COMPARISON OF OPTIMAL SELECTION STATEGIES FOR FINITE LOCUS MODELS INVOLVING MARKED QUANTITATIVE TRAIT LOCI

J. H. J. van der Werf

Animal Science, University of New England, Armidale, NSW 2351

SUMMARY

In a simulation study, BLUP selection and genotype assisted selection were compared under two genetic models: the infinitesimal model and a model in which the majority of the genetic variation stemmed from a small number of loci. When phenotypic information is available on both sexes and before first mating, genotypic selection is initially about 9% better than BLUP selection, but this advantage is lost over the longer term. Benefits from genotypic selection were smaller under a finite locus model in this case. When phenotypic information was available on females only, and after the first mating, initial benefit from genotypic selection was 30% for the infinitesimal model and up to 95% for the finite locus model. In general, genotypic selection not only increases selection accuracy, but to some extent also accommodates better variances changes. Postponing fixation of the QTL by using a lower weight for its genotypic value is generally beneficial for medium and long-term profit.

Keywords: Selection, QTL, genetic models

INTRODUCTION

Genetic evaluation systems as well as many selection strategies assume an infinitesimal model. Under this model, the trait(s) involved in selection is (are) subject to the action of very many genes at different loci, each having a relatively small effect, and genetic variance does not significantly change due to changing gene frequencies. Mäki-Tanila and Kennedy (1986) have discussed the problems that could arise when the true genetic model is based on a small number of genes. They found that BLUP was able to estimate genetic changes from short-term selection reasonably well within 3 generations, even when the genetic variance was due to as few as 2 loci. After more generations, alleles became fixed and response was underestimated. The robustness of BLUP selection in realistic breeding programs with possibly a finite number loci has not been well documented. It can be expected that weights for within and between family information would not be optimal when genetic variance changes.

DNA technology now allows a rapid detection of genes or genetic markers linked to genes with large effects. Hence, there are genes with large effects, and we will be able to select based on knowledge of major genotypes. Models used to optimize selection based on such knowledge have mostly assumed the existence of 1 QTL and all other genes are 'infinitesimal' (Gibson 1994; Garrick 1997; Dekkers and van Arendonk 1998). Results indicated that using genotype information at the QTL (genotype selection) increases genetic gain in the early generations, but in the long term mass selection methods that ignored such information would be better. Dekkers and Van Arendonk (1998) found that an optimal selection weight put on QTL-genotype should be smaller initially and increase toward the end of a time horizon considered. The reason is that with selection based on genotypes selection intensity on the 'polygenic component' is sacrificed for the benefit of quickly fixing the major gene. However, the assumption of a 'polygenic' residual genetic component is important here, as it assumes that the 'residual' genetic variance does not decrease due to gene frequency changes. The question is therefore whether findings on optimal QTL selection hold more generally. The purpose of this paper is to test the robustness of optimal QTL selection strategies against genetic models that, rather realistically, deviate from the infinitesimal model.

MATERIALS AND METHODS

Genetic model. Phenotypic records were simulated based on the model y = g + A + e, where g is the accumulated genotypic effect on n loci, A is the additive polygenic effect of a large (but unknown) number of loci each with small effect, and e is an environmental effect. Effects of A and e were drawn from random normal distributions with variance VA and Ve. Offspring of known parents were simulated as _Asire + _Adam+ MS. MS is a term for Mendelian sampling, drawn from a normal distribution with variance (_ - _Fp)VA, where Fp is the average parental inbreeding coefficient. Genotypic effects were simulated as g = Σgi, where gi is the genotypic effect at the ith biallelic locus: gi = -ai , d.ai or ai, and var(g)= Vg. Dominance (d) was either 0 or 0.5. Sampling of genotypes for base parents was based on an initial gene frequency of 0.2, and genotypes from offspring were sampled from parents' genotypes based on Mendelian rules. Total phenotypic variance was set at unity. Therefore, broad sense heritability is H2 = Vg + VA and 'polygenic heritability' is VA. Broad sense heritability (H2) was 0.35; polygenic heritability (h2) was 0.30 in the infinitesimal model and 0.10 in the finite locus model. In the 'infinitesimal' model (INFINITE), all of Vg was explained by 1 major gene (QTL). In a finite locus model (FINITE), the same major gene was present, but the other part of Vg was taken up by 19 loci. The effects of ai were derived from a geometric series, such that initial genetic variance at locus i was Vgi = αi-1 (1-α)Vg, and α describes the flatness of the distribution of genetic effects (Lande and Thompson 1990). An α-value of 0.8 was chosen, leading, for example, to gene substitution effects in the finite locus model at loci 1 (QTL), 2, 5 , 10 and 20 of 0.4, 0.35, 0.19, 0.10 and 0.04 phenotypic SD, respectively.

Selection strategies. Selection was across all (mature) age classes. Hence, generations were overlapping and generation intervals were optimized. Breeding values were obtained with best linear unbiased prediction (BLUP). For both genetic models the assumed heritability was 0.35 for BLUP selection (ignoring knowledge of QTL genotype) and 0.30 for genotypic selection, when QTL genotypes were accounted for in the model. In the latter case, knowledge of the genotype of the gene with largest effect was assumed known without error. An estimate of the jth QTL-genotypic effect ($\hat{g}_{1j}$) was obtained from the solutions for fixed class effect of QTL genotype. The selection criterion was $w.\hat{g}_{1j} + \hat{A}$, where $\hat{A}$ is the BLUP EBV for the aggregate effects of all genetic effects other than at the QTL. The term w was 1 for genotypic (QTL) selection, and 0.5 for weighted genotypic (wQTL) selection. This value was found to give maximum response by trying different values between 0.1 and 1.4 (step size 0.1). For simplicity, weights were kept constant over generations. Two alternatives cases were compared.

