

# Response to selection from using identified genes and quadratic indices in two-traits breeding goals

S. Avendaño<sup>1,3</sup>, P. M. Visscher<sup>2</sup> and B. Villanueva<sup>1\*</sup>

<sup>1</sup> *Scottish Agricultural College. West Mains Road. Edinburgh EH9 3JG. UK*

<sup>2</sup> *The University of Edinburgh. Institute of Evolutionary Biology. School of Biological Sciences.*

*West Mains Road. Edinburgh EH 9 3JT. UK*

<sup>3</sup> *Aviagen Ltd. Newbridge. Edinburgh. EH 28 8SZ. UK*

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## Abstract

Benefits from the use of optimised selection for maximising genetic gain while constraining the rate of inbreeding were evaluated through stochastic simulation for scenarios where the breeding goal includes two negatively correlated traits. One of the traits was controlled only by polygenes and had a heritability of 0.3 while the other trait was controlled by an identified additive biallelic QTL (with an initial allele frequency of 0.15) and by polygenes and had a polygenic heritability of 0.1. Optimised selection was compared to standard truncation selection both when the information on the QTL was used and when it was ignored. Extra gains in the breeding goal were observed throughout the 10 simulated generations from the combined use of optimised contributions and QTL information although, as expected, this scheme was not the most effective for improving individual traits. By generation ten, the gain in the aggregate breeding value with optimised selection was about 12% higher than with truncation selection. Optimised selection allowed extra polygenic responses in both traits but these extra responses were negative for the trait under mixed inheritance. The use of the QTL allowed not only positive gains in the trait with the lowest heritability, but also avoided the loss of the favourable allele. The effect of selecting for the QTL on each trait depended on its relative weight in the selection index and not exclusively on the inheritance model.

**Additional key words:** GAS, inbreeding, multiple traits, optimised selection, QTL.

## Resumen

### Respuesta a la selección utilizando genes identificados e índices cuadráticos para la mejora simultánea de dos caracteres

En este trabajo se han evaluado, mediante simulación estocástica, los beneficios de utilizar selección optimizada para maximizar la respuesta genética, controlando al mismo tiempo la tasa de consanguinidad, en un contexto en el cual el objetivo de mejora incluye dos caracteres correlacionados negativamente. Uno de los caracteres (con heredabilidad de 0,3) fue poligénico mientras que el segundo (con heredabilidad de 0,1) estaba controlado por un QTL bialélico y por poligenes. La frecuencia alélica inicial para el QTL fue 0,15. La estrategia de selección optimizada se comparó con la de selección clásica por truncamiento, tanto en el caso de utilizar la información del QTL, como en el caso de ignorarla. El uso simultáneo de contribuciones optimizadas y del QTL produjo una mayor ganancia en el objetivo de mejora en las 10 generaciones de selección simuladas, si bien este esquema no fue el más eficiente para mejorar los caracteres individualmente. En la generación 10, la ganancia obtenida en el objetivo de mejora con selección optimizada fue aproximadamente un 12% más alta que aplicando la selección por truncamiento. La selección optimizada produjo una respuesta poligénica adicional en ambos caracteres, mientras que esta respuesta fue negativa para el carácter controlado por el QTL. El uso del QTL no solo proporcionó respuestas positivas en el carácter con heredabilidad baja, sino que también evitó la pérdida del alelo favorable. El efecto sobre ambos caracteres derivado de seleccionar sobre el QTL para uno de ellos dependió tanto del modelo genético como de su ponderación relativa en el índice de selección.

**Palabras clave adicionales:** consanguinidad, GAS, QTL, selección optimizada, varios caracteres.

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\* Corresponding author: [beatriz.villanueva@sac.ac.uk](mailto:beatriz.villanueva@sac.ac.uk)

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## Introduction<sup>1</sup>

Breeding goals in selection programmes for livestock populations commonly include several traits. However, the vast majority of the research directed to evaluate the potential benefits of using information on identified quantitative trait loci or QTL (GAS) or on markers linked to them (MAS) in artificial selection has been focused on single-trait scenarios (e.g., Ruane and Colleau, 1995; Villanueva *et al.*, 1999, 2002; Abdel-Azim and Freeman, 2002).

The few studies that have investigated the value of GAS or MAS in breeding programmes aimed at improving several traits have found extra genetic gains in the aggregate genotype when using molecular information, at least in the early generations (De Koning and Weller, 1994; Xie and Xu, 1998; Verrier, 2001). However, these studies assumed standard truncation selection where the number of parents selected and their contributions are fixed. This could hamper the comparison between selection schemes using and ignoring QTL information as they may lead not only to different rates of genetic gain but also to different rates of inbreeding.

Dynamic selection tools that optimise genetic contributions of selection candidates for obtaining maximum genetic gain while constraining the rate of inbreeding ( $\Delta F$ ) to a pre-defined value have been used under single trait scenarios with GAS or MAS (Villanueva *et al.*, 1999, 2002). These tools are implemented as quadratic indexes in which the desired  $\Delta F$  is achieved by applying a quadratic constraint on the average coancestry of selection candidates weighted by their projected use (Woolliams *et al.*, 2002). The quadratic optimisation in GAS and MAS schemes allowed for increased genetic gains when compared to truncation selection at the same  $\Delta F$ .

