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## Efficiency of direct selection on quantitative trait loci for a two-trait breeding objective

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**Abstract** Selection on known loci affecting quantitative traits (DSQ) was compared to phenotypic selection index for a single and a two-trait selection objective. Two situations were simulated; a single known quantitative locus, and ten identified loci accounting for all the additive genetic variance. Selection efficiency of DSQ relative to trait-based selection was higher for two-trait selection, than was selection on a single trait with the same heritability. The advantage of DSQ was greater when the traits were negatively correlated. Relative selection efficiency (RSE) for a single locus responsible for 0.1 of the genetic variance was 1.11 with heritabilities of 0.45 and 0.2 and zero genetic and phenotypic correlations between the traits. RSE of DSQ for ten known loci was 1.5 to 1.8 in the first 3 generations of selection, but declined in each subsequent generation. With DSQ most loci reached fixation after 7 generations. Response to trait-based selection continued through generation 15 and approached the response obtained with DSQ after 10 generations. The cumulative genetic response after 10 generations of DSQ was only 93% to 97% of the economically optimum genotype because the less favorable allele reached fixation for some loci, generally those with effects in opposite directions on the two traits.

**Key words** Quantitative trait loci · Marker assisted selection · Multi-trait selection index

### Introduction

Nearly all commercial breeding schemes for quantitative traits are based on selecting as parents for the next generation those individuals with the most desirable estimated

aggregate breeding value. There is generally no attempt to directly select for specific alleles affecting the traits under selection. Genetic markers can be used to isolate the effects of individual chromosomal segments, even if the effect is responsible only for a small fraction of the total phenotypic variance (Sax 1923; reviewed by Soller 1990, 1991; Weller 1992). Until recently, the application of “Marker-assisted selection” (MAS) was limited by the lack of suitable segregating genetic markers in animal and plant populations of commercial interest. New techniques have been developed to determine polymorphisms in the DNA base pair sequence, including restriction fragment length polymorphisms (RFLP), DNA fingerprinting, and DNA microsatellites (Beckmann and Soller 1983; Fries et al. 1990; Georges and Massey 1991; Jeffreys et al. 1985; Litt and Luty 1989; Soller 1990; Soller 1991; Soller and Beckmann 1983; Weber and May 1989). Thus, it is now possible to find polymorphisms suitable for use as genetic markers in all commercial species.

Since MAS will require additional investment in breeding programs, it is critical to determine the additional genetic gain that could be obtained. Weller and Fernando (1991) list four ways by which MAS can contribute to genetic progress within a breed:

- 1) by increasing selection intensity,
- 2) by decreasing generation interval,
- 3) by increasing accuracy of evaluation,
- 4) by planning matings among individuals.

The first two ways may not be applicable in many species. By planned matings it is possible to utilize nonadditive genetic variation such as dominance and epistasis. However, any gain due to nonadditive genetic variation will not carry over into future generations. A priori it would seem that if the individual quantitative trait loci (QTL) affecting a quantitative trait are known, then it should be possible to devise a more efficient breeding scheme than mass selection. However, in practice this is apparently not the case. Weller and Soller (1981) studied strategies for incorporating a number of favorable genes into a single strain. They found the optimum strategy to be random mating

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among the different strains and mass selection on the number of positive alleles in each progeny. The same strategy would of course be followed if the individual QTL were not known. Thus, most studies that have attempted to estimate the expected genetic progress via MAS have concentrated on the effect of MAS on increasing the accuracy of evaluation (Lande and Thompson 1990; Smith and Webb 1981; Smith and Simpson 1986; Stam 1986; Zhang and Smith 1992). Results generally show that although the gain is significant for low heritability traits, it is insignificant for high heritability traits.

All previous studies have concentrated on expected genetic progress for a single trait. However, in practice, the commercial breeding objective is nearly always composed of several traits. Falconer (1989) noted that "negative" genetic correlations, relative to the desired direction of selection, will develop among traits under selection during the course of a breeding program. (Henceforth the economically favorable phenotype will be termed "positive" and the economically unfavorable phenotype will be termed "negative". Thus, if both traits are measured on scales in which economically favorable is positive, then a "negative" genetic correlation is one in the opposite direction to the selection objective.) Those alleles with positive effects for both traits will be the first to undergo fixation, while those alleles with positive effects on some traits and negative effects on others will not be appreciably affected by selection. Thus, genetic progress for an index of traits with major negative genetic correlations will be slow even if all of the traits have high heritability.

If the negative genetic correlation between two traits is incomplete, then it is still likely that a few QTL will have positive effects on both traits. Weller et al. (1988) found QTL with effects on pairs of traits in the direction opposite to that of the genetic correlation. Selection for these loci may be significantly more effective than the traditional selection index. Lande and Thompson (1990) computed an optimum selection index for multitrait MAS, but did not evaluate the efficiency of MAS for a multitrait breeding objective.

The goals of the study presented here were to estimate the maximum expected gain from selection on specific QTL for a two trait breeding objective, with differing heritabilities and with both positive and negative genetic and environmental correlations. Two situations were considered: a single known QTL with effects on both traits, together with background genetic variation; and all QTL with effects on both traits known.

