Dynamic selection procedures for constrained inbreeding and their consequences for pedigree development

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Summary

A novel selection algorithm for maximizing genetic response while constraining the rate of inbreeding is presented. It is shown that the proposed method controls the rate of inbreeding by maintaining the sum of squared genetic contributions at a constant value and represents an improvement on previous procedures. To maintain a constant rate of inbreeding the contributions from all generations are weighted equally and this is facilitated by modifying the numerator relationship matrix. By considering the optimization of the contributions of many generations the initial mating proportions (the genetic contributions to the next generation) are not equal to their long-term values, but are set equal to the expected long-term contributions given the current information. This is confirmed by the regression of the long-term contributions on the assigned mating proportions being close to one. The gain obtained from the selection algorithm is compared with the maximum theoretical genetic gain under constrained inbreeding. It is concluded that this theoretical upper bound is in general unattainable, but from this a concept of genetic efficiency in terms of resources and constraints is derived.

1. Introduction

The problem of optimizing genetic progress with constrained rates of inbreeding has only recently been explored, following the development of a coherent underpinning theory for predicting rates of inbreeding under selection (Wray & Thompson, 1990). Optimal designs for maximizing gain with constrained inbreeding have been developed with mass selection (Villanueva *et al.*, 1996), and with sib-indices (Villanueva & Woolliams, 1997). However, there are limitations: (i) these designs are special cases, and do not, for example, cover selection using BLUP; and (ii) they are tools for designing schemes *a priori*, but do not offer guidance for selection decisions in practice that involve a particular given set of candidates with performance and pedigree records.

Unlike the advances in the deterministic predictions for genetic gain and inbreeding, the development of dynamic selection algorithms for designing schemes *a posteriori* (Woolliams & Meuwissen, 1993; Wray & Goddard, 1994; Brisbane & Gibson, 1995) has proceeded largely without the application of genetic contribution theory (Woolliams & Thompson, 1994). The approach employed in the design of these algorithms is to describe the problem of a constrained maximum gain as a quadratic programming problem. The gain is maximized step by step, optimizing progress one generation in the future. Where the constraint has been on the rate of inbreeding the selection decision has involved consideration of the relationships between successful candidates, and has allowed different mating proportions for selected individuals. Meuwissen (1997) developed an algorithm that showed how to obtain explicit solutions for this problem, which are near-optimal using the numerator relationship matrix (**A**). The shortfalls of these procedures are that: (i) they do not achieve a constant rate of inbreeding over several generations of selection; and (ii) because of a lack of accompanying

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theory it is unclear whether consideration of only the next generation provides the optimal, feasible solution to the long-term problem.

An approach to understanding the theoretical problem is provided by the concept of long-term genetic contributions (James & McBride, 1958). Woolliams & Thompson (1994) developed this approach to show that the long-term rates of gain and inbreeding that were attributable to a generation could be described in a unified way by contributions. Furthermore, they showed that the recurrent selection problem constrained by rates of inbreeding could be recast in a form that was analogous to a previously solved problem of optimal allocation of clones in one generation (Bondesson, 1989).

This paper has four objectives. First, it seeks to improve existing methods for maximizing gain while restricting the rate of inbreeding by introducing modifications to existing algorithms (using an augmented numerator relationship matrix (A^*) and an associated constraint). Secondly, it examines the relationship of the optimal mating proportions in dynamic selection procedures with long-term contributions in order to describe the process by which individual contributions influence the way the pedigree develops. Thirdly, it extends the results of Woolliams & Thompson (1994) for deriving explicitly a theoretical upper bound to genetic progress as a function of the constraints imposed and the resources available. Finally, it develops a concept of genetic efficiency by comparing the results of applying the modified dynamic algorithm with the theoretical upper bound.

2. Methods

(i) *Simulation models*

Stochastic computer simulations were used to model the effects of dynamic selection routines on the way the pedigree develops and to compare rates of gain and inbreeding from using different selection algorithms. Populations with discrete generations were evaluated over 20 generations. An additive infinitesimal model (Bulmer, 1971) was considered. The trait under selection was assumed to be of known heritability (h^2) and the genetic evaluation was carried out using an animal model BLUP. True breeding values of unrelated individuals in the base population ($t = 0$) were obtained from a normal distribution with mean zero and variance h^2. Phenotypic values were obtained by adding a normally distributed environmental component with mean zero and variance ($1 - h^2$). In each subsequent generation, the optimum number of sires and dams were selected as described below. The number of offspring born per generation was 100 (50 males and 50 females). True breeding values of the offspring were generated as half the sum of the true breeding values of the animal's sire and dam plus a Mendelian sampling term taken from a normal distribution with mean zero and variance $(\frac{1}{2})[1 - \frac{1}{2}(F_s + F_d)] h^2$, where F_s and F_d are the inbreeding coefficients of the sire and the dam, respectively. The rates of inbreeding and response were calculated for each generation.

Three different dynamic selection algorithms were employed, all based upon the algorithm presented by Meuwissen (1997). For each algorithm, the number of sires and dams and their contributions were optimized each generation of selection in order to maximize the rate of gain subject to a constraint on the rate of inbreeding.

(a) *Algorithm I*

Algorithm I was as described by Meuwissen (1997). In brief, the algorithm uses the estimated breeding values and the numerator relationship matrix (A) to identify an optimum mating proportion for each individual i at generation t ($c_{i,t}$), where $c_{i,t} = 0$ implies that the individual is not required for breeding. It achieves this by maximizing

$$f(\mathbf{c}) = \mathbf{c}_t^T \mathbf{g}_t - \lambda \mathbf{c}_t^T \mathbf{A}_t \mathbf{c}_t,$$

where $\mathbf{c}_t$ is the vector of mating proportions of selection candidates at generation t (i.e. genetic contributions to the next generation), $\mathbf{g}_t$ is the vector of estimated breeding values, $\mathbf{A}_t$ is the numerator relationship matrix of candidates, and λ is a Lagrangian multiplier. Constraints are imposed so that mating proportions are positive (i.e. $c_{i,t} \geqslant 0$) and sum to 1 (i.e. $\Sigma_i c_{i,t} = 1$). The Lagrangian multiplier is chosen to achieve the constraint $\mathbf{c}_t^T \mathbf{A}_t \mathbf{c}_t \leqslant 2t\Delta F$, where ΔF is the intended rate of inbreeding and t is the generation number.