The objective of this study was to investigate, through Monte Carlo computer simulation, the benefits from GAS when the optimisation method imposing a constraint on  $\Delta F$  is applied on an index including two correlated traits, one of which is affected by an identified QTL. The study focused on a scenario in which benefits from the use of QTL information might be anticipated: the traits were negatively correlated and the trait affected by the QTL had a low heritability. Situations where both sexes had phenotypes available for both traits, or where the phenotypic expression of the trait affected by the QTL was sex-limited were evaluated.

## Material and Methods

Selection schemes using or ignoring information on the QTL when estimating the total breeding value were compared using stochastic simulations. Two selection procedures were used: i) standard truncation selection (T) in which a fixed number of candidates from each sex (those with the highest index values) are selected each generation; and ii) optimised selection (O) in which the number of selected candidates and their contributions are optimised to maximise genetic gain while restricting  $\Delta F$  per generation. It should be noted that the optimisation applied here differs from that described by Dekkers and Van Arendonk (1998) where the purpose was to achieve the optimal emphasis given to the QTL relative to the polygenes across generations for maximising gain in truncation selection schemes. Dekkers and Van Arendonk (1998) considered infinite populations and therefore no accumulation of inbreeding. A total of 500 replicates were run for each simulation and the results presented are the averages over all replicates.

### Genetic model

One of the traits ( $t_1$ ) was controlled only by polygenes (i.e., the infinitesimal model) while the other trait ( $t_2$ ) was controlled by an identified additive biallelic QTL (alleles A and B) and by polygenes (i.e., a mixed inheritance model). The total genetic values of the  $i^{\text{th}}$  individual for  $t_1$  and  $t_2$  were respectively  $g_1 = u_{i_1}$  and  $g_2 = u_{i_2} + v_i$ , where  $u_{k_i}$  is the polygenic effect for trait  $k$  ( $k = 1, 2$ ) and  $v_i$  is the genotypic value due to the QTL. The polygenic plus environmental variances summed to one for both traits. The genotypic value due to the QTL was  $a$ , 0 and  $-a$  for genotypes AA, AB and BB, respectively so  $a$  is defined as half the difference between the two homozygotes (Falconer and Mackay, 1996). For  $t_2$ , the additive genetic variance explained by the QTL ( $\sigma_v^2$ ) 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 variation explained by the QTL in  $t_2$  [i.e.,  $\theta = \sigma_v^2 / (\sigma_v^2 + \sigma_{u_2}^2)$ ] in the base generation was 0.1 or 0.5, which correspond to  $a$  values of 0.21 and 0.63 within QTL genotype standard deviation units. The polygenic heritabilities ( $h^2$ ) were 0.3 for  $t_1$  and 0.1 for  $t_2$ . The

<sup>1</sup> Abbreviations used: BLUP (best linear unbiased predictor), EBV (estimated breeding values), GAS (gene assisted selection), MAS (marker assisted selection), QTL (quantitative trait loci).

polygenic genetic correlation ( $\rho_u$ ) between both traits was  $-0.5$  and the environmental correlation was zero.

### Simulation of the population

The base generation ( $t=0$ ) was composed of  $N=120$  individuals (60 males and 60 females). A prior generation ( $t=-1$ ) composed also of 60 males and 60 females was simulated to create the family structure in  $t=0$ . Individuals generated at  $t=-1$  were mated at random and each produced one male and one female offspring. Generation 1 ( $t=1$ ) was obtained from the matings among selected individuals at  $t=0$ . In the base generation, the polygenic values ( $u_1$  and  $u_2$ ) were drawn from a bivariate normal distribution with correlation  $\rho_u$  and polygenic variances  $\sigma_{u_1}^2$  and  $\sigma_{u_2}^2$ . Polygenic genetic values in  $t=0$  for the  $i^{\text{th}}$  individual were generated as

$$u_{1i} = \sigma_{u_1} w_{1i} \text{ and } u_{2i} = [\rho_u w_{1i} + \sqrt{(1-\rho_u^2)} w_{2i}] \sigma_{u_2}, \text{ where } w_{1i} \text{ and } w_{2i} \text{ are random normal deviates taken from a normal distribution with variance equal to one. Phenotypic values for } t_1 (y_{1i}) \text{ and } t_2 (y_{2i}) \text{ were obtained by adding an environmental component to the total genetic value.}$$

Selection was carried out for 10 discrete generations. 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 (i.e., in the same way as for the polygenic values in  $t=0$ ) with correlation  $\rho_u$  and variances  $\frac{1}{2}\sigma_{u_k}^2(1-F)$  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 number of selection candidates was kept constant across generations.

### Estimation of breeding values

In schemes using the QTL genotype (denoted as G) it was assumed that the QTL effect and QTL genotypes for all individuals were known without error. The total estimated breeding values for  $t_1$  and  $t_2$  were respectively  $EBV_{t_1} = EBV_{u_1}$  and  $EBV_{t_2} = EBV_{u_2} + BV_{qtl}$ , where  $EBV_{u_k}$  is the estimate of the polygenic breeding value for trait  $k$  and  $BV_{qtl}$  is the known breeding value due to the QTL effect. The  $BV_{qtl}$  was  $2(1-p)a$ ,  $(1-2p)a$  and  $-2pa$  for genotypes AA, AB, BB, respectively (Falconer and Mackay, 1996), with  $p$  updated each generation. A bivariate BLUP evaluation was performed to obtain  $EBV_{u_1}$

and  $EBV_{u_2}$  simultaneously using PEST (Groeneveld *et al.*, 1990) with the base population polygenic variances ( $\sigma_{u_1}^2$  and  $\sigma_{u_2}^2$ ), and the phenotypic values for  $t_2$  corrected for the QTL effect ( $y_{2i}^* = y_{2i} - v_i$ ).