## Methods

### Simulation of a single known QTL

The selection objective consisted of two traits with phenotypic variances of  $\sigma_{p1}^2$  and  $\sigma_{p2}^2$ , genetic variances of  $\sigma_{a1}^2$  and  $\sigma_{a2}^2$ , a genetic correlation of  $r_a$ , and a phenotypic correlation of  $r_p$ .  $\sigma_{a1}^2$  and  $\sigma_{a2}^2$  were assumed to be equal to the genetic variance of the identified QTL on traits 1 and 2,  $\sigma_{Q1}^2$  and  $\sigma_{Q2}^2$ , plus the genetic variance due to other, not identified, loci. The population under selection was assumed to be diploid. It was further assumed that there were only two alleles for the QTL segregating in the population, that the effect of the QTL on both traits was codominant, and that, prior to selection, mating was random with respect to the QTL. Thus, the genetic correlation between the traits on the QTL was either 1 or -1. No epistasis between the QTL and other loci was assumed, thus, the correlation between the QTL and the other loci was zero.

$\sigma_{Q1}^2$  and  $\sigma_{Q2}^2$  were computed as  $f_1(\sigma_{a1}^2)$  and  $f_2(\sigma_{a2}^2)$ , where  $f_1$  and  $f_2$  are the fractions of the genetic variance for each trait attributed to the identified QTL. It was assumed that  $f_1 = f_2$ . Equal frequencies were assumed for the two QTL alleles; thus:

$$\sigma_{Q_i}^2 = 2p(1-p)a_i^2 = 0.5a_i^2 \quad (1)$$

where  $p$  is the allele frequency and  $a_i$  is the substitution effect of the QTL for trait  $i$ . The effects of the QTL on trait 1 were  $a_1$ , 0, and  $-a_1$ , and the effects of the QTL on trait 2 were  $a_2$ , 0, and  $-a_2$ .

The phenotypic and genetic parameters of the two traits and the QTL were used to derive the optimum linear selection index,

$$I = b_{X1} X_1 + b_{X2} X_2 + b_Q q \quad (2)$$

where  $X_1$  and  $X_2$  are the phenotypic trait values for traits 1 and 2,  $q$  is the "value" for the QTL, and  $b_{X1}$ ,  $b_{X2}$  and  $b_Q$  are the index coefficients. (Since all individuals are selected from a common population with a single mean, it is not necessary to subtract the trait means or the mean of  $q$ .) By selection index theory (Hazel 1943), the vector of optimum index coefficients,  $\mathbf{b}_I$ , is derived as follows:

$$\mathbf{b}_I = \mathbf{P}^{-1} \mathbf{G} \mathbf{v} \quad (3)$$

where  $\mathbf{P}$  is the phenotypic matrix,  $\mathbf{G}$  is the genetic variance matrix, and  $\mathbf{v}$  is the vector of economic values for the two traits and the QTL. The elements of  $\mathbf{P}$  and  $\mathbf{G}$  are given in Table 1.  $\sigma_{p1}^2$  and  $\sigma_{p2}^2$  were set equal to unity.  $r_a$  was varied from -0.8 to 0.8, and  $r_p$  was set equal to  $r_a$ .  $q$  was set equal to 2, 1, and 0 for locus effects of  $a_1$ , 0 and  $-a_1$ , respectively. Thus, the variance of the QTL =  $2(0.5)(0.5) = 0.5$ . Since the "heritability" of the QTL is 1, the phenotypic variance is equal to the genetic variance. The genetic covariances between the QTL and the two traits were  $0.5a_1$  and  $0.5a_2$ . Since, as stated, the "heritability" of the QTL is 1, the phenotypic covariances are equal to the genetic covariances. The genetic and phenotypic covariances between the two quantitative traits were derived from the corresponding variances and correlations. These values differs from the values given in Appendix 1 of Lande and Thompson (1990) because the latter measured the standard deviation of the QTL in units of the quantitative trait, while in this study the QTL was measured in units of the number of alleles with "positive" effects. Since each quantitative trait is measured in different units, this notation is more appropriate for a two-trait breeding objective. The economic values for the two traits were set equal to unity, and the economic value for the QTL was 0.

**Table 1** The genetic and phenotypic variance-covariance matrices for selection on two traits and a single QTL<sup>a</sup>

Trait	Genetic matrix			Phenotypic matrix		
	Trait 1	Trait 2	QTL	Trait 1	Trait 2	QTL
Trait 1	$\sigma_{a1}^2$	$r_a \sigma_{a1} \sigma_{a2}$	$2p(1-p)a_1$	$\sigma_{p1}^2$	$r_p \sigma_{p1} \sigma_{p2}$	$2p(1-p)a_1$
Trait 2	$r_a \sigma_{a1} \sigma_{a2}$	$\sigma_{a2}^2$	$2p(1-p)a_2$	$r_p \sigma_{p1} \sigma_{p2}$	$\sigma_{p2}^2$	$2p(1-p)a_2$
QTL	$2p(1-p)a_1$	$2p(1-p)a_2$	$2p(1-p)$	$2p(1-p)a_1$	$2p(1-p)a_2$	$2p(1-p)$

<sup>a</sup> Explanation of symbols is given in the text

Maximum genetic response will be obtained when all traits with genetic correlations with the traits in the aggregate genotype are included in the index. If the  $i^{\text{th}}$  trait of the aggregate genotype is deleted from the index, the variance of the selection index will be reduced by  $b_i^2/w_i$ , where  $b_i$  is the index coefficient for the  $i^{\text{th}}$  trait (in this case  $b_i=b_{i0}$ ), and  $w_i$  is the diagonal element for the  $i^{\text{th}}$  trait in  $P^{-1}$  (Cunningham 1969). The relative selection efficiency of the index, including the QTL information, RSE, is then computed as follows,

$$\text{RSE} = \left[ \frac{\mathbf{b}'_i \mathbf{P} \mathbf{b}_i}{\mathbf{b}'_i \mathbf{P} \mathbf{b}_i - b_i^2 / w_i} \right]^{1/2} \quad (4)$$

RSE was computed with  $r_a$  and  $r_p$  varied from  $-0.8$  to  $0.8$ ,  $f$  was varied from  $0$  to  $0.7$ ,  $h^2$  of the two traits was varied from  $0.05$  to  $1$ . Values for the other parameters were held constant.

