MAXIMISING GENETIC GAIN WITH QTL INFORMATION AND CONTROL OF INBREEDING

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INTRODUCTION

Several studies have evaluated the potential benefits of gene and marker assisted selection (GAS and MAS, respectively) in mixed inheritance models, where an identified quantitative trait locus (QTL) is segregating together with polygenes. Most of these studies have assumed fixed contributions of selection candidates and equal emphasis on estimated breeding values (EBV) for the QTL and polygenes in the selection criterion. The general finding has been that the extra short-term gains expected from GAS and MAS are not maintained in the long-term (*e.g.* Gibson, 1994).

Villanueva *et al.* (1999) used BLUP evaluation and optimised (rather than fixed) contributions of the selection candidates for maximising gains with restrictions on inbreeding. The emphasis given to the QTL EBV relative to the polygenic EBV was however fixed and therefore not optimal. In contrast, Dekkers and van Arendonk (1998) optimised the relative weight given to the QTL over generations but assumed fixed contributions of candidates and no accumulation of inbreeding.

The methods used by Villanueva *et al.* (1999) and Dekkers and van Arendonk (1998) each gave higher gain than standard GAS and largely resolved the conflict between short- and long-term gains. The objective of this study was to evaluate, through stochastic simulation, the gains obtained by combining both types of optimisation.

MATERIAL AND METHODS

Genetic and population models. A trait controlled by polygenes and a known biallelic QTL was simulated. Polygenic and environmental variances were 0.2 and 0.8, respectively. The QTL had additive (*a*) and dominance (*d*) effects as defined by Falconer and MacKay (1996). The initial frequency of the favourable allele (*p*) was 0.15. The QTL and polygenes were in linkage phase equilibrium in the initial population. Reductions in genetic variance due to selection (Bulmer effect) and inbreeding were accounted for. The number of candidates per generation was 60 per sex. Selection was carried out for 10 discrete generations.

Estimation of breeding values. All candidates were phenotyped and genotyped for the QTL prior to selection. The effect of the QTL was assumed known without error. Three types of schemes were compared. BLUP was used to derive EBVs in all cases.

1. Phenotypic conventional selection (PHE): Information on the QTL was ignored and the total EBV was obtained from standard BLUP, using the total initial genetic additive variance and phenotypic values uncorrected for the QTL.

2. Standard GAS (GAS_{STA}): The total EBV was EBV_p+BV_q, where EBV_p is the estimate of the polygenic breeding value (obtained from standard BLUP, using the polygenic variance and phenotypic values corrected for the QTL effect) and BV_q is the breeding value due to the QTL.

3. Optimal GAS (GAS_{OPT}): The total EBV was $EBV_p+\lambda BV_q$, where EBV_p and BV_q are obtained as in GAS_{STA} and λ is the optimal relative weight given to BV_q for maximising cumulated genetic gain over the planning horizon (i.e. $\Sigma= G_1+\ldots+G_{10}$, where G_i is the average total genetic value at generation i). Weights λ were obtained using optimal control theory for each sex, genotype, and generation, following the deterministic model described in Dekkers and Chakraborty (2001). Four QTL genotypes (BB, Bb, bB and bb, where the first letter indicates the allele received from the father) and two sexes were distinguished, resulting in eight variables to be optimised for each generation.

Selection procedures. For the three types of schemes described above, two types of selection procedures were considered: 1) Truncation selection, where the number of parents (10 sires and 20 dams) and the family sizes were fixed across generations ; and 2) Optimised selection, where the numbers of parents and their contributions were optimised each generation to maximise genetic gain while restricting the rate of inbreeding (Villanueva *et al.*, 1999). The rate of inbreeding was restricted to the lowest value obtained with truncation selection (4.5% per generation, in PHE schemes). The EBV used in the optimisation differed for the three types of schemes (PHE, GAS_{STA} and GAS_{OPT}) and they were obtained as described above. Weights on the QTL for GAS_{OPT} under optimised selection were derived assuming truncation selection of the number of parents selected with optimised selection under GAS_{STA}.

RESULTS AND DISCUSSION

Table 1 shows the gain obtained across generations with schemes PHE, GAS_{STA} and GAS_{OPT} under truncation and optimised selection for an additive QTL with *a*=0.5 and *d*=0. Results are averages of 500 replicates. The optimisation of contributions clearly improved the rates of gain for all three schemes. At a given generation, the lowest gain obtained with optimised selection was higher than the highest gain from truncation selection. The benefit from optimised contributions was greatest for generation 1 (54% for GAS_{STA}) and decreased over generations to 14% for GAS_{OPT} in generation 10. Optimising contributions increased the sum of genetic gains over generations (Σ), which was the objective maximised to obtain the optimal QTL weights with GAS_{OPT}, by 19.7, 17.3, and 16.8% for PHE, GAS_{STA}, and GAS_{OPT}, respectively.