In schemes ignoring the QTL genotypes (denoted as I),  $EBV_{t_1}$  and  $EBV_{t_2}$  were also obtained from a bivariate BLUP genetic evaluation but using the base population total genetic additive variances ( $\sigma_{g_1}^2 = \sigma_{u_1}^2$  and  $\sigma_{g_2}^2 = \sigma_{u_2}^2 + \sigma_v^2$ ) and the phenotypic values  $y_2$  uncorrected for the QTL effect.

### Availability of phenotypes in selection candidates

Two situations were simulated with regard to phenotypes availability: i) all selection candidates had available phenotypes for both traits (termed *full-data*), and ii) all selection candidates had available phenotypes for  $t_1$ , but only female candidates had available phenotypes for  $t_2$  (termed *sex-limited*).

### Selection methods

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 economic weight). The index on which selection was carried out was  $I_S = EBV_{t_1} + EBV_{t_2}$ .

The potential extra gains from GAS were investigated in both truncation and optimised selection schemes. Thus, in total, four schemes were evaluated depending on the selection method and the use of QTL information: truncation ignoring ( $T_I$ ) or using ( $T_G$ ) the QTL information and optimised selection ignoring ( $O_I$ ) or using ( $O_G$ ) the QTL information. Random mating among selected candidates was performed for both truncation and optimised selection.

In truncation selection schemes, the 12 highest ranked male and females based on the index  $I_S$  were selected each generation and each selected individual was mated only once. All females produced the same number of offspring (i.e., 10), hence equal contributions to the next generation were allocated to each selected candidate.

In optimised selection schemes the number of selected males and females and their contributions to the next generation were optimised for maximising the rate of gain while constraining  $\Delta F$  to a pre-defined level each generation. The optimisation algorithm described by Meuwissen (1997) was used but the constraint imposed on  $\Delta F$  was that described in Grundy *et al.* (1998).

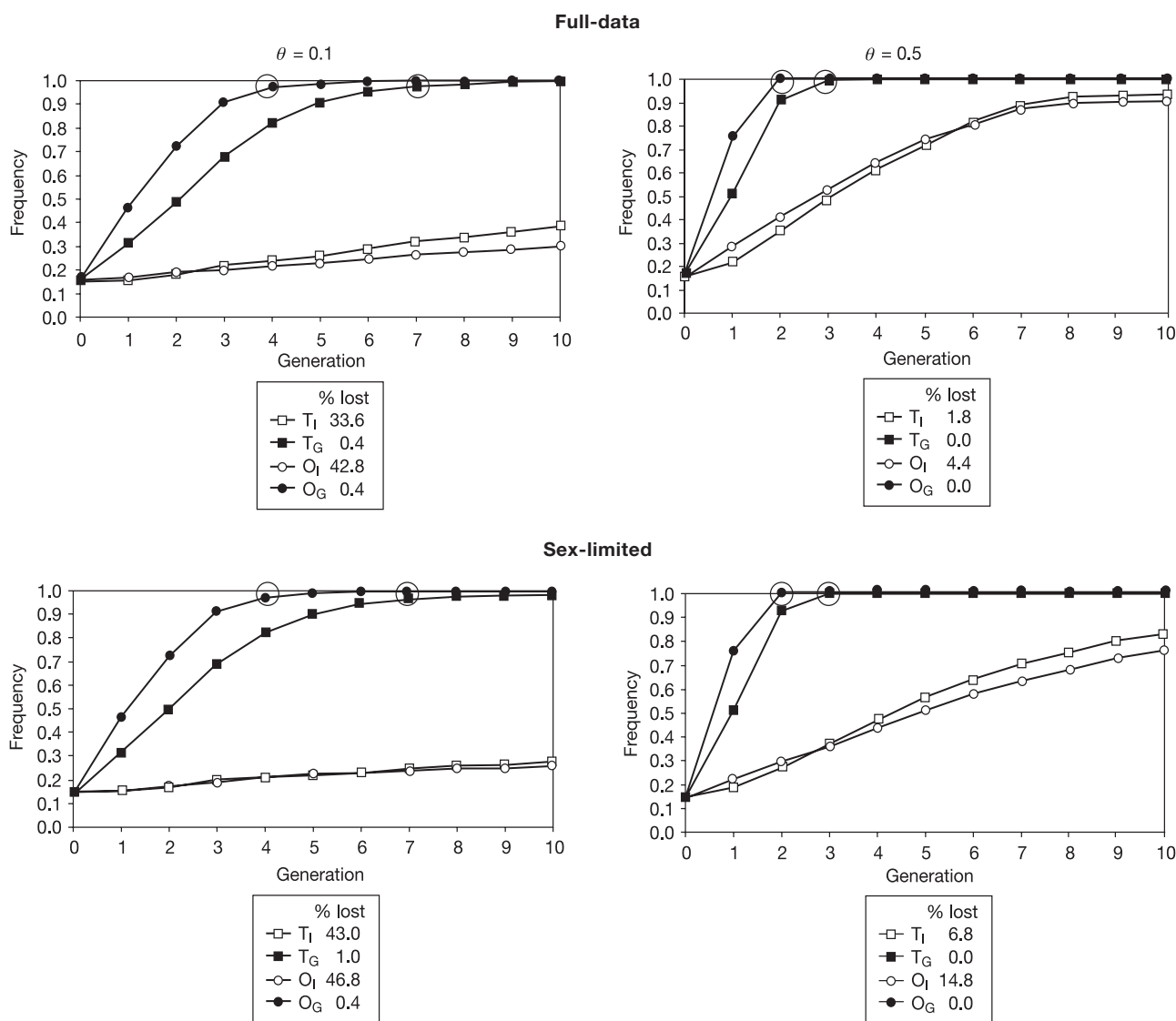
This dynamic optimisation tool receives the generic denomination of quadratic index (Woolliams *et al.*, 2002).