#### Simulation of ten QTL accounting for all the genetic variance

Previous studies have used various distributions to simulate QTL, including the geometric (Lande and Thompson 1990) and gamma (Zhang and Smith 1992) distributions. Hoeschele and VanRaden (1993) used the exponential distribution under the assumption that the frequency of loci decreases as a function of gene effect over the entire range of effects. Since it will generally not be possible to detect loci of very small effect, they suggested setting a lower bound to the distribution. The following protocol was used to obtain a similar situation and at the same time to account for all of the genetic variance associated with the two traits by ten diallelic and uncorrelated QTL.

The additive genetic variance of QTL  $j$  on trait  $i$ ,  $\sigma_{aij}^2$ , was simulated by sampling from a chi-squared distribution with ten degrees of freedom. Chi-squared deviates were multiplied by  $\sigma_{ai}^2/100$ , where  $\sigma_{ai}^2$  is the additive genetic variance for trait  $i$ , to account for the facts that the mean of the chi-squared distribution with ten degrees of freedom is approximately equal to 10 and that the sum of the variance for the ten loci should equal  $\sigma_{ai}^2$ . As in the case of a single known QTL, the phenotypic variances and standard deviations were assumed equal to unity for both traits. Thus,  $\sigma_{ai}^2 = h_i^2$ , where  $h_i^2$  is the heritability for trait  $i$ .

As with the previous simulation, the population was assumed to be diploid, and each QTL had only two alleles that acted codominantly. Thus, the QTL effects were either  $a_{ij}$  or  $-a_{ij}$  for homozygotes and 0 for heterozygote, where  $a_{ij}$  is the substitution effect for locus  $j$  on trait  $i$ . Following Hoeschele and VanRaden (1993), the initial allele frequencies for QTL  $j$ ,  $p_j$ , and  $1-p_j$  were derived by sampling from a uniform distribution.  $a_{ij}$  was then derived from the following equation:

$$\sigma_{aij}^2 = 2p_j(1-p_j)a_{ij}^2 \quad (5)$$

In order to avoid immediate fixation of rare alleles,  $p_j > 0.95$  or  $< 0.05$  were set to  $0.95$  and  $0.05$ , respectively. The relative large influence of very high and low allele frequencies on the substitution effect of the QTL was also curtailed. As shown by Hoeschele and VanRaden (1993) a dependency between  $p_j$  and  $a_{ij}$  is unavoidable if total genetic variance is considered to be fixed. The empirical distribution of  $a_{ij}$  obtained from a sample of 5000 with  $h^2=0.2$  is given in Fig. 1. The mode of the distribution is approximately 0.2. Even though the sample was quite large, this is still an empirical distribution based on a computer-generated sample. Therefore, the curve is not completely smooth. This distribution differs from that of Hoeschele and VanRaden (1993) chiefly in that there is a positive probability of detecting QTL with effects less than the mode, this is similar to the empirical results of Weller et al. (1988).

For each locus, positive effects on both traits were simulated a priori for the same allele. As explained above, since codominance is assumed, the genetic correlation for each QTL was originally equal to unity. An overall genetic correlation of  $-0.4$  was simulated by multiplying the effects of the first seven loci on the second trait by  $-1$ . Since QTL effects were simulated individually at random, the sequence of the loci with negative or positive genetic correlations is immaterial. The expected genetic variance for trait  $i$  is  $10 \sigma_{ai}^2$ , where  $\sigma_{ai}^2$  is the mean QTL variance. The expected genetic covariance is:  $3 \sigma_{a1} \sigma_{a2} - 7 \sigma_{a1} \sigma_{a2} = -4 \sigma_{a1} \sigma_{a2}$ , where  $\sigma_{a1}$  and  $\sigma_{a2}$  are the mean

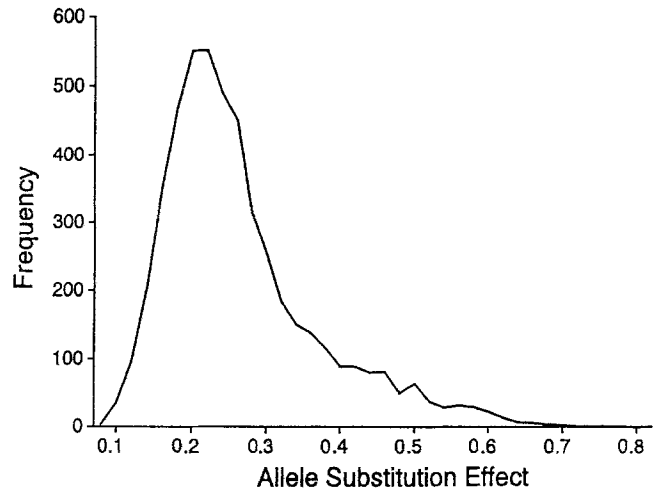


Fig. 1 The empirical distribution of QTL substitution effects in phenotypic standard deviation units obtained from a sample of 5000 with heritability of 0.2

