 were calculated by tracing back the pedigree from descendants to ancestors using the algorithm described by Woolliams & Mäntysaari (1995). The term ‘at convergence’ used throughout this paper refers to generation 8. The estimated Mendelian sampling term for selection candidate  $i$  was obtained as  $\hat{a}_i = EBV_i - [0.5(EBV_S + EBV_D)]$ , where  $EBV_i$ ,  $EBV_S$  and  $EBV_D$  are the BLUP estimated breeding values for the individual, its sire and its dam, respectively. The EBVs used to calculate  $\hat{a}_i$  were either those at the time of selection (i.e.  $EBV_{sel}$  obtained at generation 3 to estimate  $\hat{a}_{sel}$ ) or at convergence of long-term contributions of selected candidates (i.e.  $EBV_{conv}$  obtained at generation 8 to estimate  $\hat{a}_{conv}$ ).

(iv) *Comparison between potential selective advantages and between selection methods*

Linear regression models were used to compare  $\hat{a}$  and EBV as potential selective advantages for optimal and truncation selection. Bivariate regressions were conducted for (i)  $c$  on  $\hat{a}_{sel}$  and  $EBV_{sel}$ , and (ii)  $r$  on  $\hat{a}_{conv}$  and  $EBV_{conv}$ . Only selected individuals (i.e. those with  $c_i > 0$ ) were included in the analysis.

We will now illustrate procedures and notation using the example of  $r$  on  $\hat{a}_{conv}$  and  $EBV_{conv}$ . Initially, partial correlations  $\rho_{r,\hat{a}_{conv}}$  and  $\rho_{r,EBV_{conv}}$  were calculated using standard formulae. The following regression

models were then fitted:

$$r_i = u + b_{r,\hat{a}_{conv}} \hat{a}_{conv_i} + b_{r,EBV_{conv}} EBV_{conv_i} + e_i \tag{1}$$

$$r_i = u + b_{r,\hat{a}_{conv}} \hat{a}_{conv_i} + e_i \tag{2}$$

$$r_i = u + b_{r,EBV_{conv}} EBV_{conv_i} + e_i \tag{3}$$

$$r_i = u + e_i, \tag{4}$$

where  $u$  is the intercept,  $b_{r,\hat{a}_{conv}}$  and  $b_{r,EBV_{conv}}$  are regression coefficients in the models, and  $e_i$  is the residual term with variance  $\sigma_{e_r}^2(j)$  for regression model  $j$ . The impacts of  $\hat{a}_{conv}$  and  $EBV_{conv}$ , and their joint impact, were calculated as, respectively:

$$V_{r,\hat{a}_{conv}} = [\sigma_{e_r}^2(3) - \sigma_{e_r}^2(1)] / \sigma_{e_r}^2(4)$$

$$V_{r,EBV_{conv}} = [\sigma_{e_r}^2(2) - \sigma_{e_r}^2(1)] / \sigma_{e_r}^2(4)$$

$$V_{r,tot} = 1 - \sigma_{e_r}^2(1) / \sigma_{e_r}^2(4).$$

The corresponding analysis of  $c$  using  $\rho_{c,\hat{a}_{conv}}$ ,  $\rho_{c,EBV_{conv}}$ ,  $V_{c,\hat{a}_{sel}}$ ,  $V_{c,EBV_{sel}}$  and  $V_{c,tot}$  follows by analogy.

A measure of efficiency,  $\gamma$ , was also calculated for the selection schemes. This was based on the representation of genetic gain given by Woolliams & Thompson (1994) (i.e.  $\Delta G = \sum r_i a_i$ ). Because the prediction error of the Mendelian sampling term would be expected to be independent of  $r$ , this can be expressed as  $E[\Delta G] = E[\sum r_i \hat{a}_{conv_i}]$ . Therefore,  $\sum e_i^2$ , where  $e_i$  is the residual deviation from the regression model 2 for  $r$ , represents a component of  $\sum r_i^2$  that has not contributed to gain, and therefore it follows that  $\gamma = 1 - 0.25 \sum e_i^2 / \Delta F$  can be regarded as a measure of efficiency for the selection scheme in generating gain effectively from the available variation.

An additional comparison between quadratic optimization and truncation selection was established from the distributions of  $\hat{a}$  and EBV of selected and unselected individuals. The frequency distributions of both groups were plotted after arbitrarily defining 32 bin classes for  $\hat{a}_{sel}$  and 64 bin classes for  $EBV_{sel}$ . Summary distribution statistics were calculated. For  $\hat{a}_{sel}$  and  $EBV_{sel}$  under quadratic optimization, and for  $\hat{a}_{sel}$  under truncation selection, there is an overlap in the frequency distribution of those selected and unselected candidates. The degree of overlap between distributions was measured as the probability that the potential selective advantage ( $\hat{a}_{sel}$  or  $EBV_{sel}$ ) of a randomly taken individual from the selected group being equal or greater than the potential selective advantage of a randomly taken individual from the unselected group. For instance, for  $\hat{a}_{sel}$  this probability was approximated as

$$P(\hat{a}_i SELECT \geq \hat{a}_j UNSELECT) = \sum_{k=1}^{\max bin} \left[ P(\hat{a}_i SELECT)_k \left( \sum_{l=1}^{bin_i = bin_k} P(\hat{a}_j UNSELECT)_l \right) \right],$$

