

POTENTIAL BENEFITS OF USING IDENTIFIED MAJOR GENES IN TWO TRAIT BREEDING GOALS UNDER TRUNCATION AND OPTIMAL SELECTION

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INTRODUCTION

Most research investigating the benefits of gene and marker assisted selection (GAS and MAS, respectively) when quantitative trait loci (QTL) are segregating, has considered single trait scenarios (e.g. Weller, 2001). However, multi-trait breeding goals are common in animal breeding programs. Verrier (2001) has investigated the value of MAS when selection is on an index that included two negatively correlated traits. He found extra short-term gains in the aggregate genotype from MAS (relative to conventional BLUP selection) when the QTL affected both trait but MARS was found to be more efficient than BLUP to avoid loss of the favourable QTL allele. No extra gains were found when the QTL affected only one of the traits. Verrier (2001) used standard truncation selection with fixed contributions of selection candidates which could hamper the comparison of schemes as they may lead to different inbreeding levels.

Under a single trait scenario, Villanueva *et al.* (1999) used an optimisation method for maximising genetic gains while constraining inbreeding. Optimal selection in GAS schemes allowed for increased genetic gains when compared to truncation selection at the same rate of inbreeding. Moreover, when the QTL had a large effect, the joint use of BLUP estimates of breeding values and optimal selection substantially reduced the loss in long-term response often observed in GAS truncation studies (e.g. Pong-Wong *et al.*, 1998).

The objective of this study was to investigate, through Monte Carlo simulation, the benefits from GAS when the optimisation method with constrained inbreeding is applied on an index that includes two negatively correlated traits. An identified QTL affected only one of the traits, for which phenotypes were not available.

METHODS

Genetic and population models. One of the traits (t_1) was controlled by polygenes while the other trait (t_2) was controlled by an identified additive biallelic QTL (alleles A and B) and by polygenes. Hence, no pleiotropy between the traits was defined. The polygenic plus environmental variances summed up to 1 for both traits. The polygenic heritabilities were 0.3 and 0.1 for t_1 and t_2 , respectively. The genotypic value due to the QTL was a , 0 and $-a$ for genotypes AA, AB and BB, respectively and a was defined as in Falconer and Mackay (1996). The additive genetic variance explained by the QTL (σ_{v2}^2) was $2p(1-p)a^2$, where p is the frequency of the favourable allele (Falconer and Mackay, 1996). The initial p was 0.15. The proportion of the total genetic variance of t_2 explained by the QTL (θ) was 0.1 or 0.5 which corresponds to a values of 0.21 and 0.63, respectively. The polygenic genetic correlation ρ_u was -0.5 . In the base generation ($t = 0$) the polygenic values (u_1 and u_2) were drawn from a

bivariate normal distribution with correlation ρ_u and polygenic variances σ_{u1}^2 and σ_{u2}^2 . Phenotypic values for t_1 were obtained by adding an environmental component to the polygenic value. No phenotypes were available for trait 2. Selection was over 10 discrete generations and, from $t = 1$ to 10, the polygenic value for trait k ($k = 1, 2$) was generated as the parental average polygenic value plus a random Mendelian sampling term. The latter was sampled from a bivariate normal distribution with correlation ρ_u and variances $(\sigma_{uk}^2/2)(1-F/2)$, for $k = 1, 2$, where F is the average parental inbreeding coefficient. The genotype for the QTL was obtained by randomly sampling one allele from each parent. The population was composed of 60 males and 60 females.

Selection criteria and estimation of breeding values. The breeding goal was $H = BV_1 + BV_2$, where BV_k is the true breeding value for trait k (i.e. both traits had the same relative economic weight). The selection criterion was $I = EBV_1 + EBV_2$, where EBV_k is the total estimated breeding value for trait k . BLUP was used to obtain EBV_1 . For t_2 , EBV_2 was the sum of the polygenic (EBV_{u2}) and the QTL (BV_{qtl}) components. Since no phenotypes were available for t_2 , EBV_{u2} was obtained as $b_g EBV_1$ where b_g is the polygenic genetic regression of t_2 on t_1 . Schemes using or ignoring the QTL genotype when estimating breeding values were evaluated. When ignoring the QTL, b_g was $\rho_u (\sigma_{u2}^2 + \sigma_{v2}^2) / \sigma_{u1}$ (i.e. selection was on EBV_1). The BV_{qtl} was $2(1-p)a$, $[(1-p)-p]a$ and $-2pa$ for genotypes AA, AB, BB, respectively (Falconer and Mackay, 1996), with p updated each generation. For schemes ignoring the QTL genotypes, BV_{qtl} was 0.