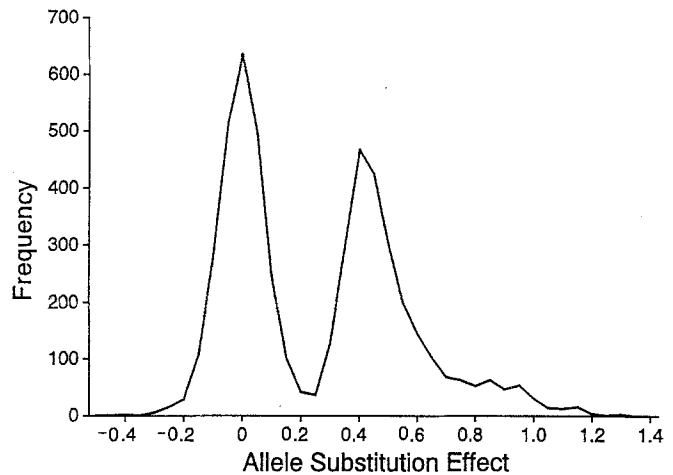


Fig. 2 The empirical distribution of the sum of the effects of allele distribution on both traits obtained from a sample of 5000 with  $h^2=0.2$  for both traits and a genetic correlation of 0

QTL standard deviations for traits 1 and 2, respectively. Thus, the expected genetic correlation is  $-0.4$ . Similarly expected genetic correlations of  $0.4$  or  $0.0$  were simulated by multiplying the effects on the second trait of the first three or five loci by  $-1$ . The empirical distribution of  $a_{1j}+a_{2j}$  obtained from a sample of 5000 with  $h^2=0.2$  for both traits and a genetic correlation of 0 is given in Fig. 2. This distribution is bimodal with one mode near zero for loci with opposite effects on both traits and a second mode at 0.4 for loci with effects in the same direction. Overall this distribution is less skewed than the distributions for the individual alleles.

Genotypes of individuals in the base population were simulated by selecting two random numbers for each locus from a uniform distribution over the range of  $(0, 1)$ . For each of the two random numbers generated for each locus of each individual the allele with a positive effect on the first trait was selected if the random value was  $< p_j$ . Otherwise, the alternate allele was selected. The genetic value of trait  $i$  for the  $m^{\text{th}}$  individual,  $G_{im}$ , was then computed as follows:

$$G_{im} = \sum_{j=1}^{10} (a_{ijk} + a_{ijl}), \quad (6)$$

where  $a_{ijk}$  and  $a_{ijl}$  are the genetic effects on trait  $i$  of the two alleles  $k$  and  $l$  at the  $j^{\text{th}}$  locus. The economic aggregate genotype for indi-

**Table 2** Parameters, symbols (in parentheses), and values used in the simulation with all QTL assumed known

Parameter	Values		
Additive genetic variance ( $\sigma_{ai}^2$ ) <sup>a</sup>	0.05	0.20	0.40
Phenotypic variance ( $\sigma_p^2$ )	1		
Economical value ( $v_i$ )	1		
Genetic correlation ( $r_a$ )	-0.40	0	0.40
Environmental correlation ( $r_e$ )	-0.40	0	0.40
Initial frequency of QTL alleles ( $p_j$ )	0.05–0.95		

<sup>a</sup> Since  $\sigma_p^2=1$ ,  $\sigma_{ai}^2=h_i^2$ , the heritability for trait  $i$

vidual  $m$ ,  $H_m$ , was then computed as follows:

$$H_m = G_{1m} v_1 + G_{2m} v_2, \quad (7)$$

where  $v_1$  and  $v_2$  are the economic values for traits 1 and 2. The economic values for the two traits were set equal in all simulations.

The environmental value of trait  $i$  for the  $m^{\text{th}}$  individual was computed as  $E_{cm} + E_{ism}$ , where  $E_{cm}$  is the environmental effect common to both traits for the  $m^{\text{th}}$  individual, and  $E_{ism}$  is environmental effect specific to trait  $i$  for the  $m^{\text{th}}$  individual.  $E_{cm}$  and  $E_{ism}$  were simulated by sampling from normal distributions with means of zero, and variances of  $E_{cm}^2$  and  $1-h_i^2-E_{cm}^2$ , respectively, where  $E_{cm}^2$  is the common environmental variance, and  $h_i^2$  is the heritability for trait  $i$ . The phenotypic value of trait  $i$  for the  $m^{\text{th}}$  individual,  $X_{im}$  is then computed as follows:

$$X_{im} = G_{im} + E_{cm} + E_{ism} \quad (8)$$

The phenotypic variance for each trait was set to unity. The initial phenotypic covariance between the traits was equal to the genetic covariance computed above plus  $E_{cm}^2$ .

#### Simulation of population and selection program

One thousand individuals were simulated for the base population as described above. Animals were randomly assigned as males or females. Fifty males and 200 females were selected for breeding the next generation. In order to reduce inbreeding, mating was disassortive with respect to the selection objective. Each male was mated to 4 females, with the males with the highest index values mated to the females with the lowest index. One thousand individuals were simulated for the next generation. The genotype of each progeny was simulated by selecting at random one allele from each parent for each loci. The environmental effect for each progeny was simulated as described previously.

Selection on  $H_m$ , denoted "direct selection of QTL" (DSQ), was compared to selection on the optimum linear selection index,  $I_m$ , based on each individual's phenotypic values for the two traits, "trait-based selection index" (TSI), computed as follows:

$$I_m = b_1 X_{1m} + b_2 X_{2m} \quad (9)$$

where  $b_1$  and  $b_2$  are the index coefficient for traits 1 and 2, respectively. Index coefficients were computed with Eq. 3 using the two-trait phenotypic and genetic variance matrices. After every generation, genetic and phenotypic variances and covariances were recomputed using the genetic and phenotypic values for the individuals simulated in that generation. These values were then used to recompute the index coefficients derived from Eq. 3.