With optimised selection,  $\Delta F$  was restricted to the value obtained in the corresponding truncation scheme. It must be noted that the input for the optimisation algorithm are the  $I_s$  values of selection candidates rather than the  $EBV$  of individual traits as in previous studies assuming single trait scenarios with polygenic (Meuwissen, 1997; Grundy *et al.*, 1998), or mixed inheritance models (Villanueva *et al.*, 1999, 2002).

## Results

### Fixation and loss of the favourable allele

The gene frequency of the favourable allele and the percentage of replicates in which it was lost are presented in Figure 1. As expected, allele fixation was faster when the QTL explained a larger proportion ( $\theta$ ) of the genetic variance. Schemes using the gene information ( $O_G$  and  $T_G$ ) fixed ( $p \geq 0.97$ ) the favourable allele within



**Figure 1.** Frequency of the favourable allele over generations for truncation and optimal schemes ignoring ( $T_I$ ,  $O_I$ ) or using ( $T_G$ ,  $O_G$ ) the QTL information for two levels of the proportion of total genetic variance explained by the QTL affecting trait 2 ( $\theta$ ). Two scenarios are considered: 1) phenotypes are available for both traits in both sexes (*Full-data*); and 2) phenotypes for trait 2 are available only for females (*Sex-limited*). Circles indicate the generation numbers where the frequency of the favourable allele is greater or equal to 0.97. The percentage of replicates where the favourable allele was lost (% lost) is indicated. Standard errors ranged from 0.00 to 0.01.

the selection period considered. Fixation was faster in  $O_G$  than in  $T_G$ . In contrast, schemes ignoring the gene information ( $O_I$  and  $T_I$ ) did not lead to fixation of the favourable allele within the selection period evaluated, although  $p$  was close to fixation in the *full-data* scenario for  $\theta=0.5$ . A trend was identified in which  $O_I$  increased  $p$  faster than  $T_I$  during initial generations, whereas the opposite was true for later generations. This was particularly evident for the *full-data* scenario with  $\theta=0.1$  and for both scenarios with  $\theta=0.5$ .

The loss of the favourable allele was only important in those schemes ignoring the gene information, particularly for  $\theta=0.1$ , and for the *sex-limited* scenario. Also, the  $O_I$  scheme consistently lost the favourable allele to a greater extent than  $T_I$ .

## Response in the breeding objective

### *Phenotypic records available in both sexes for both traits*

Table 1 shows the accumulated response in the breeding objective for the four schemes evaluated. For a particular selection scheme, the gain in  $H$  was always greater for  $\theta=0.5$  than for  $\theta=0.1$ . At each generation, schemes using the genotype information ( $O_G$  and  $T_G$ )

yielded more gain than the corresponding schemes ignoring the QTL ( $O_I$  and  $T_I$ ) at both levels of  $\theta$ . The advantage of  $G$  schemes was highest before fixation (around 12% for  $\theta=0.1$  and 50% for  $\theta=0.5$  at  $t=2$ ) and decreased after fixation (around 6% for  $\theta=0.1$  and 2% for  $\theta=0.5$  by  $t=10$ ).

Optimal selection schemes ( $O_G$  and  $O_I$ ) achieved higher gain in  $H$  than the corresponding truncation selection schemes ( $T_G$  and  $T_I$ ) at both levels of  $\theta$  during the whole selection period. By  $t=10$ , the accumulated gain in  $H$  was about 12% higher for  $O_G$  than for  $T_G$  and about 13% higher for  $O_I$  than for  $T_I$  for both  $\theta$  levels.

The comparison between  $O_I$  and  $T_G$  schemes indicates that the optimisation of contributions had a higher impact on genetic gain than the use of QTL information. The scheme  $O_I$  achieved higher accumulated gain in  $H$  than  $T_G$  during the whole selection period for  $\theta=0.1$ . For  $\theta=0.5$ ,  $T_G$  achieved higher gains than  $O_I$  until  $t=3$ , when the favourable allele is fixed in  $T_G$ . After fixation (i.e., from  $t=4$  onwards)  $O_I$  progressively outperformed  $T_G$  achieving 10% higher gain in  $H$  by generation ten. Therefore, in early generations while the gene is segregating in the  $T_G$  scheme, the importance of the use of molecular information relative to the optimisation of contributions was dependent on the size of the gene.