Table 1. Regression of  $r_i$  on  $c_i$  for quadratic optimization ( $b_{r,c}$ , with s.e. in parentheses), together with partial correlation coefficients from a bivariate regression of  $c_i$  on the initial estimate of Mendelian sampling term ( $\hat{a}_{sel}$ ) and breeding value ( $EBV_{sel}$ ), and of  $r_i$  on the ultimate estimates,  $\hat{a}_{conv}$  and  $EBV_{conv}$ , after convergence of  $r_i$ , for a range of heritabilities ( $h^2$ ) and different constraints on  $\Delta F$ , for  $N=100$

$\Delta F$	$h^2$	$r_i$ on $c_i$	$c_i$ on $\hat{a}_{sel}$ & $EBV_{sel}$		$r_i$ on $\hat{a}_{conv}$ & $EBV_{conv}$	
		$b_{r,c}$	$\rho_{c,\hat{a}_{sel}}$	$\rho_{c,EBV_{sel}}$	$\rho_{r,\hat{a}_{conv}}$	$\rho_{r,EBV_{conv}}$
0.01*	0.01	1.003 (0.017)	0.89	0.21	0.85	0.07
	0.25	1.015 (0.015)	0.90	0.05	0.85	0.05
	0.50	1.026 (0.013)	0.89	-0.01	0.81	0.01
	0.99	1.054 (0.023)	0.74	0.07	0.54	0.04
0.02‡	0.01	0.962 (0.026)	0.78	0.19	0.79	0.00
	0.25	0.970 (0.022)	0.80	0.19	0.75	0.10
	0.50	1.002 (0.019)	0.81	0.13	0.71	0.10
	0.99	1.018 (0.015)	0.70	0.05	0.52	0.03

\* Approximate significance levels for  $\rho$ : 0.027,  $P<0.05$ ; 0.036,  $P<0.01$ ; 0.046,  $P<0.001$ .

‡ Approximate significance levels for  $\rho$ : 0.037,  $P<0.05$ ; 0.049,  $P<0.01$ ; 0.063,  $P<0.001$ .

where  $p(\hat{a}_{iSELECT})_k$  is the probability of an individual  $i$  from bin  $k$  being selected and  $p(\hat{a}_{jUNSELECT})_l$  is the probability of an individual  $j$  from bin  $l$  being not selected. Likewise, the corresponding probability was calculated for  $EBV_{sel}$ .

### 3. Results

#### (i) Relationships between contributions and potential selective advantages

The regression coefficients of  $r_i$  (the long-term genetic contributions) and  $c_i$  (the contributions to the next generation) were close to 1 for all combinations of  $h^2$  and  $\Delta F$  (Table 1). This indicates that, for quadratic indices,  $c_i$  values are unbiased or nearly unbiased predictors of  $r_i$ , as previously demonstrated by Grundy *et al.* (1998b). Table 1 also shows the partial correlations between the contribution and estimates of Mendelian sampling term ( $\hat{a}$ ) and breeding value (EBV) for the quadratic index on two occasions, after selection and after contributions have converged. The correlation between  $\hat{a}$  and the contribution, after adjustment for EBV, was consistently much greater than the correlation between EBV and the contribution, after adjustment for  $\hat{a}$ . The partial correlations for  $\hat{a}$  were all  $>0.50$ , with values as large as 0.90, whereas the partial correlations with EBV were rarely  $>0.15$  and always  $<0.20$ .

However, judging the impact of each of the potential selective advantages from the partial correlations is complex, because  $\hat{a}$  and EBV are themselves correlated, and the reduction in variance of the dependent variate  $r_i$  or  $c_i$  is related to the square of the corre-

lations. For the range of parameters considered, Table 2 shows that regression on EBV, following regression on  $\hat{a}$ , reduced the residual variance by at most 4% of the unadjusted variance of  $c_i$ , and by at most 1% of the unadjusted variance of  $r_i$ . However, regression on  $\hat{a}$ , following regression on EBV, reduced the unadjusted variance by at least 20% and as much as 60% of the unadjusted variance. Table 2 also shows patterns in the proportion of the variance in contributions explained by the regressions on  $\hat{a}$  and EBV. This proportion declined as the value of the constraint on  $\Delta F$  increased. For  $r_i$ , the proportion of the variance explained by the joint regression was notably lower for  $h^2=0.99$  than for other heritabilities simulated, but this pattern was not evident for  $c_i$ .

In summary, the simple regressions of  $r_i$  ( $c_i$ ) on  $\hat{a}_{conv}$  ( $\hat{a}_{sel}$ ) was almost as effective as the joint regression for predicting contributions. However, enough data were generated to show that the regressions on EBV were of statistical significance, even though their impact on the residual variance of the contributions was small. The empirical relationship between long-term contributions and  $\hat{a}_{conv}$  or  $EBV_{conv}$  is illustrated in Fig. 1, which includes all the observations generated across replicates for  $h^2=0.25$  and  $\Delta F=0.01$  or 0.02.

The efficiency for the schemes in Table 2, described by  $\gamma$ , depended most strongly on  $\Delta F$  with only small differences between  $h^2=0.01$ , 0.25 and 0.50, with  $\gamma=0.96$ , 0.84 and 0.55, approximately, for  $\Delta F=0.005$ , 0.01 and 0.02. For  $h^2=0.99$ ,  $\gamma$  was always slightly lower than the corresponding values of  $\gamma$  observed for other values of  $h^2$  for the same  $\Delta F$ . Thus, the lowest  $\gamma$  observed for quadratic optimization in this study was 0.47 for  $\Delta F=0.02$  and  $h^2=0.99$ .