DSQ was continued for 10 generations and TSI for 15 generations. The individual alleles were followed in both selection methods. The mean breeding value in each generation was calculated for both DSQ and TSI. The genetic response per generation was computed as the difference between the mean breeding values of the current and previous generations. The gene frequencies of the ten QTL were monitored in order to detect allele fixation. The maximum obtainable genetic response in economic units was also calculated for each simulation.

The selection procedure was repeated 15 times for each parameter set. Environmental and genetic correlations of -0.4, 0, and 0.4

**Table 3** Efficiency of selection with a single known QTL for a two-trait breeding objective, relative to index selection on the phenotypes, as a function of the proportion of the genetic variance due to the known QTL. Heritabilities for the traits were 0.45 and 0.20. The QTL has two alleles with initial frequencies of 0.5. Efficiencies are given for genetic correlations,  $r_a$ , of -0.40 and 0.40. Phenotypic correlations were set equal to the genetic correlations

Proportion	Correlations <sup>a</sup>	
	-0.40	0.40
0.00	1.000	1.000
0.10	1.163	1.070
0.20	1.342	1.157
0.30	1.546	1.240
0.40	–	1.327
0.50	–	1.419
0.60	–	1.516
0.70	–	1.621

<sup>a</sup> Relative efficiency is not listed for parameter combinations outside the parameter space

**Table 4** Comparison of selection efficiencies for a single trait and a two-trait selection objective, as a function of the heritabilities, when a single QTL was known. The QTL has two alleles with initial frequencies of 0.5. The proportion of the additive genetic variance due to the QTL was set at 0.10 or 0.30. For two-trait selection, the genetic and phenotypic correlations were -0.40, and the heritability of the traits were equal

Heritability	Proportion=0.10		Proportion=0.30	
	Two traits	One trait	Two traits	One trait
0.05	2.668	1.678	4.472	2.549
0.10	1.948	1.348	3.162	1.872
0.20	1.464	1.152	2.236	1.422
0.45	1.124	1.035	1.491	1.110
0.80	1.011	1.003	1.118	1.010

and heritabilities of 0.05, 0.2, and 0.4 were simulated. The parameter values used are given in Table 2. In order to compare the results of this study to previous studies, selection on a single trait was also simulated for both a single known QTL and all known QTL. In the single trait simulations heritability was varied from 0.05 to 0.8 for a single known QTL and from 0.05 to 0.4 for the simulations with all QTL assumed known.

## Results

### Estimation of relative selection frequency (RSE) for a single known QTL

RSE as a function of  $f$  is given in Table 3 for  $r_a=-0.4$  and 0.4 and heritabilities of 0.45 and 0.2. In all cases, it was assumed that  $r_p=r_a$ . As expected, RSE increases with increase of  $f$ . Since a genetic correlation of unity is assumed for the QTL, the maximum possible  $f$  under the restrictions given are 0.3 for  $r_a=-0.4$  and 0.7 for  $r_a=0.4$ . At greater values than these limits, the single identified QTL would re-

**Table 5** The effect of the genetic and phenotypic correlations between the two traits on the relative selection efficiency of indices including information on a single QTL, as compared to the phenotypic selection index. Heritabilities were 0.45 and 0.20. The QTL has two alleles with initial frequencies of 0.5. The proportion of the additive genetic variance due to the QTL was set at 0.10 or 0.30

$r_a=r_p$	Proportion of the genetic variance	
	0.10	0.30 <sup>a</sup>
-0.80	1.281	—
-0.60	1.209	—
-0.40	1.163	1.546
-0.20	1.133	1.424
0.00	1.111	1.346
0.20	1.093	1.288
0.40	1.077	1.240
0.60	1.062	1.193
0.80	1.040	1.127

<sup>a</sup> Relative efficiency is not listed for parameter combinations outside the parameter space

sult in a genetic correlation greater than the assumed values. For the values tested, the gain in selection efficiency due to DSQ with  $r_a=-0.4$  was more than twice the gain with  $r_a=0.4$ . For  $f=0.1$ ,  $h_1^2=0.45$  and  $h_2^2=0.20$ , a selection index including a single known QTL accounting for only 0.045 of the total variance for trait 1 increases RSE by 16% if  $r_a=-0.4$ .

Comparison of RSE for a single trait and a two-trait selection objective as a function of heritability are given in Table 4. The proportion of the additive genetic variance due to the QTL was set at 0.10 or 0.30. For two-trait selection, the genetic and phenotypic correlations were  $-0.40$ , and the heritability of the traits was equal. Previous studies have shown that the RSE of DSQ increases as a function of the proportion of the additive genetic variance associated with the QTL (Lande and Thompson 1990; Smith and Simpson 1986; Stam 1986). This also occurred with two genetically correlated traits. The increase in selection efficiency was generally three times greater for the two-trait selection objective, than for the single trait objective.

The effect of the genetic and phenotypic correlation between the two traits on RSE is given in Table 5. Heritabilities for the two traits were 0.45 and 0.20. RSE was computed for  $f=0.1$  and  $f=0.3$ . The genetic and phenotypic correlations were assumed to be equal for all simulations. RSE decreased with increase in the genetic correlation. At  $r_a=0.8$ , RSE for the two-trait objective is only slightly greater than for a single trait with  $h^2=0.45$ . However, with  $f=0.1$ , the gain in selection efficiency increases sevenfold from  $r_a=0.8$  to  $r_a=-0.8$ . For  $f=0.3$ , there is a twofold gain in RSE from  $r_a=0.4$  to  $r_a=-0.4$ . As explained above,  $r_a<-0.4$  is outside the parameter space for  $f>0.3$ . Values for RSE for these combinations are therefore not given.