The combination of optimal contributions and genotype information (i.e., the  $O_G$  scheme) resulted in

**Table 1.** Total accumulated genetic gain in the breeding goal over generations ( $t$ ) for truncation and optimal schemes ignoring ( $T_I$ ,  $O_I$ ) or using ( $T_G$ ,  $O_G$ ) the QTL information for two levels of the proportion of the total genetic variance explained by the QTL affecting trait 2 ( $\theta$ ). Phenotypic records were available for both traits in both sexes (*Full-data*) or in both sexes for trait 1 but only in females for trait 2 (*Sex-limited*)<sup>a</sup>

$t$	$\theta=0.1$				$\theta=0.5$			
	$T_I$	$T_G$	$O_I$	$O_G$	$T_I$	$T_G$	$O_I$	$O_G$
<i>Full-data</i>								
1	0.341	0.374	0.538	0.600	0.411	0.618	0.663	1.025
2	0.674	0.743	0.873	1.001	0.855	1.284	1.113	1.647
3	0.974	1.077	1.197	1.374	1.268	1.666	1.547	1.971
4	1.247	1.385	1.500	1.687	1.664	1.967	1.965	2.268
5	1.515	1.676	1.804	1.984	2.025	2.245	2.344	2.560
10	2.703	2.870	3.059	3.223	3.314	3.413	3.737	3.791
<i>Sex-limited</i>								
1	0.336	0.372	0.529	0.598	0.372	0.614	0.595	1.023
2	0.654	0.736	0.868	0.978	0.769	1.281	0.995	1.641
3	0.943	1.065	1.191	1.345	1.133	1.659	1.369	1.955
4	1.212	1.372	1.501	1.655	1.489	1.957	1.744	2.254
5	1.474	1.656	1.794	1.946	1.833	2.226	2.101	2.543
10	2.631	2.851	3.029	3.161	3.139	3.390	3.551	3.768

<sup>a</sup> Standard errors ranged from 0.002 to 0.020.

the highest gains in  $H$  in both the short and the long term at both levels of  $\theta$ . When compared to traditional truncation selection ( $T_I$ ), the  $O_G$  scheme gave 19% and 14% higher cumulated gain in  $H$  at  $t = 10$  for  $\theta = 0.1$  and  $\theta = 0.5$ , respectively.

#### Phenotypic records for trait 2 only available on females

When only females had available phenotypes in the trait controlled by the QTL ( $t_2$ ) the ranking among schemes was the same as that described in the scenario where both sexes had available phenotypes in both traits (Table 1). Although the absolute values for the gains in  $H$  were lower for the *sex-limited* scenario than for the *full-data* scenario the differences were relatively small. Also, the optimisation of contributions had similar benefits to those found in the *full-data* scenario.

Except for optimised selection with  $\theta = 0.1$ , the benefit of using the QTL information was greater in the *sex-limited* than in the *full-data* scenario. The advantage of G schemes over I schemes in accumulated gain in  $H$  at  $t = 10$  was 8.4% ( $T_G$  over  $T_I$ ) and 4.3% ( $O_G$  over  $O_I$ ) for  $\theta = 0.1$  and 8.0% ( $T_G$  over  $T_I$ ) and 6.1% ( $O_G$  over  $O_I$ ) for  $\theta = 0.5$ , respectively. As in the *full-data* scenario, the  $O_G$  scheme achieved the highest cumulated gains in  $H$  in the short and long term for both levels of  $\theta$ . For the *sex-limited* scenario, the advantage of  $O_G$  over truncation selection ignoring the QTL ( $T_I$ ) at  $t = 10$  was 20% for both  $\theta$  levels. This represents a 6% increase for the same comparison under the *full-data* scenario for  $\theta = 0.5$ .

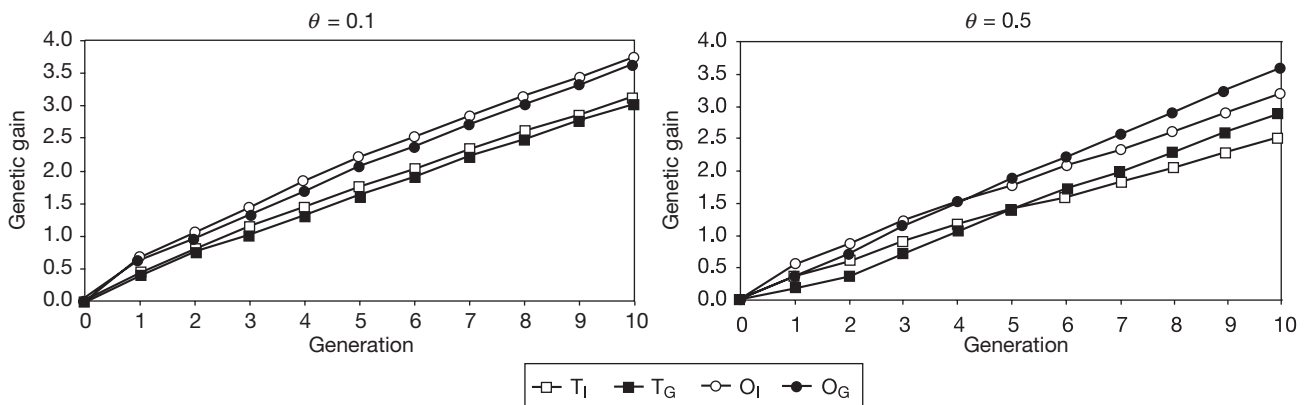
### Total and polygenic responses in individual traits

Comparisons between schemes in terms of genetic gains for the individual traits included in the breeding objective are presented only for the *full-data* scenario as similar results were found for the *sex-limited* scenario.