Case A: Phenotypes were measured on both sexes before selection, and first progeny could be dropped at the age of 1 year. Fifteen years of selection were simulated with 100 males and 100 females born each year. Each year, 10 males and 50 females were selected.

Case B: Phenotypes were measured on females only and at the age of 3 years, whereas first progeny were dropped at 2 years of age. Twenty-five years of selection were simulated with 100 males and 100 females born each year. Each year, 10 males and 50 females were selected.

Five hundred replicates were simulated for case A and two hundred for case B. Alternative A could refer to meat sheep with selection on commonly measured traits and assuming a somewhat (artificially) high female reproductive rate. Alternative B could refer to dairy cattle. Different alternatives were compared for genetic mean in years 5, 10 and 15, and for the sum of the genetic means over years. The last figure reflects accumulated profit over the whole time period considered, with no discounting.

RESULTS AND DISCUSSION

Relative values for genetic means in different years, and accumulated profit for BLUP and genotype assisted selection are in Table 1 for each of the cases and genetic models considered. In case A, benefits from utilizing QTL-genotypic information were limited. Only during the first years, reasonable effects were found (up to 9.5% higher means under the INFINITE model). BLUP selection resulted in about equal means in the long term. Results agree partly with Gibson (1994) in that initial benefit of genotypic selection was lost over the long term. However, in our case genotypic selection was not surpassed by BLUP selection, and would not be so after year 15 as the QTL was fixed by both selection methods. A difference with previous authors might be explained by the fact that genotypic selection would be more efficient for the 'polygenic' part as the model accommodates the loss of variance due to fixation of the QTL. This argument would not be relevant when comparing genotypic and mass selection. Weighted genotypic selection resulted in additional overall profit over BLUP selection. Essentially, the QTL is fixed at a slower rate with this strategy. An optimal selection strategy fixes the major gene near the end of the period considered. Optimum weights would be higher for shorter evaluation periods.

Table 1 Genetic mean in years 5, 10 and 15, and accumulated profit over years for QTL and weighted QTL selection relative to BLUP selection for two genetic models

Case		Finite Locus Model[1]		Infinite Locus Model[2]	
		QTL/BLUP	wQTL/BLUP	QTL/BLUP	wQTL/BLUP
A	Year 3	1.050	1.046	1.095	1.067
	Year 5	.999	1.020	1.060	1.054
	Year 10	.973	.992	.998	1.021
	Year 15	.979	.992	.990	1.013
	Overall Profit	.983	1.000	1.009	1.025
B	Year 5	1.841	1.876	1.346	1.250
	Year 10	1.442	1.462	1.116	1.091
	Year 15	1.305	1.345	1.081	1.088
	Year 25	1.130	1.168	1.005	1.033
	Overall Profit	1.284	1.305	1.074	1.081

[1] Finite locus model for 'polygenic' component; $V_A = .10$; $V_g = .25$; $V_{qtl} = .05$

[2] Infinitesimal model for polygenic effects: $V_A = .30$; $V_g = V_{qtl} = .05$

BLUP and genotype selection methods resulted in about 25% more genetic gain than mass selection, at all stages under the INFINITE model (not shown). Under the FINITE model, BLUP was about

17% superior to mass selection and this value decreased only slightly (from 19% to 16%) over the period considered. Benefits from genotypic selection were slightly smaller under a finite locus model.

In case B, benefits from genotypic selection were much larger, as phenotypic information was only on females and established after first mating. Under the INFINITE model, benefits were about 30%, similar to those found by Meuwissen and Goddard (1996) for such cases. However, under the FINITE model, benefits from genotypic selection were substantially higher (up to 95%) initially. This was partly because BLUP selection was much less efficient under the finite locus model. BLUP weights were not properly weighted with changing variances due to gene frequency changes. Selection in case B depends more on relatives information than in case A. Genotypic selection would be less affected by variance changes, as the main variance change was at the QTL, which was accommodated in the model. With genotypic selection the QTL was fixed more rapidly under the FINITE model than under the INFINITE model (10 vs 15 years), whereas with BLUP selection gene frequencies in year 25 were 0.89 for the INFINITE model and 0.77 for the FINITE model. Tempering the fixation of the QTL with weighted genotypic selection was advantageous in all cases. The existence of partial dominance (d=0.5) changed little to the overall results.

It is not easy to make more general inferences from this study as only a particular finite locus model was investigated. There is only one infinitesimal model, and there are an infinite number of finite locus models. There is good experimental evidence that genetic variance is due to very many loci (eg. Franklin 1997). Nevertheless, evidence from QTL detection work suggests that there are some genes with large effects. Long-term selection experiments (e..g. Keightley 1998) do not rule out changes of variances as observed in this study under the FINITE model. However, mutation, epistatic effects and linkage between loci all have an effect on genetic variance. Further modeling work with finite locus models with multiple QTL may reveal how important such effects are in selection. This study has shown that one of the advantages of genotype assisted selection may be that changes in variance are better accommodated. This could even be more important when multiple QTL are fitted.

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