For an individual with mating proportion $c_{i,t}$ the desired number of offspring was $200c_{i,t}$ (since 100 was the total number of candidates per generation and the contributions sum to a half for each sex). The actual number was achieved through a process of: (i) reducing the desired real number to the largest integer below it and then allocating a mate at random to produce a single offspring per mating; and (ii) adding further offspring to parents with the greatest deviations from the desired number until the numbers of offspring sum to 100, again allocating mates at random. The sex of the offspring was randomly determined.

(b) *Algorithm II*

Algorithm I controls the increase in average coancestry and hence it constrains the absolute increase in inbreeding coefficient from time $t-1$ (F_{t-1}) to time t (F_t), rather than the rate of inbreeding. This increase

in the inbreeding coefficient approximates ΔF only when F_{t-1} is small. In Algorithm II a straightforward modification of Algorithm I to achieve the restriction on ΔF was applied by setting the constraint, $C_t = 1 - (1 - 2\Delta F)^t$.

(c) *Algorithm III*

In contrast to the previous algorithms, Algorithm III controls the total increase in squared genetic contributions each generation to constrain ΔF. This was achieved by modifying Algorithm I by replacing $\mathbf{A}$ with an augmented matrix $\mathbf{A}^*$. The augmented matrix for individuals in the generation $t+1$ was calculated as

$$\mathbf{A}^*_{t+1} = \mathbf{Z}_t \mathbf{A}^*_t \mathbf{Z}_t^{\mathrm{T}} + \mathbf{D},$$

where $\mathbf{D}$ is diagonal with elements equal to $\frac{1}{2}$ and $\mathbf{Z}_t$ is a gene flow matrix (Hill, 1974) identifying parents of generation $t+1$. With the offspring in rows and parents in columns, the elements of $\mathbf{Z}_t$ are either $\frac{1}{2}$ (parents) or 0 (otherwise) (Thompson, 1977; Wray & Thompson, 1990). For $t = 0$ (base population), $\mathbf{A}^*_0 = \mathbf{I}$. By augmenting $\mathbf{A}$ the diagonal terms are no longer scaled by one minus the average inbreeding of the parents and hence the base is in effect re-defined each generation. Therefore, each generation can be used to constrain ΔF to a constant value as the differential treatment of generations arising from this dependence on the average inbreeding of the parents is removed. A proof that $\mathbf{c}_t^{\mathrm{T}} \mathbf{A}^*_t \mathbf{c}_t$ can be used to constrain the rate of inbreeding is presented in Appendix A.

The constraint applied in this algorithm is $\mathbf{c}_t^{\mathrm{T}} \mathbf{A}^*_t \mathbf{c}_t \leqslant t\Delta C$, where ΔC is set to $2\Delta F [1 - 3\Delta F + 12(\Delta F)^2]$; this is approximately equal to ΔF for small values of ΔF but is marginally greater than ΔF for larger ΔF, due to second-order effects (see Appendix B). Henceforth $\mathbf{A}^*_t$, $\mathbf{A}_t$ and $\mathbf{c}_t$ will be abbreviated as $\mathbf{A}^*$, $\mathbf{A}$ and $\mathbf{c}$, respectively.

(d) *Relationship between mating proportions and long-term contributions*

The total number of parents selected each generation was obtained along with the 'effective' number (N) of each sex which was derived from $(4\mathbf{c}^{\mathrm{T}}\mathbf{c})^{-1}$ (Robertson, 1965). For each replicate using $\mathbf{A}^*$, the long-term contributions ($\mathbf{r}$) were calculated using the program used by Woolliams & Mäntysaari (1995) for individuals born at generation 15. The long-term contribution of an individual i was defined as the proportion of genes in generation 20 that derived from that ancestor. The regression of r_i on c_i was calculated for each replicate using only those individuals for which $c_i > 0$. In addition, $\mathbf{r}^{\mathrm{T}}\mathbf{r}$, $\mathbf{c}^{\mathrm{T}}\mathbf{c}$ and their ratio were calculated for ancestors in generation 15.

Generation 15 was chosen since this is the last generation whose contributions are near convergence by the end of the simulation ($t = 20$).

To obtain the regression of $\mathbf{r}$ on $\mathbf{c}$, the results for generation 15 were subdivided by sex, replicate and the number of parents selected. The regression coefficients and their associated standard errors were calculated within each category and were pooled using weights inversely proportional to the sampling variance. An analysis of variance found no significant differences in slope due to number of parents.

(e) *Parameters*

The schemes were run for a range of heritabilities (0·01, 0·25 and 0·99) and constraints on the rate of inbreeding (0·006 25, 0·025 and 0·05). A minimum of 100 replicates were run for each combination and results presented are averages over replicates.

(ii) *Upper bounds for rate of progress and efficiency*

Bondesson (1989) solved an allocation problem concerning the planting of optimal proportions (k_i) of clones with known genetic values (A_i) to maximize gain ($\Sigma k_i A_i$) in a single crop with a constraint on genetic diversity (namely $\Sigma k_i^2 \leqslant \gamma^{-1}$). Here γ has a lower bound of one attained when only one clone is planted throughout the crop. This problem is equivalent to a recurrent selection problem with constrained inbreeding if we consider Mendelian sampling terms (a_i) rather than genetic values and long-term contributions (r_i) rather than clonal proportions. For infinite populations (Bondesson, 1989) the solution to the problem of obtaining maximum genetic gain under constrained diversity was obtained by maximizing

$$\int ar(a)\,\phi(a)\,\mathrm{d}a,$$

where the integration is bounded by $-\infty$ and $+\infty$, subject to the constraints:

(i) $r(a) \geqslant 0$ (i.e. all contributions are non-negative),

(ii) $\int r(a)\,\phi(a)\,\mathrm{d}a = 1$ (i.e. the total contribution over all individuals is one),

(iii) $\int [r(a)]^2 \phi(a)\,\mathrm{d}a = \gamma^{-1}$ (i.e. the diversity is constrained),

$$\left.\right\} (1)$$

where $\phi(a)$ is the density function for the Mendelian sampling terms and $r(a)$ is the total long-term contribution in the population for individuals with Mendelian sampling term a.