Table 2. The proportion of variance explained by multivariate regression of  $c_i$  and  $r_i$  on  $\hat{a}$  and EBV at selection and convergence of  $r_i$ , respectively, for a range of heritabilities ( $h^2$ ) and different constraints on  $\Delta F$ , for  $N=200$

$\Delta F$	$h^2$	$c_i$ on $\hat{a}_{sel}$ & $EBV_{sel}$			$r_i$ on $\hat{a}_{conv}$ & $EBV_{conv}$		
		$V_{c,\hat{a}_{sel}}$	$V_{c,EBV_{sel}}$	$V_{c,tot}$	$V_{r,\hat{a}_{conv}}$	$V_{r,EBV_{conv}}$	$V_{r,tot}$
0.005	0.01	0.60	0.01	0.88	0.40	0.00	0.87
	0.25	0.57	0.00	0.89	0.40	0.00	0.85
	0.50	0.53	0.00	0.88	0.39	0.00	0.80
	0.99	0.35	0.00	0.75	0.23	0.00	0.49
0.010	0.01	0.56	0.03	0.71	0.41	0.00	0.77
	0.25	0.52	0.02	0.76	0.35	0.01	0.75
	0.50	0.50	0.01	0.77	0.33	0.00	0.70
	0.99	0.34	0.00	0.71	0.22	0.00	0.47
0.020	0.01	0.47	0.02	0.51	0.47	0.00	0.69
	0.25	0.43	0.04	0.58	0.30	0.01	0.63
	0.50	0.41	0.03	0.62	0.26	0.01	0.59
	0.99	0.37	0.00	0.69	0.25	0.00	0.47

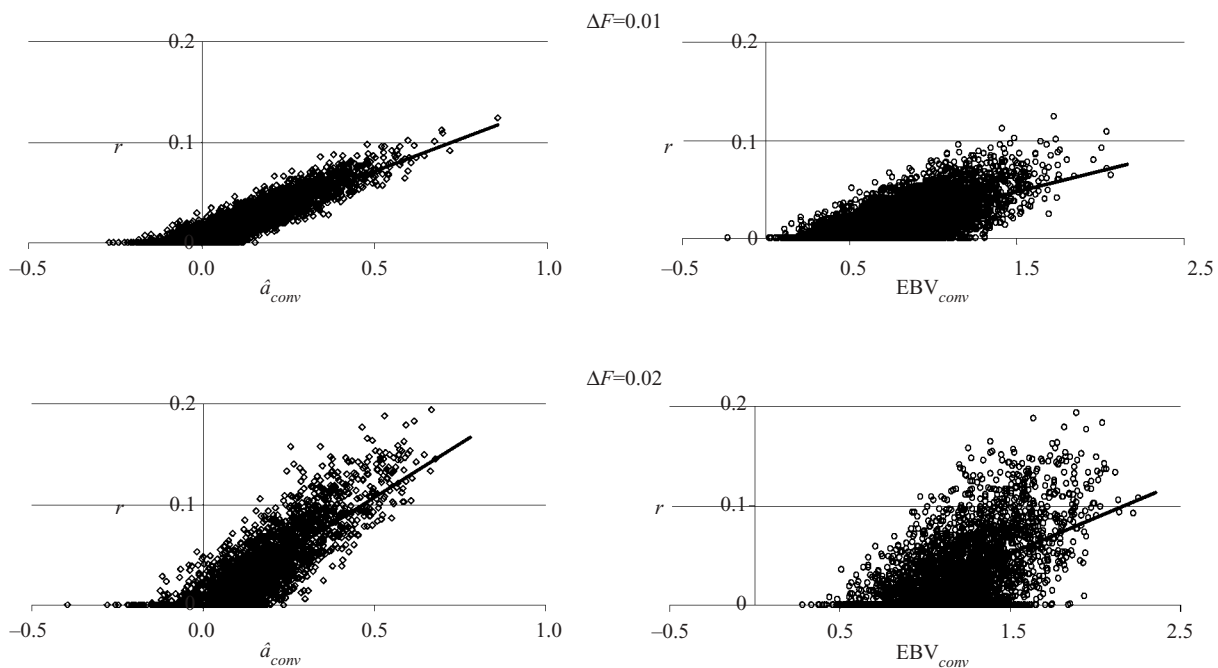


Fig. 1. Relationship between long-term contributions ( $r$ ) and estimated Mendelian sampling terms ( $\hat{a}_{conv}$ ) or estimated breeding values ( $EBV_{conv}$ ) at the convergence of the long-term contributions under quadratic optimization for  $N=100$ ,  $h^2=0.25$  and two  $\Delta F$  constraints.