RSE with a single known QTL for a two-trait breeding objective, relative to index selection on the phenotypes, as a function of heritabilities of the two traits is given in Table 6. The genetic and phenotypic correlations between the

**Table 6** Efficiency of selection with a single known QTL for a two-trait breeding objective, relative to index selection on the phenotypes, as a function of heritabilities of the two traits. The QTL has two alleles with initial frequencies of 0.5. The genetic and phenotypic correlations between the traits were  $-0.40$ . The proportion of the additive genetic variance due to the QTL was set at 0.10 or 0.30

Proportion	$h_2^2$	$h_1^2$			
		0.05	0.20	0.45	0.80
0.1	0.05	2.668	1.425	1.087	1.008
	0.10	2.023	1.523	1.124	1.015
	0.20	1.425	1.464	1.163	1.027
	0.30	1.214	1.320	1.163	1.033
	0.45	1.087	1.163	1.124	1.033
	0.60	1.036	1.080	1.078	1.025
	0.80	1.008	1.027	1.033	1.011
	1.00	1.000	1.006	1.009	1.002
0.3	0.05	4.472	2.089	1.285	1.034
	0.10	3.281	2.326	1.405	1.066
	0.20	2.089	2.236	1.547	1.123
	0.30	1.612	1.925	1.575	1.164
	0.45	1.285	1.546	1.491	1.189
	0.60	1.130	1.306	1.356	1.175
	0.80	1.034	1.123	1.189	1.118
	1.00	1.001	1.030	1.069	1.044

traits is  $-0.40$ .  $f$  was set at 0.10 and 0.30. Similar to single-trait simulations (Lande and Thompson 1990; Smith and Simpson 1986; Stam 1986), RSE is highest when heritabilities are low for both traits. Contrary to the results for single-trait simulations, RSE is still relatively high for two traits with moderate heritabilities (0.2 to 0.5), provided that they are negatively correlated. Since  $f$  is computed relative to the genetic variances of the two traits, the effect of the QTL relative to the phenotypic variance increases as a function of the heritabilities. Nevertheless, for both  $f$  values, RSE is maximum when both heritabilities are 0.05. As the heritability of one trait increases, the heritability of the other trait at which RSE is maximum also increases, but not symmetrically. For example, with  $f=0.1$ , and  $h_1^2=0.2$ , maximum RSE as a function of  $h_2^2$  is obtained at 0.1.

#### Comparison of response to selection on ten QTL accounting for all of the genetic variance and trait-based selection

Response for 15 generations of TSI and 10 generations of DSQ, computed as the mean genetic level of the population in economic units, are given in Table 7. Genetic and phenotypic correlations were assumed to be equal for all simulations. The heritabilities of the traits were 0.40 and 0.20, and a monetary value of one was assumed for each unit of the phenotypic standard deviation. Aggregate genotype values are the means of 15 simulations. Responses to the first generation of TSI were close to the values expected by selection index theory (Falconer 1989). As expected, genetic gains increased with increase in the genetic correlations. Total genetic response was always greater by

**Table 7** Response for 15 generations of selection, computed as the mean genetic level of the population in economic units, for trait-based selection index (TSI) and direct selection on quantitative trait loci (DSQ) when all the QTL are known. Genetic and phenotypic correlations were assumed equal for all simulations. The heritabilities of the traits were 0.40 and 0.20, and a monetary value of one was assumed for each unit of the genetic standard deviations. Aggregate genotype values are the means of 15 simulations

Generation	$r_a=r_p=-0.40$		$r_a=r_p=0.00$		$r_a=r_p=0.40$	
	TSI	DSQ	TSI	DSQ	TSI	DSQ
1	0.00	0.00	0.00	0.00	0.00	0.00
2	0.48	0.83	0.56	0.98	0.68	1.21
3	0.90	1.43	1.02	1.75	1.28	2.07
4	1.30	1.90	1.52	2.42	1.87	2.90
5	1.65	2.20	2.01	2.98	2.38	3.64
6	1.90	2.36	2.41	3.33	2.91	4.07
7	2.08	2.44	2.74	3.55	3.33	4.31
8	2.20	2.50	3.01	3.65	3.66	4.47
9	2.27	2.52	3.19	3.70	3.91	4.54
10	2.34	2.53	3.32	3.74	4.08	4.55
11	2.39	-	3.43	-	4.22	-
12	2.42	-	3.51	-	4.33	-
13	2.45	-	3.58	-	4.39	-
14	2.47	-	3.63	-	4.43	-
15	2.48	-	3.66	-	4.46	-

DSQ. Most of the genetic response was obtained in the first generations, especially for DSQ. By generation 15 cumulative response by TSI was nearly equal to that obtained by DSQ after 10 generations.

In most cases, the genetic variances increased during the first few generations of TSI but not DSQ. Under the assumed model, two alleles at each locus and codominance, the genetic variance is greatest when frequencies of both alleles are 0.5. Thus, selection for rare alleles increases variance, while selection for alleles with high frequency reduces variance. Due to the dependency in the model between substitution effect and allele frequency, most loci with large effects will have extreme allele frequencies. The genetic variances of both traits decreased after generation 2–4 by both selection methods. The reduction in the variances was larger with DSQ than with TSI. In most cases, the genetic correlation between the traits became more negative during selection, although in some simulations the genetic correlation increased.

The effect of the genetic and phenotypic correlations on the efficiency of DSQ, relative to TSI is given in Table 8. Heritabilities for the traits were 0.40 and 0.20. Selection efficiencies were derived by dividing the cumulative genetic response by DSQ at each generation by the cumulative genetic response obtained by TSI. RSE decreased at each generation and was close to 1.1 by generation 10 for all three sets of correlations. RSE was slightly lower with negative correlations and nearly equal for the other two cases.