Selection procedures. Schemes including or ignoring the QTL information were evaluated under standard truncation or optimal selection. With truncation selection, the 12 candidates from each sex with the highest I were selected each generation. With optimal selection, numbers selected and their contributions were optimised to maximise genetic gain while restricting inbreeding rate (ΔF) per generation (Grundy *et al.*, 1998). Selected candidates were mated at random. Thus, four schemes were evaluated : truncation ignoring (T_1) or using (T_G) the QTL and optimal selection ignoring (O_1) or using (O_G) the QTL. The ΔF was restricted to the value obtained in the corresponding truncation schemes (0.06 for both O_1 and O_G schemes).

RESULTS AND DISCUSSION

Table 1 shows the accumulated response in H for the four strategies evaluated and two θ values. Schemes using the genotype information (O_G and T_G) yielded more short and long-term gains than the corresponding schemes ignoring the QTL (O_1 and T_1). With truncation selection, Verrier (2001) did not find extra gains from MAS when the QTL affected only one trait. However, he considered selection on one marker than on the QTL, available phenotypes in both traits and a lower economic weight for the trait affected by the QTL.

Optimal selection always achieved higher gain in H than the corresponding truncation selection scheme. For a QTL of small effect ($\theta = 0.1$), O_1 achieved even higher gains than T_G (including in the first generation), due to higher selection differentials allowed in the optimised schemes. Conversely, when the QTL had a larger effect ($\theta = 0.5$), T_G yielded higher gains than O_1 , since the BV_{qtl} had a higher weight in the selection criterion and a higher proportion of candidates were homozygous for the favourable genotype. Combining optimal contributions

and genotype information (O_G) resulted in the highest gains in H (up to 48 % at $t = 10$ and $\theta = 0.5$ over T_I). Fixation of the favourable allele only occurred in those methods using genotype information, with a faster rate for $\theta = 0.5$ (table 1). As expected, schemes ignoring the QTL kept p around its initial value (0.15), losing the favourable allele in 58.4 % (T_I) and 63.0 % (O_I) of the replicates at both levels of θ .

Table 1. Total accumulated gain in the breeding goal over generations (t) for truncation and optimal selection using (T_G , O_G) or ignoring (T_I , O_I) QTL information, and two levels of θ . The generation in which the favourable allele was fixed is indicated in bold ^A

T	$\theta = 0.1$				$\theta = 0.5$			
	T_I	T_G	O_I	O_G	T_I	T_G	O_I	O_G
1	0.289	0.330	0.419	0.483	0.285	0.588	0.422	0.885
2	0.604	0.688	0.764	0.887	0.599	1.265	0.759	1.559
3	0.881	1.005	1.073	1.244	0.874	1.611	1.063	1.865
4	1.142	1.302	1.369	1.556	1.138	1.892	1.360	2.163
5	1.396	1.584	1.665	1.851	1.395	2.156	1.652	2.459
10	2.517	2.732	2.933	3.123	2.519	3.298	2.921	3.730

^A Standard errors ranged from 0.002 to 0.020. Averages over 500 replicates.