#### Genetic gains in trait 1

Figure 2 shows the total gain in  $t_1$  (i.e., polygenic gain) across generations. Optimal schemes ( $O_I$  and  $O_G$ ) clearly yielded higher gains than truncation schemes ( $T_I$  and  $T_G$ ) throughout the whole selection period for both levels of  $\theta$ .

For  $\theta = 0.1$ , schemes ignoring QTL information achieved higher gain than the corresponding schemes using this information, although differences between schemes were small. In contrast, for  $\theta = 0.5$  the ranking between G and I schemes depended upon the frequency of the favourable allele. In early generations while the allele is segregating in all the schemes,  $O_I$  and  $T_I$  schemes achieved, respectively, higher gains in  $t_1$  than  $O_G$  and  $T_G$  schemes. Conversely, after fixation in the G schemes (i.e., from  $t = 4$ ), these schemes achieved higher accumulated polygenic gain in  $t_1$  than their corresponding I schemes and the extra gains ranged from 11% to 13% at  $t = 10$ . Thus for  $\theta = 0.5$ , the lower (polygenic) gain of the  $O_G$  and  $T_G$  schemes while the gene is segregating suggests negative consequences in  $t_1$  from selecting on the QTL affecting  $t_2$ , but not to a degree to which the long-term gain in  $t_1$  would be compromised.



**Figure 2.** Accumulated total (polygenic) genetic gain in trait 1 over generations for truncation and optimal schemes ignoring ( $T_I$ ,  $O_I$ ) or using ( $T_G$ ,  $O_G$ ) the QTL information for two levels of the proportion of total genetic variance explained by the QTL affecting trait 2 ( $\theta$ ). Phenotypic records were available for both traits in both sexes. Standard errors ranged from 0.00 to 0.02.

Genetic gains in trait 2

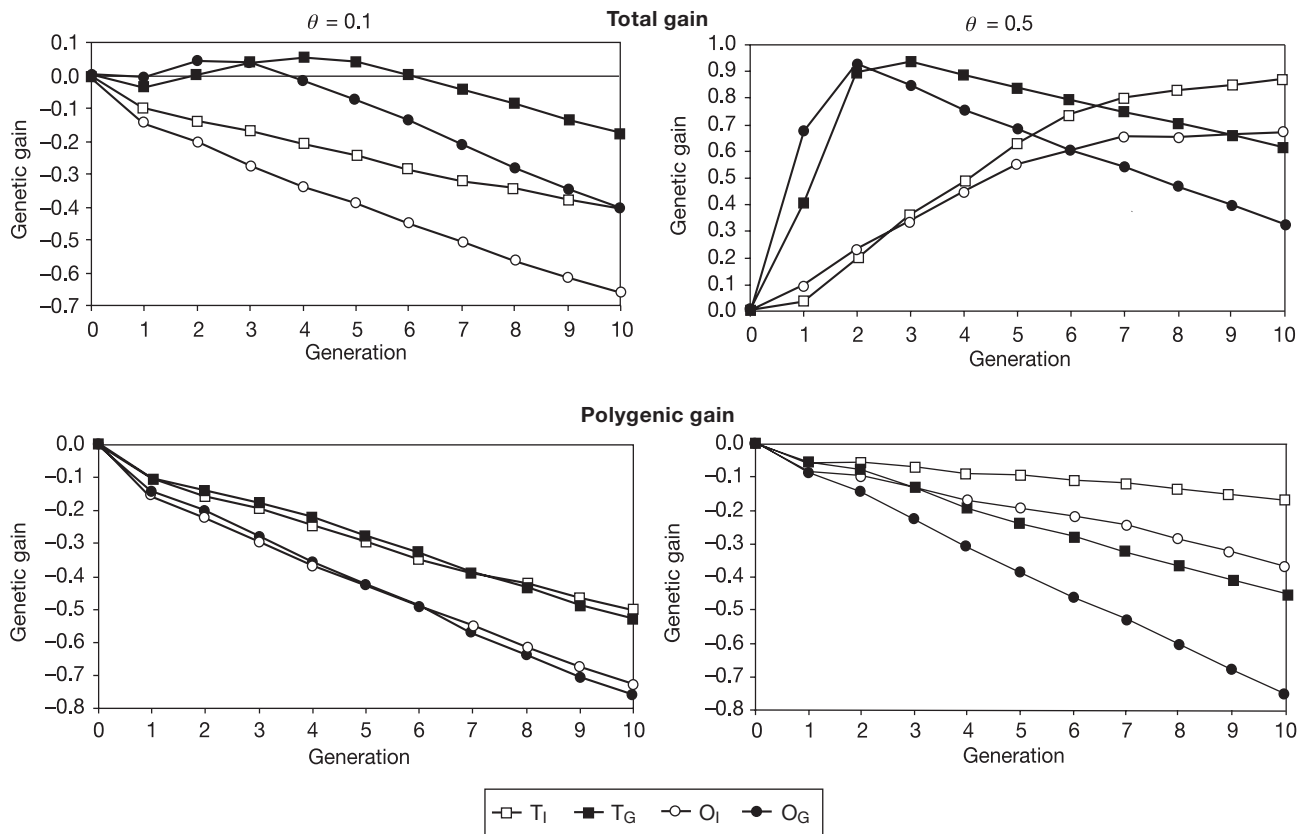
Figure 3 shows the total and polygenic gains for  $t_2$ . When the QTL had a small effect (i.e.,  $\theta = 0.1$ ), the total response in  $t_2$  in schemes using QTL information was only positive after  $t = 1$  and while the favourable allele was segregating (i.e., up to  $t = 4$  in  $O_G$  and up to  $t = 6$  in  $T_G$ ). Schemes ignoring the QTL led to negative total response in  $t_2$  throughout the whole selection period. The negative response was driven by the negative sign of  $\rho_u$ . Hence, the  $T_G$  scheme was the «best» with respect to  $t_2$  as it allowed positive total responses for a longer period and gave lower negative responses after fixation when compared to  $O_G$  and the schemes ignoring the QTL. As for  $t_1$ , with  $\theta = 0.1$  the  $O_I$  scheme achieved the highest total response in  $t_2$ , although in the undesired direction.