Fig. 2 compares the relationships between  $r$  and  $\hat{a}_{conv}$ , and between  $c$  and  $\hat{a}_{sel}$  for  $h^2=0.25$  and  $\Delta F=0.01$  or  $0.02$ . The  $c$  value was plotted against  $\hat{a}_{sel}$  (i.e. at generation 3) and superimposed on the plot of  $r$  against  $\hat{a}_{conv}$ . For  $\Delta F=0.01$ , the regression lines of  $c$  and  $\hat{a}_{sel}$ , and of  $r$  and  $\hat{a}_{conv}$  are very similar ( $b_{c,\hat{a}_{sel}}=0.132\pm 0.0007$ ;  $b_{r,\hat{a}_{conv}}=0.129\pm 0.0007$ ), although, for  $\Delta F=0.02$ , there was a greater discrepancy ( $b_{c,\hat{a}_{sel}}=0.247\pm 0.0027$ ;  $b_{r,\hat{a}_{conv}}=0.213\pm 0.0023$ ). For the broader range of parameters for  $\Delta F$  and  $h^2$  considered in this study, the results (not shown) suggest that  $b_{c,\hat{a}_{sel}}$  is a reasonable estimator of  $b_{r,\hat{a}_{conv}}$  for the

quadratic index. Discrepancies were largest for  $h^2=0.01$  where  $b_{c,\hat{a}_{sel}}$  was more clearly greater than  $b_{r,\hat{a}_{conv}}$ .

#### (ii) Estimated Mendelian sampling terms of selected and unselected candidates under quadratic optimization

The frequency distribution of the estimated Mendelian sampling at the time of selection ( $\hat{a}_{sel}$ ) of selected and unselected candidates born in generation 3 across the 100 replicates for  $N=100$  is presented in Fig. 3. For  $\Delta F=0.01$ , the proportion of selected candidates

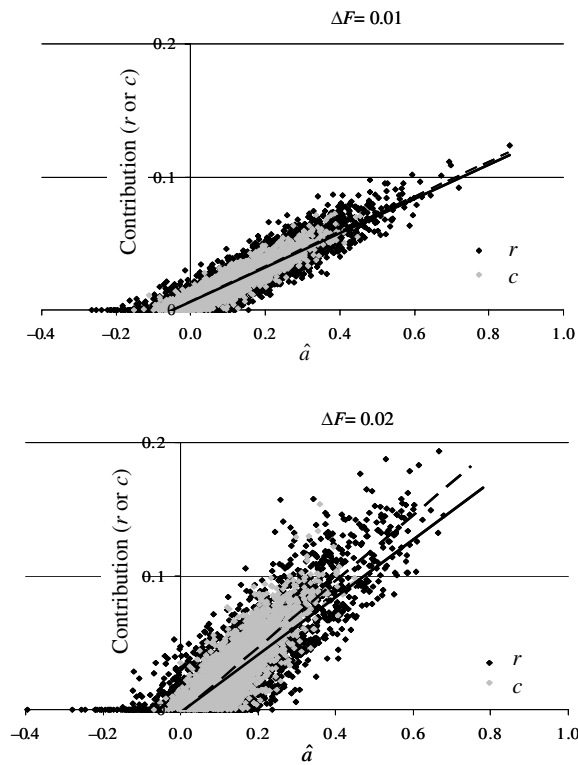


Fig. 2. Relationship between long-term contributions ( $r$ ) and estimated Mendelian sampling terms at convergence ( $\hat{a}_{conv}$ ) (solid line) and between mating proportions ( $c$ ) and estimated Mendelian sampling term at selection time ( $\hat{a}_{sel}$ ) (broken line) under quadratic optimization for  $N=100$ ,  $h^2=0.25$  and two  $\Delta F$  constraints.

( $p$ ) was 0.5943. For  $\Delta F=0.02$ ,  $p$  was reduced to 0.3584. The mean  $\hat{a}_{sel}$  was higher for selected candidates than for unselected candidates, and the difference in  $\hat{a}_{sel}$  between the groups was similar for both  $\Delta F$  constraints (i.e. about 0.56 standard deviations of the true Mendelian sampling term in the base population).

The coefficient of right skewness of the distribution of  $\hat{a}_{sel}$  for selected candidates was about 0.7 for both levels of inbreeding constraint. However, the degree of left skewness of the distribution of non-selected candidates changed with the  $\Delta F$  restriction ( $-0.77$  for  $\Delta F=0.01$  and  $-0.58$  for  $\Delta F=0.02$ ). Thus, a greater  $\Delta F$  resulted in a more symmetric distribution of those individuals that remained unselected.

(iii) *Qualitative comparison between optimal selection and truncation selection*

Table 3 shows a comparison of the relationship of  $r_i$  with the potential selective advantages for selection using quadratic optimization and for truncation. It shows that the joint regression on the potential selective advantages explained a much greater proportion of the unadjusted variance when selection used quadratic optimization (0.841 as against 0.486). Furthermore, although this was almost entirely explained by