Different results were obtained when the phenotypic and genetic correlations were not equal. The effect of the environmental correlation on the RSE of DSQ with a constant genetic correlation is given in Table 9. The genetic

**Table 8** The effect of equal genetic and phenotypic correlations on the efficiency of direct selection on quantitative trait loci with all QTL known for a two-trait selection objective, relative to trait-based selection. Heritabilities for the traits were 0.40 and 0.20. Results are the means of 15 replicates

Generation	$r_a=r_p=-0.40$	$r_a=r_p=0.00$	$r_a=r_p=0.40$
1	-	-	-
2	1.739	1.754	1.762
3	1.588	1.722	1.618
4	1.466	1.590	1.552
5	1.332	1.487	1.533
6	1.241	1.383	1.399
7	1.173	1.292	1.296
8	1.137	1.215	1.223
9	1.107	1.161	1.161
10	1.078	1.125	1.115

**Table 9** The effect of the environmental correlation on the efficiency of direct selection on quantitative trait loci with all QTL known for a two-trait selection objective, relative to trait-based selection. The genetic correlation was  $-0.4$  for all simulations. Heritabilities for the traits were 0.40 and 0.20. Results are the means of 15 replicates

Generation	Environmental correlations		
	$-0.4$	0	0.4
1	-	-	-
2	1.739	1.960	2.275
3	1.588	1.878	2.098
4	1.466	1.683	1.935
5	1.332	1.523	1.695
6	1.241	1.404	1.520
7	1.173	1.315	1.413
8	1.137	1.238	1.322
9	1.107	1.195	1.242
10	1.078	1.147	1.179

correlation was  $-0.4$  for all simulations. RSE is greatest when the phenotypic and genetic correlations are in opposite directions. Under these circumstances TSI is least efficient. As in the previous table, RSE decreases at each generation, but with  $r_e=0.4$ , RSE=1.18 even after 10 generations.

Cumulative genetic response with DSQ and maximum obtainable genetic response, in economic units, for different genetic correlations are given in Table 10. The maximum obtainable response is the difference between the average genetic mean of the base population and the genetic mean of the most economically favorable genotype. The phenotypic correlations were set equal to the genetic correlations, and the heritability of the two traits was 0.40 and 0.20. Cumulative responses were less than the maximum obtainable genetic response for all simulations because in most simulations the less favorable allele reached fixation for at least one of the loci. Most of these were loci in which the allele effects on the two traits were in opposite directions.

The proportion of loci reaching fixation during the first 15 generations of TSI and 10 generations of DSQ are given

**Table 10** Cumulative genetic response with direct selection on quantitative trait loci and maximum obtainable genetic response, in economic units, for different genetic correlations. The phenotypic correlations were set equal to the genetic correlations, and heritabilities of the two traits were 0.40 and 0.20. Results are the means of 15 replicates

Genetic correlation	Cumulative genetic response	Maximum obtainable genetic response	Percent of maximum obtainable response reached
-0.40	2.53	2.71	93.4
0.00	3.74	3.84	97.4
0.40	4.55	4.88	93.2

**Table 11** Proportion of loci reaching fixation during the first 15 generations of trait-based selection index (TSI), and direct selection on quantitative trait loci (DSQ) when all QTL were known. The heritabilities of the two traits were 0.40 and 0.20. Results are based on 15 replicates

Generation	$r_a=r_p=-0.40$		$r_a=r_p=0.00$		$r_a=r_p=0.40$	
	TSI	DSQ	TSI	DSQ	TSI	DSQ
1	0.00	0.00	0.00	0.00	0.00	0.00
2	0.00	0.00	0.00	0.01	0.00	0.01
3	0.00	0.07	0.00	0.06	0.01	0.07
4	0.06	0.23	0.03	0.13	0.03	0.15
5	0.07	0.37	0.05	0.27	0.11	0.27
6	0.11	0.51	0.09	0.47	0.14	0.49
7	0.14	0.68	0.12	0.67	0.17	0.71
8	0.19	0.80	0.17	0.78	0.19	0.83
9	0.27	0.91	0.22	0.87	0.20	0.95
10	0.32	0.95	0.25	0.91	0.24	0.98
11	0.37	—	0.36	—	0.31	—
12	0.46	—	0.40	—	0.38	—
13	0.51	—	0.42	—	0.43	—
14	0.57	—	0.47	—	0.51	—
15	0.60	—	0.54	—	0.59	—

**Table 12** The effect of heritability on the efficiency of direct selection on quantitative trait loci with all QTL known for a two-trait or single trait selection objective relative to trait-based selection. The genetic correlation was -0.4, the environmental correlation was 0, and the heritability of the two traits was equal for the two-trait simulations. Results are the means of 10 replicates

Generation	Two traits			Single trait		
	$h^2=0.05$	$h^2=0.20$	$h^2=0.40$	$h^2=0.05$	$h^2=0.20$	$h^2=0.40$
1	—	—	—	—	—	—
2	5.10	2.55	1.95	4.10	2.16	1.55
3	4.50	2.40	1.82	3.84	2.03	1.57
4	4.15	2.08	1.67	3.52	1.98	1.50
5	3.58	1.87	1.46	3.27	1.91	1.47
6	3.14	1.63	1.32	3.08	1.78	1.41
7	2.71	1.45	1.23	2.85	1.62	1.37
8	2.42	1.36	1.18	2.71	1.48	1.30
9	2.21	1.29	1.15	2.50	1.35	1.23
10	2.02	1.25	1.13	2.27	1.24	1.16

in Table 11. The heritability of the two traits was 0.40 and 0.20. Genetic and phenotypic correlations were set equal at either -0.4, 0 or 0.4. Nearly complete fixation was obtained for DSQ, but for TSI no more than 0.6 of the loci reached fixation even after 15 generations. As expected, loci for which allele effects on both traits were in the same direction reached fixation earlier. For both DSQ and TSI, fixation was slowest with zero correlations.