With  $\theta = 0.1$ , the polygenic gain in  $t_2$  followed the same trend that of  $t_1$  (see also Fig. 2) but in opposite direction. Optimal schemes ( $O_G$  and  $O_I$ ) achieved higher gains than truncation selection schemes ( $T_G$  and  $T_I$ )

and the differences between schemes using or ignoring the QTL information were relatively small. Therefore, it should be emphasized that for a gene of small effect, the trends in polygenic responses in both traits were practically determined only by the selection method, that is, truncation or optimal selection.

When the QTL had a large effect (i.e.,  $\theta = 0.5$ ) the four schemes evaluated yielded positive total responses in  $t_2$  during the whole selection period. The maximum accumulated gain in  $O_G$  and  $T_G$  was observed at generations two and three, respectively, which are the generations where the QTL was fixed (see also Fig. 1). After fixation the total response decreased steadily in both schemes although at a higher rate in the  $O_G$  scheme. Schemes ignoring the QTL showed increasing cumulative gains during the whole selection period as the favourable allele was still segregating in the last generation of selection.

As for the case where the QTL had a smaller effect (i.e.,  $\theta = 0.1$ ), negative polygenic gains were observed in  $t_2$  for all selection schemes and these were higher



**Figure 3.** Accumulated total and polygenic genetic gains in trait 2 over generations for truncation and optimal schemes ignoring ( $T_I$ ,  $O_I$ ) or using ( $T_G$ ,  $O_G$ ) the QTL information for two levels of the proportion of total genetic variance explained by the QTL affecting trait 2 ( $\theta$ ). Phenotypic records were available for both traits in both sexes. Standard errors ranged from 0.00 to 0.01.

with optimal than with truncation selection. However, in contrast with the results for  $\theta = 0.1$ , G schemes ( $O_G$  and  $T_G$ ) achieved significant higher polygenic negative responses than their corresponding I schemes ( $O_I$  and  $T_I$ ) both in the short and the long term when  $\theta = 0.5$ . Thus, in this case, both the selection method and the use of genotype information determined the ranking among schemes relative to polygenic gain.

Summarising, for  $\theta = 0.1$ , optimal schemes achieved the greatest accumulated polygenic responses in both traits, positive in  $t_1$  and negative in  $t_2$  (Figs. 2 and 3) and the differences between schemes using or ignoring the QTL were very small. For  $\theta = 0.5$ , the combination of both optimal selection and the use of the QTL information (i.e., the  $O_G$  scheme) yielded the greatest accumulated polygenic response in both traits, again positive in  $t_1$  and negative in  $t_2$ .

The reason for the  $T_G$  scheme achieving higher gains in  $H$  than  $O_I$  before fixation for  $\theta = 0.5$  (i.e.,  $t = 2$  and  $3$ , Table 1) is explained by the notable increase in total gain in  $t_2$  clearly driven by QTL gain (Fig. 3). As mentioned above, after fixation in  $T_G$  the total gain in  $t_2$  was reduced, while in  $O_I$  the gene segregates throughout the whole selection period, thus, allowing an increase in total gains in  $t_2$  up until  $t = 10$ . In addition, the polygenic gains in  $t_1$  for  $O_I$  were always higher than for  $T_G$  (Fig. 2) hence, allowing higher gains in  $H$  after fixation.

## Discussion

This study has evaluated the combined benefits of using QTL genotype information and quadratic optimisation for maximising gain while constraining  $\Delta F$  when selection is applied on a selection index including two negatively correlated traits. This represents an extension of the work of Villanueva *et al.* (1999) based on a single trait scenario. The study focused on a practical scenario which might benefit from the use of QTL information: a trait with high heritability affected by polygenes (e.g., a production trait) negatively correlated to a trait with low heritability for which a QTL has been identified (e.g., a fitness-related trait).