For both selection procedures (truncation and optimised contributions), the optimisation of the weight given to the QTL (GAS_{OPT}) prevented the long-term loss in response at $t=10$ that was observed with standard QTL selection (GAS_{STA}). With truncation selection the favourable allele was fixed ($p≥0.99$) by $t=10$ for the three schemes. At this point, the gain from PHE was 2% higher than that from GAS_{STA} but 1% lower than that from GAS_{OPT}. The weights given to the QTL used in optimised selection were obtained based on truncation selection. The optimisation of contributions led to a faster increase in p (relative to truncation selection) and the early loss of polygenic gain in GAS schemes was not completely recovered. At $t=8$, where the favourable allele was fixed for all three schemes, the gain from GAS_{OPT} was slightly, but not significantly, lower (0.2%) than the gain from PHE. However, this represents a significant improvement over standard GAS, which produced 3% lower gain than PHE. The highest value for Σ was obtained in schemes GAS_{OPT} for both truncation and optimised selection, although differences were limited; GAS_{OPT} resulted in 5.8 and 2.1% greater Σ than PHE and GAS_{STA}, respectively, for truncation selection and 3.1 and 1.6% greater Σ for optimised selection.

Table 1. Total accumulated genetic gain over generations (t) from truncation and optimised BLUP selection for three types of scheme: phenotypic (PHE), standard GAS (GAS $_{STA}$) and optimal GAS (GAS $_{OPT}$) for an additive QTL ($a = 0.5$, $d=0$). The last row shows the sum of gains over generations.

	Truncation selection			Optimised selection		
T	PHE	GAS_{STA}	GAS_{OPT}	PHE	GAS_{STA}	GAS_{OPT}
1	0.332	0.440	0.422	0.498	0.677	0.603
2	0.733	0.957	0.869	0.971	1.280	1.128
3	1.115	1.351	1.286	1.416	1.588	1.603
4	1.467	1.639	1.653	1.823	1.880	1.966
5	1.802	1.888	1.959	2.186	2.173	2.267
6	2.099	2.128	2.215	2.504	2.453	2.534
7	2.364	2.347	2.446	2.783	2.706	2.789
8	2.612	2.567	2.667	3.047	2.963	3.040
9	2.838	2.777	2.874	3.289	3.209	3.285
10	3.045	2.980	3.082	3.523	3.443	3.522
Σ	18.406	19.075	19.473	22.040	22.371	22.736

The advantage of GAS_{OPT} over both GAS_{STA} and PHE was also observed when the favourable allele was completely dominant (Table 2). The extra early gain from using the genotype information was lost in the long term with standard QTL selection (GAS_{STA}) but maintained with optimal QTL selection (GAS_{OPT}). As with an additive QTL, the extra long-term response of GAS_{OPT} relative to PHE was higher with truncation than with optimised selection although the optimisation of contributions always led to higher absolute gains than truncation selection.

Here the optimisation of selection decisions was carried out in two steps. First, optimal weights on the QTL breeding value were obtained using the Dekkers and van Arendonk (1998) model, which assumes fixed contributions and constant polygenic genetic variances. Secondly, contributions were optimised. Simultaneous optimisation of both the QTL weights and contributions is expected to lead to further benefits from GAS, both in the short and in the long term

Table 2. Total accumulated genetic gain over generations (*t*) from truncation and optimised BLUP selection for three types of scheme: phenotypic (PHE), standard GAS (GAS $_{STA}$) and optimal GAS (GAS $_{OPT}$) for a dominant QTL (*a = d* = 0.5). The last row shows the sum of gains over generations.

	Truncation selection			Optimised selection		
T	PHE	GAS$_{STA}$	GAS$_{OPT}$	PHE	GAS$_{STA}$	GAS$_{OPT}$
1	0.458	0.566	0.521	0.758	0.656	0.710
2	0.904	0.964	0.945	1.162	1.127	1.177
4	1.557	1.528	1.603	1.756	1.830	1.853
6	2.072	2.021	2.126	2.306	2.397	2.408
8	2.532	2.468	2.591	2.821	2.909	2.919
10	2.969	2.892	3.015	3.295	3.389	3.396
Σ	18.635	18.412	19.144	21.232	21.735	21.975

CONCLUSION

Combined optimisation of contributions of selection candidates and weights on the QTL across generations allows substantial increases in gain at a fixed rate of inbreeding and avoids the conflict between short- and long-term responses in GAS schemes. Most of the increase in gain is produced by optimising contributions. The optimisation of the QTL weights has a greater impact on avoiding the long-term loss with GAS.

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