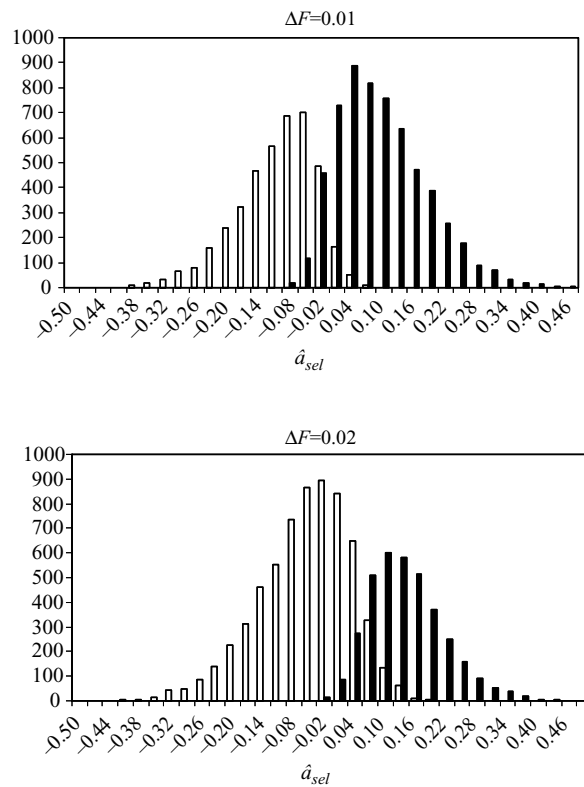


Fig. 3. Frequency distribution of Mendelian sampling terms at selection time ( $\hat{a}_{sel}$ ) for selected and unselected candidates under quadratic optimization for  $N=100$ ,  $h^2=0.25$  and two  $\Delta F$  constraints.

$\hat{a}_{conv}$  for quadratic optimization, both selective advantages contributed to the reduction for truncation selection, with  $EBV_{conv}$  making slightly more impact.

The relationship between long-term contributions and estimated Mendelian sampling terms or estimated breeding values at convergence of  $r$  (i.e. generation 8) across replicates are shown for truncation selection in Fig. 4 for  $h^2=0.25$  and  $\Delta F=0.01$ . The simple correlations between  $r$  and  $\hat{a}_{conv}$ , and between  $r$  and  $EBV_{conv}$  were 0.63 and 0.69, respectively, whereas the corresponding values for quadratic optimization were 0.92 and 0.65. The efficiencies  $\gamma$  for selection using quadratic optimization and for truncation were also very different (0.95 and 0.50, respectively) (Table 3). This was reflected in 1.13-fold greater  $\Delta G$  using quadratic optimization.

The comparison between the frequency distributions of  $\hat{a}_{sel}$  and  $EBV_{sel}$  for selected and non-selected candidates under quadratic optimization and truncation selection across generations and replicates is presented in Fig. 5 for  $\Delta F=0.01$ . Distributional parameters are given in Table 4. It should be realized that the overlap between the frequency distributions of  $EBV_{sel}$  for selected and unselected candidates for truncation selection is purely an artefact created from the use of pooled data across replicates because, in a single replicate, every selected candidate will have

Table 3. Comparison of the parameters describing the relationship of  $r$  with  $\hat{a}_{conv}$  and  $EBV_{conv}$  for selection using quadratic optimization and truncation, for  $h^2=0.25$ ,  $\Delta F=0.01$  and  $N=100$ . Significance levels are those for the corresponding parameters in Table 1

Selection method	$\rho_{r,\hat{a}_{conv}}$	$\rho_{r,EBV_{conv}}$	$V_{r,\hat{a}_{conv}}$	$V_{r,EBV_{conv}}$	$V_{r,tot}$	$\gamma$
Optimization	0.85	0.05	0.415	0.000	0.841	0.92
Truncation	0.33	0.38	0.063	0.087	0.486	0.50

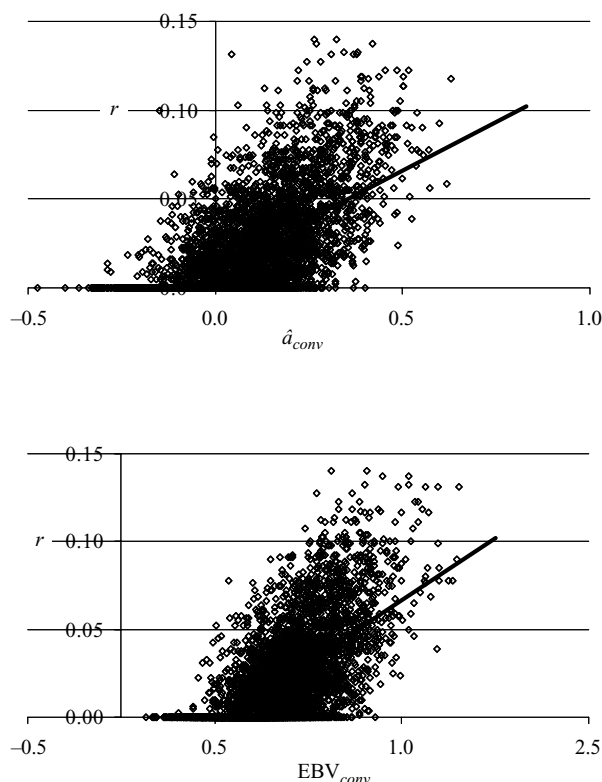


Fig. 4. Relationship between long-term contributions ( $r$ ) and estimated Mendelian sampling terms ( $\hat{a}_{conv}$ ) or estimated breeding values ( $EBV_{conv}$ ) at convergence of the long-term contributions under truncation selection for  $N=100$ ,  $h^2=0.25$  and  $\Delta F=0.01$ .

higher  $EBV_{sel}$  than every unselected candidate. However, this is not the case for the frequency distributions of  $\hat{a}_{sel}$ , for which, even under truncation selection, some overlapping can occur between selected and unselected candidates. For quadratic optimization the overlapping between selected and unselected candidates is a property of the method and can occur for both  $\hat{a}_{sel}$  and the  $EBV_{sel}$  within a single replicate.