The use of a quadratic index for optimising the contributions of selection candidates gave similar benefits over truncation selection for improving the aggregate genotype to those found previously in single trait scenarios under mixed inheritance models (Villanueva *et al.*, 1999, 2002). Also, optimal selection gave higher

absolute polygenic response than truncation selection in both traits. However, the polygenic negative correlation between the traits determined the sign of the responses, which was positive in  $t_1$  and negative in  $t_2$ . While the maximisation of genetic gains is an intrinsic property of quadratic optimisation, for this set up with two negatively correlated traits, the extra polygenic responses in the negative direction in the trait with lower heritability ( $t_2$ ) might be seen as undesirable. This would be the case if  $t_2$  was related to reproductive success or to other component of overall fitness. The only benefit of quadratic optimisation with respect to truncation selection for the trait affected by the QTL effect arose from a faster fixation of the favourable allele when QTL information was used. However, the faster the allele was fixed, the earlier the polygenic gains in the undesired direction in  $t_2$  started to become evident. In contrast, truncation selection using the QTL information was equally effective in fixing the favourable allele, and its sub-optimality from the point of view of the management of contributions avoided more dramatic negative responses in  $t_2$ .

The use of QTL information allowed increased gains in the aggregate breeding value across all generations of selection. Thus, for the scenarios simulated, the previously reported conflict between the short- and long-term gains when information from identified genes is used (Gibson, 1994) was not observed. This was also the case when 10 extra generations of selection were simulated for the scenario *full-data* with  $\theta = 0.5$  to enable the long-term comparisons being held after the favourable allele was fixed in I schemes (results not shown).

The effect of using the QTL information on the polygenic gain of each of the traits in the breeding goal appeared to be more related to the trait heritability (i.e., the relative weight in the breeding goal) than to the particular inheritance model. The use of QTL information had a greater effect on the trait with the highest heritability ( $t_1$ ). Significant amounts of disequilibrium between QTL alleles and polygenes (results not shown) were found (particularly with  $\theta = 0.5$ ) for this trait (which had a complete polygenic inheritance) and that reduced its polygenic gain before fixation in both optimal and truncation selection. After fixation, G schemes behaved as in a complete polygenic model and gave greater gains than I schemes. Also, G schemes were also free from any bias when estimating *EBVs* for  $t_1$ , whereas I schemes were subject to such bias throughout the whole selection process for  $\theta = 0.5$  (Villanueva *et al.*, 1999). For the



trait under QTL control (i.e., the trait with the lowest heritability), the disequilibrium was much lower and G schemes achieved greater gains than the corresponding I schemes across all generations, hence indicating that polygenic gains was not compromised by the use of the QTL information (even for  $\theta = 0.5$ ).

The most important benefit from using the QTL information arose from counteracting the effects of the negative polygenic correlation and allowing for positive total gains in  $t_2$  while the QTL was still segregating (Fig. 3). In particular, for a gene explaining 50% of the total genetic variance in  $t_2$ , the total gain was positive for the ten generations of selection analysed, both with truncation and optimised selection. After fixation, the total gain in  $t_2$  was solely determined by the polygenic gain and its direction was determined by the sign of the polygenic correlation (i.e., negative), which explains the decreasing total gain in  $t_2$  in later generations.

The loss of the favourable allele in truncation schemes was much lower than that found by Verrier (2001). In his study, MAS was only able to avoid allele loss when the QTL explained 20% of the total genetic variance and when the marker was very close to the QTL (i.e., a recombination rate of 0.02). In this case, the beneficial allele was lost for  $T_G$  and  $T_1$  schemes in 37% and 53% of the replicates, respectively. The corresponding percentages in our GAS study were 0.4% and 33.6% (Fig. 1). The higher loss found by Verrier (2001) was due to the fact that MAS rather than GAS was applied and to that, in his case, the trait affected by the QTL not only had the lowest heritability, but also had the lowest weight in the breeding goal.

The loss of the favourable allele was greater in  $O_1$  schemes than in  $T_1$  schemes. This effect is likely to be related to the lower relative weight of the trait under QTL effect in the breeding goal (i.e., lower  $h^2$ ). Quadratic optimisation allocates greater contributions to individuals with higher index values (Avendaño *et al.*, 2004) and the ranking of candidates will be dominated by the trait with the highest  $h^2$ , that is, the trait under complete polygenic inheritance ( $t_1$ ). Also, as mentioned previously, greater disequilibrium was created for this trait such that gametes carrying the favourable allele had a lower polygenic mean in  $t_1$ . In consequence, until fixation, candidates with genotypes carrying the favourable allele will have a lower selective advantage compared

to candidates carrying the unfavourable allele. By including the QTL information in the selection decisions the extra allele loss in optimal schemes disappears. A similar phenomenon would be expected if the traits had the same heritability but different relative weights in the breeding goal.

The genetic gains in the breeding goal for the schemes using the QTL might be considered as upper limits as, in practice, markers rather than identified genes are more likely to be used. The gains found here for GAS truncation schemes doubled those found by Verrier (2001) for MAS. Extra independent information on the QTL effect could be used in MAS schemes to approach the upper limit given by GAS as it has been showed in single trait scenarios (Villanueva *et al.*, 2002). Gains would be also lower than those presented here if the assumption of a complete knowledge of the QTL effect is relaxed. These decreased gains from using markers or from estimating QTL effects would affect the comparisons between schemes using and ignoring the QTL but not the comparisons between optimised and truncation schemes.

This study has implications on the optimal use of QTL information in practical breeding programmes where more than one trait contributes to the total economic value. For the scenarios considered, the joint use of optimised contributions of selection candidates and QTL information led to extra gains in the aggregate genotype both in the short and in the long term. Benefits from selection on the quadratic index in GAS schemes can be also expected with alternative genetic models including allelic QTL interactions (e.g., recessive, dominant or overdominant), pleiotropic effects and multiple QTL.

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