When finite population sizes and constraints on rates of inbreeding are considered then the number of individuals in an interval a to $a + \delta a$ is $2T\phi(a)\delta a$ (where T is total number of candidates per sex, and

the 2 arises from considering both sexes). The problem can be recast to provide the optimum solution to the recurrent selection problem considered here of maximizing ΔG with a constraint on ΔF as $\Delta G = 2TE[r_i a_i]$ and $\Delta F = 2TE[r_i^2]$ (Woolliams & Thompson, 1994). Here we will assume $\Delta F = \frac{1}{2}\Delta C$, as for the majority of cases the difference between the two is small. Thus the solution to the constrained maximization problem is obtained by maximizing

$$\Delta G = \int 2Tar(a)\,\phi(a)\,\mathrm{d}a$$

subject to the constraints

(i) $r(a) \geqslant 0$;
(ii) $\int 2Tr(a)\,\phi(a)\,\mathrm{d}a = 1$;
(iii) $\int 2T[r(a)]^2\,\phi(a)\,\mathrm{d}a = 4\Delta F$.

Multiplying through the third constraint by $2T$ and substituting $r^*(a) = 2Tr(a)$ we recover the form of constraint equations from (1) with $\gamma^{-1} = 8T\Delta F$. Since the minimum rate of inbreeding with T candidates per sex is $(8T)^{-1}$, the constraint that $\gamma \leqslant 1$ is satisfied. Therefore, the maximum ΔG is identical to the solution of Bondesson (1989) with γ replaced by $(8T\Delta F)^{-1}$.

Assuming a normally distributed Mendelian sampling term, and expressing gain in terms of i (mean deviation of individuals with values exceeding the truncation point) and x (deviation of the truncation point from the mean), the expression of Bondesson (1989) for the maximum theoretical (ideal) gain (ΔG_{ideal}) can be rewritten for recurrent selection as

$$\Delta G_{ideal} = (i-x)^{-1}$$

and the values for i and x are such that γ is the solution of

$$\gamma = 2p(i-x)^2(1+x^2-ix)^{-1},$$

where p is the proportion selected. The solution for x can be found by using the Newton–Raphson method.

The above expression for ΔG_{ideal} assumes a standard deviation of Mendelian sampling terms of one. Making this expression more general the maximum theoretical genetic gain per unit time can be expressed in terms of base phenotypic standard deviation, resources available (i.e. number of candidates) and risk (i.e. rate of inbreeding) as

$$\Delta G_{ideal} = i(k)^{-1}\sqrt{\tfrac{1}{2}h^2},$$

where $k = i(i-x)$. This equation can be used to check whether the proposed method (Algorithm III) not only constrains ΔF but also maximizes ΔG. The genetic response (ΔG_{obs}), averaged over replicates, was estimated from the sum of the products of the Mendelian terms and the long-term contributions of the candidates in generation 3 (i.e. $\Delta G_{obs} = \Sigma r_{i,3} a_{i,3}$). Generation 3 was chosen for this evaluation as the

impact of the Bulmer effect has largely taken place and yet the reduction in genetic variance associated with the mean level of inbreeding is negligible. The ratio of ΔG_{obs} to ΔG_{ideal} can be considered as a measure of relative genetic efficiency.

(iii) *Relative efficiencies of other selection procedures*

Under the same constraints on resources and the rate of inbreeding, the rates of gain obtained using Algorithm III were compared with deterministic predictions of maximum gain with optimized mass selection and with optimized sib-indices. These deterministic predictions used the methods of Villanueva & Woolliams (1997), but with one exception in that the Mendelian sampling variance was not reduced due to inbreeding. The models for mass and sib-index selection assumed equal full- and half-sub family sizes and constant numbers selected per generation with hierarchical mating where appropriate (i.e. when the optimum mating ratio was greater than one).

3. Results

(i) *Augmented relationship matrix*

A comparison of rates of inbreeding and response obtained with Algorithm I (using **A**), Algorithm II (using **A** and a modified constraint) and Algorithm III (using **A*** and a modified constraint) is shown in Table 1 for a heritability of 0·25 and a desired rate of inbreeding of 0·025. The sum of the squared contributions ($\mathbf{r}^{\mathrm{T}}\mathbf{r}$) and consequently the rate of inbreeding ($\frac{1}{4}\mathbf{r}^{\mathrm{T}}\mathbf{r} = \Delta C$) were maintained at their predefined levels throughout the period of selection with Algorithm II and Algorithm III, but increased over time with the standard **A** when the constraint was not modified (Algorithm I). The optimal numbers selected were the same for both sexes and were also constant with **A*** and the standard **A** with modified constraint, but declined over time when Algorithm I was used. Despite the inability to constrain the rate of inbreeding when using Algorithm I, there was little difference in the rate of response achieved by generation 20 amongst the three methods.

Different schemes that covered a broad range of heritabilities (0·01, 0·25 and 0·99) and possible constraints (given the number of candidates available for selection) on ΔF (0·05, 0·025 and 0·006 25) were simulated with Algorithm III. In all these cases the desired ΔF was achieved.