The degree of overlap between frequency distributions of selected and unselected candidates differed between selection methods and depended on the selective advantage used by the selection method. For quadratic optimization,  $p(\hat{a}_{iSEL} \geq \hat{a}_{jUNSEL})$  was 0.988, whereas  $p(EBV_{iSEL} \geq EBV_{jUNSEL})$  was 0.839. By contrast, for truncation selection, using pooled

observations,  $p(\hat{a}_{iSEL} \geq \hat{a}_{jUNSEL})$  was 0.832, whereas  $p(EBV_{iSEL} \geq EBV_{jUNSEL})$  was 0.955. Thus, at selection time, the probability that the selective advantage of a selected candidate will be equal to or greater than that of an unselected candidate was higher when the selective advantage was  $\hat{a}_{sel}$  under quadratic optimization and when it was  $EBV_{sel}$  under truncation selection. Other definitions of this probability (e.g. excluding the same selective advantage bin, thus  $p(\hat{a}_{iSEL} > \hat{a}_{jUNSEL})$ ) made no qualitative difference to the result presented.

#### 4. Discussion

This study has empirically demonstrated that, when selection uses quadratic optimization, the selection advantage for candidates is the estimated Mendelian sampling term. From initial selection to convergence of genetic contributions, quadratic optimization attempts to allocate contributions of selected candidates according to the best available information on their estimated Mendelian sampling term, not their breeding value. Therefore, with quadratic optimization, candidates are selected or culled according with the estimate of their independent and unique superiority or inferiority with respect to the parental average. This contrasts with BLUP truncation selection, in which the fate of candidates depends upon their EBVs and so their selective advantage is not independent of the parental average.

Grundy *et al.* (1998b) postulated the relationship between long-term contributions and Mendelian sampling terms under constrained inbreeding from a theoretical standpoint, and stated that the maximum gain could be obtained with an exact linear allocation of long-term contributions of selected candidates according to their Mendelian sampling terms (Fig. 6). In the ideal outcome, a candidate will have a long-term contribution greater than zero only if its  $a$  is greater than the value ( $u$ ) at the intercept of the regression line of  $r$  on  $a$ , and its converged contribution will be given by the regression equation (i.e. for a candidate  $i$ ,  $r_i = b(a_i - u)$ , where  $b$  is the regression slope). For a tight  $\Delta F$  constraint, both  $u$  and  $b$  will be lower than for a more relaxed constraint.

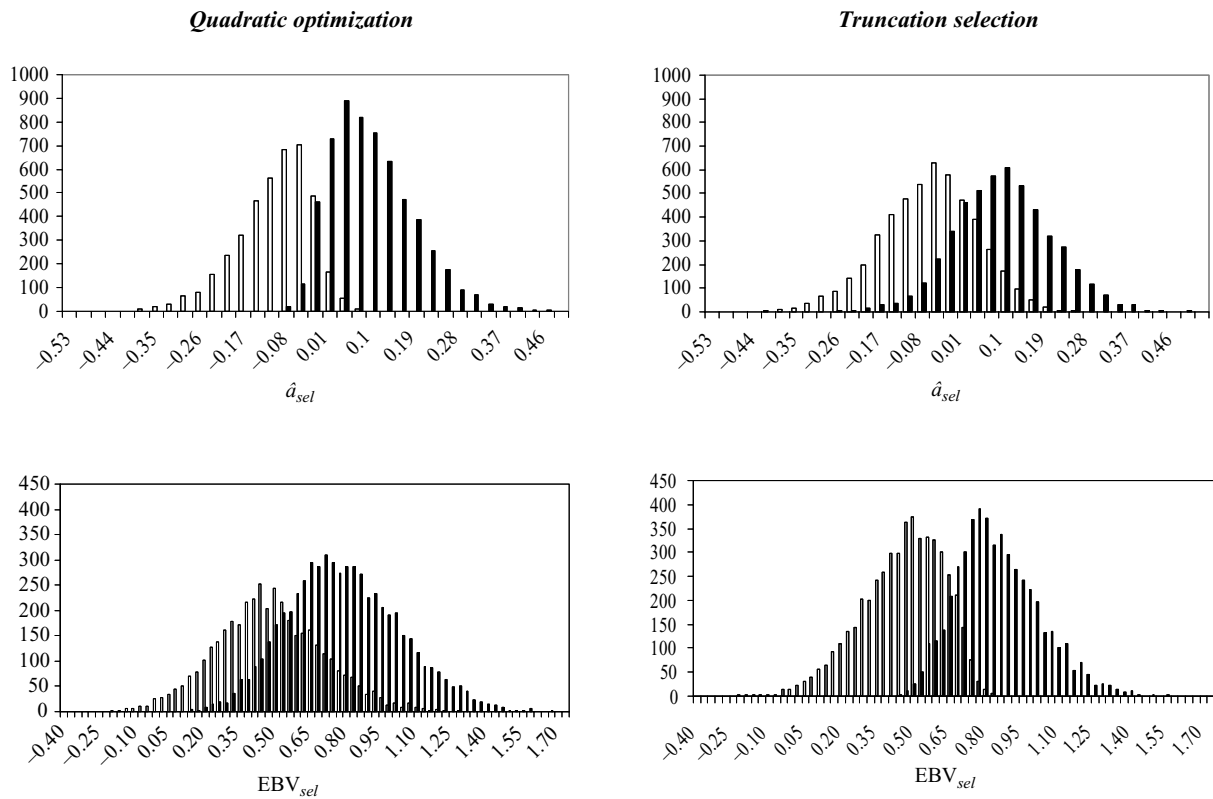


Fig. 5. Frequency distributions of estimated Mendelian sampling terms ( $\hat{a}_{sel}$ ) and estimated breeding value at selection time ( $EBV_{sel}$ ) for selected and unselected candidates under quadratic optimization and truncation selection for  $N=100$ ,  $h^2=0.25$  and  $\Delta F=0.01$ .