The effect of heritability on the efficiency of DSQ with all QTL known for a two-trait or single-trait selection objective, relative to TSI, is given in Table 12. The genetic correlation was -0.4 for the two-trait simulations, the environmental correlation was zero, and heritability of the two traits were equal. In the early generations, RSE was higher for two-trait selection, but at later generations the differences were minimal. The difference in efficiency between single and two-trait selection was greater for low heritability traits.

## Discussion

The current study assumed that QTL genotype was known without error. Although segregating genetic markers can be used to derive unbiased estimates of linked QTL effects (Weller 1986; Fernando and Grossman 1989), the estimates will also have an estimation error variance. Although bracketing QTLs with genetic markers does improve the accuracy of the estimate, some error will remain even with a dense genetic marker map. Furthermore, the current optimum method for genetic evaluation is the Best Linear Unbiased Prediction, which includes information from all known relatives (Wiggans et al. 1988). Inclusion of information from relatives can have a significant impact for low heritability traits. Thus, in practice trait-based selection is slightly more efficient than the scheme described, while direct selection on QTL can only be approximated by MAS with a dense map of genetic markers. Thus, the results presented should be considered upper limits for the gains possible with MAS.

The results presented in this study for single-trait selection were not significantly different from those obtained from previous studies (Lande and Thompson 1990; Smith and Webb 1981; Smith and Simpson 1986). In general, previous results have shown that for high heritability traits, the expected gain by MAS is small. Expected gains are greater if MAS is used to increase selection intensity and decrease generation interval (Kashi et al. 1986; Kashi et al. 1990; Meuwissen and Van Arendonk 1992) or to select individuals without records for the quantitative trait (Stam 1986). For low heritability traits, expected gains are relatively higher, but the likelihood of identifying QTL for these traits is also less. A markedly different situation was found for two-trait selection. Even with relatively high heritabilities, the RSE of DSQ as compared to TSI was greater than 1.1 for most of the cases studied. This is equivalent to a 10% increase in genetic gain per generation and compares very favorably with other techniques that have been

suggested to increase rates of genetic gain, such as multiply ovulation and embryo transplant based nucleus herd breeding schemes, sexed semen, and more complex methods of genetic evaluation (Nicholas and Smith 1983; Van Vleck 1981; Wiggans et al. 1988).

Similar to single-trait selection, RSE of DSQ with two-trait selection is greater for low heritability traits and when the genetic and environmental correlations are in opposite directions. In this case, the genetic and phenotypic correlations may also be in opposite directions, and selection on phenotype will not be very efficient. The effects of heritability and the correlations on DSQ with all QTL identified were generally similar to the results obtained with a single identified QTL. In the current study it was assumed that all loci had effects on both traits and that all effects were codominant. This led to the result that the genetic correlation for a specific QTL was either 1 or -1. A more realistic situation may be that some loci will only have significant effects on a single trait or that there will be different dominance relationships for the two loci. In this case, genetic correlations will not be complete.

Most previous studies considered only the result of a single generation of DSQ. For example, for single-trait selection, in which the QTL accounting for all of the additive genetic variance were known, Lande and Thompson (1990) found selection efficiencies similar to the efficiencies of generation 2 in Table 12. This study considered 15 generations of TSI and 10 generations of DSQ with all QTLs known. During the course of a breeding program, allele frequencies change, which affects the variance due to the known QTL. The rate of loci fixation, especially for alleles with favorable effects on both traits, was rapid. Thus, the gain obtained by DSQ, as compared to TSI, decreases from generation to generation. If selection is continued, TSI "catches up" with DSQ, although the lag is 1 generation at the beginning and increases to 7 generations. This is, of course, a highly significant difference, especially for large farm animals.

Zhang and Smith (1992) considered the result of several generations of MAS, but only for single-trait selection, and assumed incomplete linkage between the QTL and the genetic markers. They found that under their circumstances selection index was more efficient than MAS alone. Clearly incomplete linkage between the markers and QTL reduces the efficiency of MAS.

The rapid rate of allele fixation corresponds to the results of Weller and Soller (1981) that mass selection on several identified loci is remarkably efficient. Although only a single generation of selection was considered for cases in which only a single QTL was known, the multilocus results indicate that if only a single QTL is identified, a locus of the type considered would rapidly reach fixation in a finite population. Similar results were found by Saefuddin and Gibson (1991) who considered several generations of selection for a single trait with a single known QTL and background polygenic variation. Although response was greater in the early generations for an index including direct selection on the QTL, they found that response in the later generations was greater with phenotypic

selection. However, they note that their index was not optimal because it did not account for covariances between the QTL and the polygenic variation.

With ten identified QTLs, random initial allele frequency, and some loci with effects in opposing directions on the two traits, the less favorable allele reached fixation in a few cases. It is possible that a genotype closer to the optimum at fixation could be obtained by selecting for individuals with the maximum number of loci with the more desirable genotype, rather than on the aggregate genotype. This would of course result in less economic progress in the early generations.

Although disassortative mating was employed, it is likely that very similar results would have been obtained by random mating among the selected individuals. With a population of this size, the increase in inbreeding per generation with random mating would be minimal.

RSE for DSQ was significantly higher with a negative genetic and positive phenotypic correlation. Although this situation is not common in practice, there are examples for traits of economic importance, such as milk production and somatic cell concentration (Weller et al. 1992).

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