(ii) *Relationship of **r** with **c***

The regression of the long-term contributions from animals born in generation 15 to generation 20 on the original mating proportions assigned to animals born

Table 1. *Rates of inbreeding (ΔF) per generation (t), sum of squared contributions ($\mathbf{r}^T\mathbf{r}$), effective numbers of parents of each sex (N), and rates of genetic gain (ΔG, phenotypic standard deviation units) when using Algorithm I (with standard $\mathbf{A}$), Algorithm II (with standard $\mathbf{A}$ and modified constraint) or Algorithm III (with the augmented $\mathbf{A}$ and modified constraint)[a]*

	Algorithm I				Algorithm II				Algorithm III			
t	ΔF	$\mathbf{r}^T\mathbf{r}/4$[b]	N	ΔG	ΔF	$\mathbf{r}^T\mathbf{r}/4$	N	ΔG	ΔF	$\mathbf{r}^T\mathbf{r}/4$	N	ΔG
0	—	0·024	10·1	—	—	0·021	10·1	—	—	0·021	10·9	—
4	0·026	0·025	8·8	0·310	0·024	0·021	9·2	0·309	0·023	0·023	9·6	0·303
8	0·030	0·028	8·1	0·295	0·026	0·023	9·2	0·283	0·025	0·023	9·6	0·291
12	0·033	0·032	7·3	0·273	0·025	0·023	9·3	0·258	0·024	0·023	9·7	0·268
16	0·036	0·036	6·7	0·253	0·025	0·023	9·3	0·239	0·024	0·023	9·5	0·242
20	0·044	—	6·0	0·241	0·025	—	9·3	0·220	0·025	—	9·8	0·220

The rate of inbreeding per generation was constrained to 0·025.
[a] Standard errors were 0·011 for ΔG, 0·001 for ΔF and 0·2 for N.
[b] The long-term contributions were calculated as the contributions from individuals born in generation t to generation $t+5$.

Table 2. *The regression coefficient of long-term contributions on mating proportions for different constraints on the rate of inbreeding (ΔF) and heritabilities (h^2)[a]*

	ΔF		
h^2	0·05	0·025	0·00625
0·01	0·93	0·96	0·98
0·25	0·94	0·97	0·98
0·99	1·05	1·04	1·02

[a] Standard errors ranged from 0·01 to 0·05.

Table 3. *The ratio of the sum of squared contributions to the sum of squared mating proportions for different constraints on the rate of inbreeding (ΔF) and heritabilities (h^2)[a]*

	ΔF		
h^2	0·05	0·025	0·00625
0·01	2·33	1·89	1·41
0·25	1·92	1·72	1·35
0·99	1·30	1·27	1·19

[a] Standard errors were less than 0·0002 for the sum of the squared long-term contributions and 0·0004 for the sum of the squared mating proportions.

in generation 15 is shown in Table 2 for a range of heritabilities and constraints on the rate of inbreeding. The regression of r_i on c_i was close to one for all the cases considered. As heritability decreases so the regression coefficients became smaller.

(iii) *Relationship of $\mathbf{r}^T\mathbf{r}$ with $\mathbf{c}^T\mathbf{c}$*

The ratio of $\mathbf{r}^T\mathbf{r}$ to $\mathbf{c}^T\mathbf{c}$ is presented in Table 3. The ratio decreased with increased heritability and in-

Table 4. *The efficiency (%) of the observed genetic response relative to the predicted ideal ($\Delta G_{obs}/\Delta G_{ideal}$) for different constraints on the rate of inbreeding (ΔF) and heritabilities (h^2)[a]*

	ΔF		
h^2	0·05	0·025	0·00625
0·01	10·6	13·4	10·8
0·25	45·7	44·5	44·2
0·99	87·4	87·3	81·4

ΔG_{obs} was calculated as the sum of products of the long-term contributions and Mendelian sampling terms of individuals born at generation 3.
[a] Standard errors for ΔG_{obs} ranged from 0·05 to 0·005.

creased severity of the restriction on the rate of inbreeding. As heritability tended to one, and as the restriction on the rate of inbreeding became more severe, so the ratio tended to one.

(iv) *Efficiency of genetic gain*

Table 4 shows the efficiency of the genetic response obtained with Algorithm III (ΔG_{obs}) relative to the deterministic predictions of the ideal genetic response (ΔG_{ideal}). When the heritability is close to unity ($h^2 = 0·99$) the responses obtained with Algorithm III as a proportion of the ideal ranged between 81% and 87%. As the heritability decreased, there was a dramatic drop in efficiency, approximately related to $\sqrt{h^2}$, with little variation across the different constraints on the rate of inbreeding.

There was variation in efficiency over replicates, and in some replicates the gain exceeded the upper bound (ΔG_{ideal}) (i.e. the efficiency was greater than one). For example when the heritability is close to one ($h^2 = 0·99$) the gain derived from the ideal solution was exceeded in 3%, 12% and 16% of the replicates,

Table 5. *Asymptotic genetic responses obtained with Algorithm III, constrained sib-index and mass selection for different constraints on the rate of inbreeding (ΔF) and heritabilities (h^2)[a]*

Selection	h^2	ΔF		
		0·05	0·025	0·00625
Algorithm III	0·01	0·019	0·015	0·009
	0·25	0·350	0·309	0·167
	0·99	1·772	1·147	0·633
Sib-index	0·01	1·00	1·00	0·77
	0·25	0·93	0·87	0·81
	0·99	0·71	0·91	0·83
Mass	0·01	0·79	0·87	0·77
	0·25	0·91	0·84	0·81
	0·99	0·65	0·84	0·73

The responses sib-index and mass selection are expressed as a proportion of those with Algorithm III.
[a] Standard errors for ΔG obtained with Algorithm III ranged from 0·05 to 0·005.

for rates of inbreeding of 0·00625, 0·025 and 0·05, respectively. Therefore it is possible for a particular generation within a replicate to produce more gain than the upper bound, but this is due to the random sampling of matings (even though the average relationship $\mathbf{c}_t^{\mathrm{T}} \mathbf{A}_t^* \mathbf{c}_t$ is $\leqslant C_t$), an effect that is more prominent when the number of mates is small (e.g. $\Delta F = 0·05$). However, a persistent breaking of the upper bound cannot be sustained over several generations as these matings also yield more inbreeding.