Table 4. *Distributional parameters of  $\hat{a}_{sel}$  and  $EBV_{sel}$  for selected and unselected candidates when selection uses quadratic optimization and truncation. All parameters are calculated after pooling data over replicates*

Parameter	Optimization		Truncation	
	Unselected	Selected	Unselected	Selected
$\hat{a}_{sel}$				
Mean	-0.119	0.080	-0.076	0.078
Mode	-0.077	0.046	-0.069	0.051
Variance	0.006	0.007	0.010	0.011
Quartiles				
25 %	-0.164	0.015	-0.143	0.007
Median	-0.106	0.067	-0.071	0.075
75 %	-0.063	0.132	-0.009	0.143
$EBV_{sel}$				
Mean	0.462	0.772	0.442	0.833
Mode	0.427	0.734	0.495	0.743
Variance	0.051	0.057	0.029	0.030
Quartiles				
25 %	0.309	0.604	0.334	0.711
Median	0.452	0.758	0.462	0.813
75 %	0.610	0.931	0.515	0.942

The present study is the first presenting empirical evidence of relationship between long-term contributions and Mendelian sampling terms with quadratic

optimization. The primary evidence that, under quadratic optimization, the selective advantage is the Mendelian sampling comes from the analysis of the relationships between contributions (i.e. either  $c$  or  $r$ ),  $\hat{a}_{conv}$  and  $EBV_{conv}$ . Not only were the partial correlations coefficients involving  $\hat{a}_{conv}$  much greater than those involving the  $EBV_{conv}$  irrespective of the  $\Delta F$  constraint but also a simple regression of contributions on  $\hat{a}_{conv}$  performed as well as the bivariate regression on both potential selective advantages. By contrast, under truncation selection, there was no clear distinction between selective advantages in their relationship with contributions. Additionally, at selection time, the probability that a selected candidate had an equal or greater  $\hat{a}_{sel}$  than an unselected candidate was greater with quadratic optimization than under truncation selection. However, the opposite was true for  $EBV_{sel}$ , supporting the hypothesis that the two approaches to selection work on different underlying selective advantages. The observation that the joint regression of  $\hat{a}_{conv}$  and  $EBV_{conv}$  predicted  $r$  notably better than  $EBV_{conv}$  alone is not surprising given the results of Woolliams *et al.* (1999b). They showed that the regression coefficients of  $r$  on  $EBV_{sel}$  and  $(EBV_{conv} - EBV_{sel})$  were different and so the two variables  $\hat{a}_{conv}$  and  $EBV_{conv}$  give better a opportunity to approximate this complex relationship than  $EBV_{conv}$  alone.



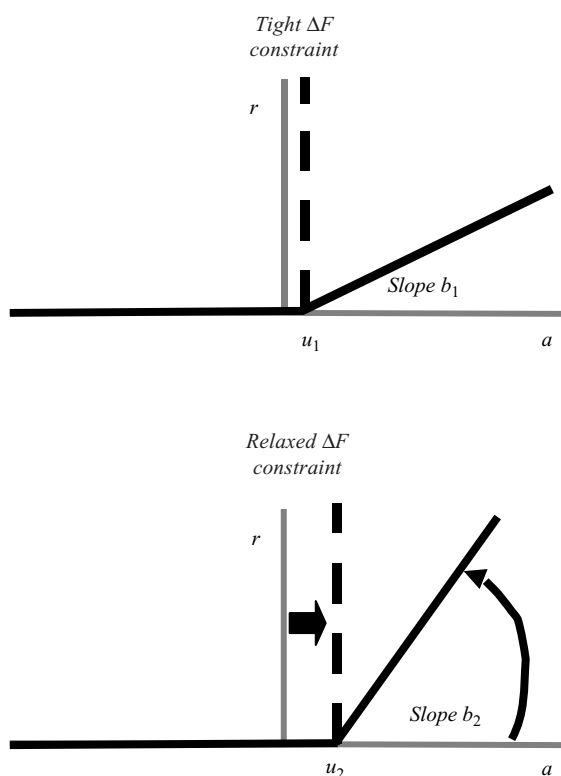


Fig. 6. Ideal outcome for the optimization of genetic gain for constrained rate of inbreeding ( $\Delta F$ ) according with Grundy *et al.* (1998a), adapted from Woolliams *et al.* (2002).

The expression for genetic gain of Woolliams & Thompson (1994) made explicit that sustained genetic gain arises from creating a covariance between the  $r$  and  $a$  (i.e.  $E(\Delta G) = \sum r_i a_i$ ), exploiting the Mendelian sampling term variance (i.e. the new genetic variation created each generation). It is therefore reasonable that an algorithm for maximizing gain should relate contributions to the Mendelian sampling terms or at least to their best available estimate. Figs 1 and 2 explicitly show that quadratic optimization attempts to maximize this covariance from selection time to the convergence of the long-term contributions.