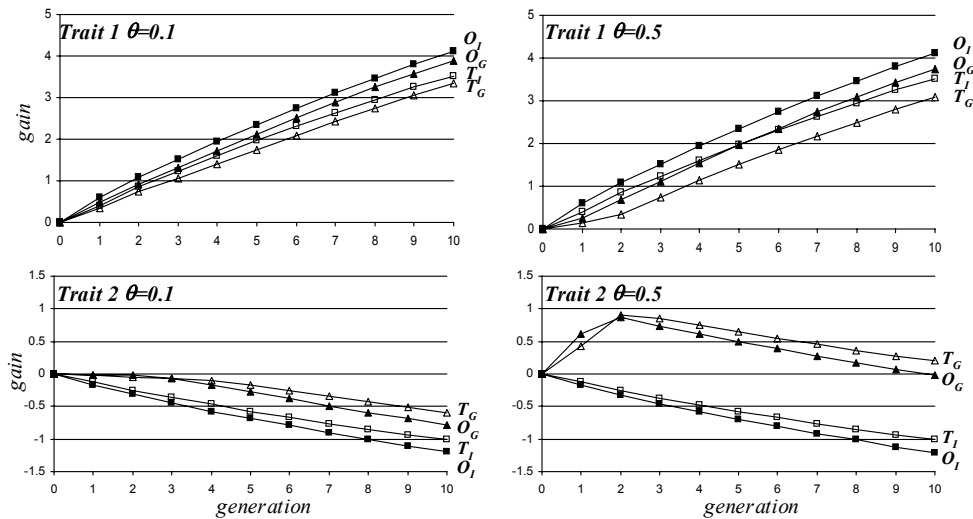


Figure 1. Total genetic responses for both traits across generations for truncation and optimal selection using (T_G , O_G) or ignoring (T_I , O_I) QTL information and two levels of θ

The total response over generations for both traits is presented in figure 1. The scheme giving the highest gain in t_1 was O_I since the optimisation on I operates with candidates ranked on EBV_1 (i.e. $BV_{qtl} = 0$ and $EBV_{u2} = b_g EBV_1$). This scheme also produced the highest response in t_2 , but due to the negative sign of the correlation, this response was in the undesired direction.

For a QTL of large effect ($\theta = 0.5$), before fixation ($t = 1$ to 3) the T_1 scheme had higher average t_1 than O_G because candidates with high BV_{qtl} were high ranked on I . After fixation, O_G achieved higher response than T_1 since the ranking on I was determined by EBV_1 . The schemes using the QTL yielded higher average breeding value for t_2 than the schemes that ignored it. In early generations ($t < 3$), when the favourable allele was still segregating ($p < 0.95$), T_G and O_G were able to prevent the negative response in t_2 when the QTL had the smallest effect ($\theta = 0.1$), and to obtain positive responses when the QTL effect was increased ($\theta = 0.5$). The response in t_2 was in the undesired direction, driven by the negative ρ_u , for schemes ignoring the QTL, and for schemes using the QTL after fixation, since the system works as a polygenic model. The optimised scheme using the QTL (O_G) fixed the gene faster than the corresponding truncation scheme (T_G) and produced higher a gain in t_2 for $t < 3$. After $t = 3$, the optimisation scheme also gave higher gain in t_2 than truncation selection, but in the undesired direction. The optimisation was more effective in improving t_1 , which was the primary trait in I (i.e. higher heritability).

CONCLUSIONS

Under this scenario with no pleiotropy at the QTL and no phenotype available for the trait affected by the QTL, the scheme combining genotype information and optimal selection (O_G) achieved the highest gains in H although this scheme was not the most efficient for improving each trait individually. For a gene of small effect optimisation of genetic contributions for maximising gain, had a higher impact on H than using the QTL. Finally, schemes that ignored genotype information lost the favourable QTL allele with a high probability.

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REFERENCES

- Falconer, D. and Mackay, T. (1986) Introduction to Quantitative Genetics. Longman, England.
Grundy, B., Villanueva, B. and Woolliams, J.A. (1998) *Genet. Res. Camb.* **72** : 159-168.
Pong-Wong, R. and Woolliams, J.A. (1998) *Genet. Sel. Evol.* **30** : 313-337.
Verrier, E. (2001) *Genet. Sel. Evol.* **33** : 17-35.
Villanueva, B., Pong-Wong, R., Grundy, B. and Woolliams, J.A. (1999) *Genet. Sel. Evol.* **31** : 313-337.
Weller, J.I. (2001) Quantitative Trait Loci Analysis in Animals. CABI Publishing.