(v) *Comparison of Algorithm III with other selection procedures*

Deterministic predictions for the maximum predicted gains with constrained inbreeding with mass (Villanueva *et al.*, 1996) and sib-indices (Villanueva & Woolliams, 1997) selection were calculated for a range of constraints on the rate of inbreeding and heritabilities. The models were slightly modified to produce an asymptotic rate of response (i.e. Bulmer equilibrium) by ignoring the reduction in Mendelian sampling variance by inbreeding. The asymptotic responses obtained from Algorithm III (which uses BLUP), mass and sib-index selection are presented in Table 5. The efficiencies of constrained mass selection with respect to Algorithm III were always lower than one, ranging from 0·65 to 0·91. Sib-indices were more efficient than mass selection, with efficiencies with respect to Algorithm III ranging from 0·71 to 1.

4. Discussion

It has been shown that the rate of inbreeding can be restricted at a predefined level for successive generations of selection. This constant rate is achieved by setting the mating proportions ($\mathbf{c}$) to values consistent with the expectations of their long-term contributions ($\mathbf{r}$) at the time of selection, which in turn is indicated by the regression of long-term contributions on mating proportions being close to one. However, even when the heritability is close to one, $\mathbf{c}^{\mathrm{T}}\mathbf{c}$ does not equal $\mathbf{r}^{\mathrm{T}}\mathbf{r}$. This can be interpreted as an inability to achieve the ideal solution where $\mathbf{c}$ equals $\mathbf{r}$ and $\mathbf{c}^{\mathrm{T}}\mathbf{c}$ equals $\mathbf{r}^{\mathrm{T}}\mathbf{r}$. The impact of this failure to achieve the ideal solution was shown to be primarily dependent on heritability and largely independent of the constraint on inbreeding. A theoretical response associated with the ideal solution was derived and hence the loss of response was quantified as an efficiency, defined as the ratio of the observed response to the ideal theoretical response.

(i) *The use of A* to control pedigree development*

Rates of inbreeding are determined by the contributions of the current generation and the contributions of ancestral generations that have yet to converge. In this respect all generations have equal importance in controlling rates of inbreeding and contributions from all these generations need to be given equal weight. With Algorithm I, the weighting factor associated with each generation in $\mathbf{A}$ is unequal since the contributions of later generations are down-weighted by a term that is approximately $\frac{1}{2}(1-F_{t-1})$, where F_{t-1} is the average inbreeding coefficient of the preceding generation. As a result the sum of the squared contributions ($\mathbf{r}^{\mathrm{T}}\mathbf{r}$) of later generations is allowed to inflate, thereby increasing ΔF (as observed in Meuwissen, 1997). Removal of the terms containing F_{t-1} in the augmented $\mathbf{A}^*$ is a natural approach to the problem arising from consideration of genetic contributions and avoids the problems of Meuwissen (1997). The weighting factor for the contributions at any generation remains stable over time with the value $\frac{1}{2}$.

An alternative approach using the standard $\mathbf{A}$ was examined using Algorithm II where $C_t = 1-(1-2\Delta F)^t$. This continuous modification to the increment applied to the constraint over time ensures that the value of the constraint is consistent with the predicted course of ΔF over time. With this correction to the method of Meuwissen (1997) a constant rate of inbreeding was achieved. However, although for the cases studied the results were similar to those obtained with Algorithm III there is a fundamental difference between these algorithms. In Algorithm II animals are weighted through $\mathbf{A}$ according to their known relationship with the base, whereas in Algorithm III this information relating to the absolute level of inbreeding (F) is not used. The ability to control the rate of inbreeding without reference to the base generation, and thus F, reinforces the distinction that the rate of inbreeding is an expression of the rate of dispersion (a

process constrained through $\mathbf{c}_t^{\mathrm{T}} \mathbf{A}_t^* \mathbf{c}_t$), whereas the inbreeding coefficient is the cumulated effect of random drift (Falconer & Mackay, 1996).

(ii) *Genetic efficiency*

Although Algorithm III is able to constrain the rate of inbreeding to a predefined level, the question arises as to whether maximization of the function $f(\mathbf{c}) = \mathbf{c}_t^{\mathrm{T}} \mathbf{g}_t - \lambda \mathbf{c}_t^{\mathrm{T}} \mathbf{A}_t^* \mathbf{c}_t$ yields the maximum possible genetic gain. The ideal response under constrained inbreeding (ΔG_{ideal}) was derived assuming that (i) the genes from the current generation can be completely mixed throughout all individuals in the next generation and (ii) that breeding values are known without error. Even when the accuracy is one, with a dioecious population and within a single generation this mixing process can not be achieved, as parental genes are present only in their offspring. Hence, the selection of the current generation is not independent of previous generations with contributions still converging. Furthermore, this dependence is increased when the accuracy is less than one. However, the selection decisions obtained from Algorithm III are not achieved by considering only the current generation but by the simultaneous optimization of the contributions from the current and previous generations (Appendix C).

Therefore Algorithm III may be viewed as an empirical upper bound to response (ΔG_{ub}), in contrast to the over-prediction of the ideal response of ΔG_{ideal}. The deviation of ΔG_{ideal} from ΔG_{ub} is dependent on the population structure, and for the case where both sexes are measured once before selection (Table 4 and results not shown for $h^2 = 0.5$), $\Delta G_{ub} \approx \rho \, \Delta G_{max}$ where ρ is the accuracy of the Mendelian sampling term for a selected individual. We have described in Appendix D an improved prediction that was within 0·01 for all schemes in Table 4.

As an aside, since $\mathbf{c} = \mathbf{r}$ represents an ideal outcome, it is possible to view $(\mathbf{c}^{\mathrm{T}}\mathbf{c})(\mathbf{r}^{\mathrm{T}}\mathbf{r})^{-1}$ as a measure of the efficiency of the scheme or the efficiency of the dispersal of genes throughout the population. The results of this study show that contrary to the speculation of Woolliams & Thompson (1994), this ideal appears unattainable even with a heritability of one, except in the special case of the extreme lower bound for inbreeding (0·0025 in this example). In this special case there is no selection and each parent is required to be replaced by two offspring (there is no variation in family size), and hence $\mathbf{c}$ is identical to $\mathbf{r}$ (results not shown). The results shown by Meuwissen (1997) tend to obscure the lack of correspondence between $\mathbf{c}^{\mathrm{T}}\mathbf{c}$ and $\mathbf{r}^{\mathrm{T}}\mathbf{r}$ since the apparent close relationship between $\mathbf{c}^{\mathrm{T}}\mathbf{c}$ and $\mathbf{r}^{\mathrm{T}}\mathbf{r}$ in his results arises from the bias produced by using $\mathbf{A}$ in which

contributions from later generations are inflated and, consequently, failing to constrain ΔF to be constant over multiple generations.