The most obvious qualitative difference between truncation selection and quadratic optimization arises from the usage of selected candidates. Whereas, in truncation selection, all individuals with an EBV above a certain truncation point are allocated the same mating proportions, in quadratic optimization, the usage is allowed to vary among selected candidates. Toro & Nieto (1984) first proposed the idea of allowing unequal contributions of selected candidates as an alternative to truncation selection under mass selection. By using a quadratic optimization approach they minimized the sum of squares of contributions of selected candidates while maintaining a predefined selection intensity. This approach allowed the maximization of the effective population size (judged

by the mating proportions), by allocating optimal contributions according to ranking scores. The allocation of higher contributions to individuals with higher selective advantage is an important property of quadratic optimization with predefined levels of  $\Delta F$ .

The true Mendelian sampling term of selected candidates is unknown and so the quadratic optimization relies on the use of their best estimates at the time of selection. Thus, at selection time contributions to the next generation are allocated according to the initial  $a$  estimates (Woolliams *et al.*, 2002). This means that the accuracy of the estimate of the Mendelian sampling term is one of the relevant parameters in determining the degree of 'noise' in the optimization system (i.e. the amount of departure from the ideal solution (Fig. 6)). Departures from the ideal solution, represented by the scatter around the straight lines in Fig. 1, have been regarded by Woolliams *et al.* (2002) as unavoidable 'contribution errors'. As indicated in the Methods, these can be used to give a measure of efficiency for a selection scheme, describing with what efficiency the loss of genetic variance is harnessed to produce desired gain. Benchmark efficiency values of 0.917 and 0.837 were obtained for  $h^2 = 0.25$  with schemes constrained to  $\Delta F$  of 0.01 and 0.02, respectively. These are indeed high efficiencies and the results suggest that schemes with more relaxed constraints (i.e. higher  $\Delta F$ ) might be less efficient in the exploitation of genetic variation even when using quadratic indices. This indicates that the degree to which  $\Delta F$  is constrained controls the amount of departure from the ideal solution, which was expected as the theoretical ideal outcome was derived under a constrained assumption. By contrast, under truncation selection, an efficiency of only 0.50 was found for  $\Delta F = 0.01$  and  $h^2 = 0.25$ .

We have shown that the outcome of the quadratic optimization at selection time, summarized by  $b_{c,\hat{a}_{sel}}$ , is a good estimator of the optimization outcome that would be obtained if converged long-term contributions and the best estimate of the Mendelian sampling term ( $b_{r,\hat{a}_{conv}}$ ) were available. Greater deviations from the ideal outcome observed for the relationship of  $r$  on  $\hat{a}_{conv}$  reduces the ability to manage individual contributions independently in a dynamic multiple generational selection process. As stressed by Woolliams *et al.* (2002), changing an individual's contribution will affect the contribution of all its ancestors and changing the contribution of a male or female parent through its offspring will affect the contribution of its mates. Therefore, although the estimate of the Mendelian sampling term will be more accurate as information accumulates, the management of an individual contribution becomes less and less independent as selection progresses.

An alternative way of assessing the impact of  $\rho_a$ , the accuracy of the estimate of the Mendelian sampling

term, on the outcome of the optimization process is by observing the change in the 'effective number of parents' from selection to convergence of contributions. The sum of squares of mating proportions and the sum of squares of the long-term contributions of selected candidates can be regarded as the 'effective number of parents' of equal contribution (e.g. Robertson, 1965) at selection time,  $N_c = [\sum c^2]^{-1}$ , and at convergence,  $N_r = [\sum r^2]^{-1}$ , respectively. For instance, for  $\Delta F = 0.01$  and  $h^2 = 0.01$ ,  $N_c$  was 43.2,  $N_r$  was 26.7 and  $\rho_a$  increased from 0.052 at selection time to 0.103 at convergence. By contrast, for  $\Delta F = 0.01$  and  $h^2 = 0.99$ ,  $N_c$  was 33.1,  $N_r$  was 26.4 and  $\rho_a$  was 0.968 both at selection time and at convergence. This indicates that, for a given  $\Delta F$  constraint, the process of building up of  $\rho_a$  (thus, the agreement between the initial and the converged solution) is controlled by the heritability of the trait.

Our results provide the relevant empirical validation for the theoretical optimal solution of Grundy *et al.* (1998b) for the optimization problem under constrained  $\Delta F$  formulated in terms of  $r$  and  $a$ . It should be emphasized that our observations on the outcome and mechanics of quadratic optimization are drawn from an ongoing use of dynamic selection in the breeding scheme, and the same outcome might not be achieved after only a single generation application of the method. Importantly, this study clearly provides evidence that the outcome of the quadratic optimization relies on the accuracy of the knowledge of the Mendelian sampling terms at the time of selection. Therefore, there is a need for developing such deterministic predictions for the accuracy of predicted Mendelian sampling terms in order to obtain predictions of gain in a constrained optimization context.

Mendelian linear indices were proposed by Woolliams & Thompson (1994) as a way of explicitly altering the amount of weight given to family information for the flexible management of genetic gain and inbreeding. These indices rely on the decomposition of EBVs and the reweighing of the estimated Mendelian terms, progressively reducing weights given to more distant ancestors. Grundy *et al.* (1998a) found them to be useful for managing gain and inbreeding. Although the concept of using Mendelian sampling terms as a selective advantage was a step in the right direction, the implementation of the concept is most effectively done through the quadratic index rather than the linear index described by Grundy *et al.* (1998a).

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