(iii) *The use of selected individuals*

With Algorithm III the degree of relationship between the mating proportions ($\mathbf{c}$) and breeding values ($\mathbf{g}$), termed the usage solution, is dependent on the constraint imposed on ΔF. The form of the distribution of mating proportions is summarized by the linear regression of $\mathbf{c}$ on $\mathbf{g}$, which is a perfect linear regression for the ideal genetic gain (Bondesson, 1989). The general form of the solution with Algorithm III with regard to the constraint on ΔF is that as a less severe constraint is imposed there is: (i) an increase in the value of the intercept as fewer individuals are used; (ii) an increase in the slope of the line as usage of selected individuals becomes more unequal and; (iii) an increase in the goodness of fit of the regression line as more emphasis is placed on breeding value.

The general form of this distribution of mating proportions differs from those solutions obtained with truncation selection where all individuals with breeding values ($\mathbf{g}$) above the truncation point are used uniformly. Comparison of these two forms of solution indicates that truncation selection is less efficient (i.e. yields less response) than Algorithm III when schemes are compared at the same rate of inbreeding (Toro & Nieto, 1984).

(iv) *Comparison with other studies*

In recent years several selection methods have been developed to control inbreeding by placing a direct constraint on either the cumulative inbreeding (Wray & Goddard, 1994; Brisbane & Gibson, 1995) or the rate of inbreeding (Meuwissen, 1997; Villanueva & Woolliams, 1997). These procedures are more efficient than standard truncation selection. The procedure of Villanueva & Woolliams (1997) was for sib-indices that yielded empirical efficiencies lower than those obtained with Algorithm III, as might be expected given the lower accuracy of sib-index selection. However, in addition, their scheme is static, with constant numbers selected and equal full-sub family sizes, which reduces the possible response as all selected individuals are assigned the same mating proportions.

Dynamic procedures have also been proposed (Wray & Goddard, 1994; Brisbane & Gibson, 1995; Meuwissen, 1997) that are based on optimizing the number and usage of parents each generation, an idea first proposed by Toro & Nieto (1984). The procedure of Wray & Goddard (1994) was aimed at maximizing the long-term selection response, which was obtained

by weighting the rate of inbreeding against the selection differential. Their algorithm was sub-optimal although the contribution of the parents given their selection was determined optimally. Wray & Goddard (1994) demonstrate an advantage of their procedure over standard BLUP of 7% by generation 30, $h^2 = 0.4$, and selection only on males. Meuwissen (1997) reported a greater advantage in response over BLUP (up to 60%) at the same rate of inbreeding. The results presented here (Table 1) indicate that similar increases in response will be achieved with Algorithm III.

For the practical application of the method in animal breeding, a model that includes reproductive limits and overlapping generations needs to be considered. An extension to include reproductive limits can be accommodated within the optimization by the inclusion of additional constraints and achieved either by considering fixed contributions (Meuwissen, 1997) or through the use of an Evolutionary Algorithm (Grundy *et al.*, 1997*b*). Additional constraints can also be used within the procedures to account for overlapping generation structure (Grundy *et al.*, 1997*a*; Meuwissen, 1998) and as shown by Meuwissen (1998) yield extra benefit compared to truncation selection.

Appendix A. A proof that $\mathbf{c}_t^{\mathrm{T}} \mathbf{A}_t^* \mathbf{c}_t$ can be used to constrain ΔF

Wray & Thompson (1990) show that the asymptotic rate of inbreeding is approximately $\frac{1}{4} \mathbf{r}^{\mathrm{T}} \mathbf{r}$, where $\mathbf{r}$ is the long-term contribution vector of individuals in generation one. An examination of the proof reveals that this result is independent of the structure of the base. The proof is derived from the relationship that $\frac{1}{2} \mathbf{r} = \mathbf{D}_1 \mathbf{R}_{1,t}^{\mathrm{T}} \mathbf{1}$, as $t \to \infty$, where $\mathbf{D}_1$ is $\frac{1}{2} \mathbf{I}$, $\mathbf{R}_{j,t} = \Pi_{k=j}^{t-1} \mathbf{Z}_k$ is the matrix of contributions relating descendants at generation t to ancestors from generation j ($j < t$) with the $\mathbf{Z}$ matrix defined as in Materials and Methods and $\mathbf{1}$ is a column vector with elements of one. ΔF is assumed to be a property of the breeding scheme and as such is invariant to the precise choice of the base generation, i.e. which individuals are assumed to be unrelated. Hence any generation can be considered as a base and all generations (other than 0) can thus be considered as being one generation removed from the base. Therefore, the $\mathbf{r}^{\mathrm{T}} \mathbf{r}$ of any generation can be used for the estimation of ΔF if the $\mathbf{D}_t$ component in $\mathbf{A}$ is set to $\frac{1}{2} \mathbf{I}$ each generation.

The total contribution to generation $t+1$ of ancestors born at generation j is $\mathbf{r}_{j,t+1} = \mathbf{c}_t^{\mathrm{T}} \mathbf{R}_{j,t}$, where $\mathbf{c}_t$ is the vector of mating proportions at generation t. Following Wray & Thompson (1990) and substituting $\mathbf{A}^*$ for $\mathbf{A}$, the squared contributions for candidates in generation t can be expressed as:

$$\mathbf{c}_t^{\mathrm{T}} \mathbf{A}^* \mathbf{c}_t = \mathbf{c}_t^{\mathrm{T}} (\tfrac{1}{2} \mathbf{R}_{t,t} \mathbf{R}_{t,t}^{\mathrm{T}} + \tfrac{1}{2} \mathbf{R}_{t-1,t} \mathbf{R}_{t-1,t}^{\mathrm{T}} + \cdots + \mathbf{R}_{0,t} \mathbf{R}_{0,t}^{\mathrm{T}}) \mathbf{c}_t$$

$$= \frac{1}{2} \sum_{j=0}^{t} \mathbf{c}_t^{\mathrm{T}} \mathbf{R}_{j,t} \mathbf{R}_{j,t}^{\mathrm{T}} \mathbf{c}_t + \tfrac{1}{2} \mathbf{c}_t^{\mathrm{T}} \mathbf{R}_{0,t} \mathbf{R}_{0,t}^{\mathrm{T}} \mathbf{c}_t$$

$$= \frac{1}{2} \sum_{j=0}^{t} \mathbf{r}_{j,t+1}^{\mathrm{T}} \mathbf{r}_{j,t+1} + \tfrac{1}{2} \mathbf{r}_{0,t+1}^{\mathrm{T}} \mathbf{r}_{0,t+1}.$$

Note that $\mathbf{R}_{t,t} \mathbf{R}_{t,t}^{\mathrm{T}} = \mathbf{I}$ and the $\mathbf{R}_{0,t} \mathbf{R}_{0,t}^{\mathrm{T}}$ has been split into two terms. Similarly for generation $t+1$,

$$\mathbf{c}_{t+1}^{\mathrm{T}} \mathbf{A}^* \mathbf{c}_{t+1} = \frac{1}{2} \sum_{j=0}^{t+1} \mathbf{r}_{j,t+2}^{\mathrm{T}} + \tfrac{1}{2} \mathbf{r}_{0,t+2}^{\mathrm{T}} \mathbf{r}_{0,t+2}.$$

Let $\Delta C = \mathbf{c}_{t+1}^{\mathrm{T}} \mathbf{A}^* \mathbf{c}_{t+1} - \mathbf{c}_t^{\mathrm{T}} \mathbf{A}^* \mathbf{c}_t$ (which is held constant over generations), $\Delta r_j^2(t+1) = \mathbf{r}_{j,t+2}^{\mathrm{T}} \mathbf{r}_{j,t+2} - \mathbf{r}_{j,t+1}^{\mathrm{T}} \mathbf{r}_{j,t+1}$ and $\Delta r_{t+1}^2(t+1) = \mathbf{r}_{t+1,t+2}^{\mathrm{T}} \mathbf{r}_{t+1,t+2} = \mathbf{c}_{t+1}^{\mathrm{T}} \mathbf{c}_{t+1}$, then the increment in the constraint can be considered as a set of increments in the squared contributions:

$$\Delta C = \frac{1}{2} \sum_{j=0}^{t+1} \Delta r_j^2(t+1) + \tfrac{1}{2} \Delta r_0^2(t+1). \qquad (\mathrm{A}\ 1)$$

Under near-equilibrium conditions that hold over the period of convergence, the contributions converge ($\Delta r_j^2(t) \to 0$ as t increases) at an approximately constant rate and hence $\Delta r_j^2(t) \approx \Delta r_{j+1}^2(t+1) = \Delta_{t-j}$, i.e. each of the increments in contributions from an ancestral generation to successive generations of descendants depends only on the number of generations that separate the ancestral generation from their descendants. Convergence implies that (i) Δ_{t-j} decreases to zero as $t-j$ increases and (ii) $\Sigma_{t-j=s}^{\infty} \Delta_{t-j}$ tends to zero as $t-j$ increases for sufficiently large s. Hence $\Delta C = \frac{1}{2} \Sigma_{k=0}^{t+1} \Delta_k + \frac{1}{2} \Delta_{t+1}$, which converges to half the total increment in squared contributions for a single generation, i.e. from (A 1)

$$\Delta C = \tfrac{1}{2}(\Delta r_{t+1}^2(t+1) + \cdots + \Delta r_0^2(t+1)) + \tfrac{1}{2} \Delta r_0^2(t+1)$$

$$\approx \tfrac{1}{2}(\Delta r_t^2(t) + \Delta r_t^2(t+1) + \cdots + \Delta r_t^2(t+s)) = \tfrac{1}{2} \mathbf{r}_{t,\infty}^{\mathrm{T}} \mathbf{r}_{t,\infty},$$

where s is sufficiently large and $\mathbf{r}_{t,\infty}$ is the long-term contribution vector of individuals in generation t. Therefore from Wray & Thompson (1990), $\Delta C \approx 2\Delta F$. This equivalence is refined in Appendix B.

Appendix B. Calculation of ΔC

Following Woolliams & Thompson (1994) the asymptotic rate of inbreeding can be expressed as

$$\Delta F = (1-\alpha) X_1 (2 - X_0)^{-1},$$

where α is the extent of non-random mating as defined by Kimura & Crow (1963) and X_0 and X_1 are the

mean of the diagonal elements of the contribution matrices (Wray & Thompson, 1990) of the base and first generation, respectively. The rate of inbreeding can also be expressed as a function of the increment applied to the constraint (ΔC) by using the following relationships:

$\alpha = -\frac{1}{2}\Delta C$ since $\alpha \approx -\Delta F$ for random mating (Robertson, 1965),

$X_1 = \Delta C$ (Appendix A),

$X_0 = 2\Delta C$ since X_0 refers to the base generation and the base generation has twice the contribution of any other generation (Wray & Thompson, 1990). Thus

$$\Delta F = (1 + \Delta C/2)\,\Delta C[2(1 - \Delta C)]^{-1},$$

which leads to

$$\Delta C = 2\Delta F[1 - 3\Delta F + 12(\Delta F)^2].$$

Appendix C. A proof that the constrained maximization of genetic response using estimated breeding values of the current generation is identical to the simultaneous constrained maximization of genetic contributions using Mendelian sampling terms from the current and all ancestral generations

Woolliams & Thompson (1994) decomposed the estimated breeding value of an individual into the weighted sum of estimated Mendelian sampling terms of itself plus all its ancestors. Given that these ancestors are not all distinct the coefficients relating the descendant and a particular ancestor can be defined as the genetic contributions of those ancestors. Thus at generation t, the vector of estimated breeding values of the current generation ($\mathbf{g}_t$) is

$$\mathbf{g}_t = \mathbf{a}_t + \sum_{j=0}^{t-1} \mathbf{R}_{j,t}\,\mathbf{a}_j,$$

where $\mathbf{a}_t$ and $\mathbf{a}_j$ are the vectors of estimated Mendelian sampling terms of the candidates and the ancestors born in generation j, respectively and $\mathbf{R}_{j,t}$ is defined in Appendix A. Furthermore, the total contribution in generation $t+1$ from ancestors born at generation j can be expressed as $\mathbf{r}_{j,t+1} = \mathbf{c}_t^{\mathrm{T}}\mathbf{R}_{j,t}$, where $\mathbf{c}_t$ is the vector of mating proportions at generation t. Thus $\mathbf{c}^{\mathrm{T}}\mathbf{g} = \Sigma_{j=0}^{t}\mathbf{r}_{j,t+1}^{\mathrm{T}}\mathbf{a}_j$.

Following Appendix A the squared contributions for candidates in any generation can be expressed as

$$\mathbf{c}^{\mathrm{T}}\mathbf{A}^*\mathbf{c} = \frac{1}{2}\sum_{j=0}^{t}\mathbf{r}_{j,t+1}^{\mathrm{T}}\mathbf{r}_{j,t+1} + \frac{1}{2}\mathbf{r}_{0,t+1}^{\mathrm{T}}\mathbf{r}_{0,t+1}.$$

After several generations $\frac{1}{2}\mathbf{r}_{j,t+1}^{\mathrm{T}}\mathbf{r}_{j,t+1}$ becomes constant and increments in $\frac{1}{2}\Sigma\mathbf{r}_{j,t+1}^{\mathrm{T}}\mathbf{r}_{j,t+1}$ tend to $\frac{1}{2}\mathbf{r}_{j,\infty}^{\mathrm{T}}\mathbf{r}_{j,\infty}$ for any generation j, and $\frac{1}{2}\mathbf{r}_{0,t+1}^{\mathrm{T}}\mathbf{r}_{0,t+1}$ also tends to a constant. Hence after convergence of the base generation

contributions, maximizing $\mathbf{c}^{\mathrm{T}}\mathbf{g} - \lambda\mathbf{c}^{\mathrm{T}}\mathbf{A}^*\mathbf{c}$ is equivalent to maximizing

$$\sum_{j=0}^{t}\mathbf{r}_{j,t+1}^{\mathrm{T}}\mathbf{a}_j - \tfrac{1}{2}\lambda\sum_{j=0}^{t}\mathbf{r}_{j,t+1}^{\mathrm{T}}\mathbf{r}_{j,t+1} = \sum_{j=0}^{t}(\mathbf{r}_{j,t+1}^{\mathrm{T}}\mathbf{a}_j - \tfrac{1}{2}\lambda\mathbf{r}_{t,t+1}^{\mathrm{T}}\mathbf{r}_{j,t+1}).$$

Thus the problem is attempting to maximize the same function simultaneously for multiple generations. The opportunity for doing so increases as j increases since the contributions converge over time and these earlier generations contribute very little to the variation in $\mathbf{c}^{\mathrm{T}}\mathbf{g}$ for feasible $\mathbf{c}$. There is no separate constraint on each generation; only the aggregate rate of inbreeding is subject to constraint.

In the linear function the Lagrangian multiplier λ is the weighting factor between the two components for all generations. When a fixed overall rate of inbreeding is imposed there is a slight departure from this simultaneous optimization, since the value of λ required for each generation in isolation to achieve the target rate of inbreeding is related to the standard deviation of the estimated breeding values, which slowly changes with inbreeding (unpublished results). However, the importance of this change is limited since the variation among possible solutions at any given time arises from the small number of generations for which contributions are converging rapidly and λ will vary very little for those generations. It may therefore be concluded that the procedure has only a small departure from optimality in the problem of maximizing gain with constrained inbreeding.

Appendix D. An empirical upper bound for response

Assume a population is propagated from $\frac{1}{2}N_c$ males and $\frac{1}{2}N_c$ females [$N_c = (\mathbf{c}^{\mathrm{T}}\mathbf{c})^{-1}$] and with each parent having a family size $S = T(\frac{1}{2}N_c)^{-1}$, where T is the number of candidates. The selection proportion assuming an infinite population size is $(T\mathbf{c}^{\mathrm{T}}\mathbf{c})^{-1}$.

In order to maintain individual contributions over generations two offspring from each family are selected to replace each parent. The selection intensity will be lower than that assuming optimality between and within family selection and this would imply a loss in response. An estimate of this loss scaled by the accuracy of selection is $i_w(i_p)^{-1}$, where i_w is the within-family selection intensity, i_p is the proportionate selection intensity and ρ is the accuracy of the Mendelian sampling terms when the contributions converge. Let N_r be the numbers of males still represented at convergence [$(\mathbf{r}^{\mathrm{T}}\mathbf{r})^{-1}$]. Some of the initial loss associated with within-family selection can be recovered by the thinning out over generations of the numbers of individuals before the fixation of their contributions. Let i_b be the increase in intensity associated with the change in the numbers represented from N_c and N_r. This thinning out is more pronounced with lower heritability since the increase in accuracy

of the Mendelian sampling terms ($\delta\rho$) over time is higher and so there is greater opportunity for reducing the numbers selected.

Thus the expected upper bound to response (ΔG_{ub}) accounting for both accuracy and dispersion of genes can be expressed as

$$\Delta G_{ub} = (i_w\rho + i_b\,\delta\rho)\,(i_p)^{-1}\,\Delta G_{ideal},$$

where ΔG_{ideal} is the idealized response.

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