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EFFICIENCY OF MARKER ASSISTED SELECTION

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ABSTRACT

Genetic markers can be used in breeding programmes in a variety of ways. Here we emphasize marker assisted introgression in crossbred populations, and marker assisted selection in outbred populations. As marker typing costs reduce, the value of their use in a breeding programme will be dominated by returns rather than their costs. Under certain conditions, markers can replace phenotypic selection in introgression programmes, thus obviating the need for rearing individuals in order to measure their phenotype. Studies in dairy cattle populations indicate that marker assisted selection is economically efficient under realistic assumptions regarding costs and benefits.

INTRODUCTION

Genetic markers can be utilized in artificial selection programmes in a variety of ways: for use in crossbreeding schemes, through marker assisted introgression, for use in outbred populations through marker assisted selection, and for use as tools in quality control (e.g., Visscher et al., 1996a). For the purpose of this study, we concentrate on the use of genetic markers in marker assisted introgression (MAI) programmes in crossbred populations. We will briefly discuss the efficiency of marker assisted selection (MAS) programmes in outbred populations. We will focus on the potential genetic gains of the marker assisted selection programmes, since an assessment of the future cost (in particular the cost of marker genotyping) of such a programme is highly speculative, although likely to be less in future than today.

Marker assisted introgression using backcrossing is an efficient way to incorporate a desired allele from a donor population into a commercial (elite) population (Hospital et al., 1992). Markers are used to keep track of the allele which is introgressed, and to select against the remainder of the donor genome, since it is usually associated with inferior performance for traits which are not associated with the trait gene which is desired. An example from pig breeding is introgression of an allele for increased litter size from the prolific, but slow growing and fat, Meishan breed into commercial (nucleus) dam lines (Rothschild et al., 1994).

After a number of generations of backcrossing to reduce the undesirable effects of the background genotype, the final backcross population is intercrossed to create individuals which are homozygous for the desired allele. Relative to a continuously selected nucleus population, the population with the desired alleles is superior because of those alleles, but inferior with respect to other loci. This is because (i) at each backcross generation fewer individuals can be selected for economic merit because of pre-selection for the allele to be introgressed, (ii) there may be a genetic lag due to using older individuals for breeding in the crossbred population, and (iii) the initial difference between the donor and recipient population in overall economic merit may have been large. These points were clearly described by Gama et al. (1992), who investigated the introgression of a transgene into a nucleus pig population. Gama et al. used markers only to identify the transgene, and did not use markers to select against the 'background genotype', i.e. the remainder of the donor genotype at each generation.

The economic efficiency of the introgression process depends on the genetic value of the final commercial product relative to nucleus populations which are under continued selection, and the extra costs associated with the introgression. The aim of

this study is to provide some insight into the parameters which drive the economic efficiency.

METHODS

The method of Gama et al. (1992), who investigated the genetic lag in a transgene introgression programme for pig nucleus populations, was extended to select on genomic proportion using markers during the backcrossing and intercrossing phase. This was achieved by calculating the amount of variance in genomic composition during backcrossing (Hill, 1993), the proportion of that variance which can be explained by markers (Visscher, 1996), and a genetic model in which the total genetic variance is partitioned into a between breed component which depends on the initial breed difference, and a within breed component.

RESULTS

Genetic lag was calculated for a typical pig nucleus population, using parameters from Gama et al. (1992). In the crossbred population throughout the backcrossing phase the same males were used as in the nucleus and at the same time. Selection intensities were lower in the crossbred population because females (during backcrossing and intercrossing) and males (intercrossing) were preselected on their marker genotype for the locus at which the allele of interest was segregating. A typical set of results when the original breed difference is large is shown in Table 1. Until generation of intercrossing of 5 (i.e. 3 generations of backcrossing, followed by 2 generations of intercrossing), selection on markers to reduce lag during backcrossing and intercrossing is just as good, or even superior, to phenotypic selection. After that, there is little variation in genomic composition left to be utilized by markers. With a large

Table 1: Genetic lag, in number of generations of gain in the nucleus population, for progeny born at generation T+2, when intercrossing to make the desired allele homozygous is performed at generation T. Initial breed difference is 20 SD, h^2 in nucleus is 0.25 and selection on 5 markers per chromosome.

	T									
Selection	1	2	3	4	5	6	7	8	9	10
None	26.1	14.4	8.5	5.6	4.1	3.4	3.0	2.8	2.7	2.7
Mass	24.9	10.6	5.0	2.7	1.8	1.4	1.2	1.2	1.1	1.1
Markers	26.1	10.3	4.6	2.5	1.8	1.8	1.9	2.1	2.2	2.4

number of rounds of backcrossing, both random selection and marker selection will asymptote to a lag of about 2.7 generations of selection.

DISCUSSION

We are clearly at a transitory phase in the exploitation of genomic information in breeding programmes. The current technology provides tools to locate genes and genomic regions that have the potential to be exploited in breeding programmes. However, it is not yet clear what genetic architecture we may expect in each population we study. Likewise it is not clear what technology we will be using in five or ten years time or what its cost will be. Nonetheless, there are currently areas where we can see that markers can already be exploited to advantage.

The lag in polygenic breeding value between a selected nucleus population and a crossbred population with an introgressed allele was investigated assuming a simple genetic model. For the example given, genetic lag was of the order of 1.1 to 2.7 generations of genetic progress in the nucleus population, which implies that the effect of the allele to be introgressed has to be worth at least that amount. This is in

agreement with the results of Gama et al. (1992), who reported the lag for a breeding programme in which a transgene was incorporated into a commercial pig line. Under our assumed genetic model, genetic markers are sufficient to select individuals during the first few backcross generations, so that rearing animals to measure their phenotypes is not required. Two or more markers per chromosome of 100 cM is sufficient to explain the variance in genomic proportion during the backcross and intercross phase. When the initial breed difference is smaller, there is less (or no) advantage in using markers to reduce lag at the early stages of backcrossing.

In outbred populations, it is more difficult to predict genetic gain through marker assisted selection than for introgression programmes. The possible improvement depends on how much segregation there is among QTL, the number of marked QTL, and the size of their individual effects, i.e. it depends more critically on the genetic model. Moreover, because most MAS schemes in outbred populations aim to use marker information by incorporating it into an index to improve selection accuracy, the genetic gains also depend on how well the size of effect and location of the QTL have been measured (Smith and Simpson, 1986; Kennedy et al., 1992). Meuwissen and Van Arendonk (1992) show that by accounting for between 4% and 13% of the within-family genetic variance, genetic gains can be increased by between 8% and 26% in nucleus breeding schemes. Outside nucleus schemes, however, where selection accuracy is already high (e.g. with progeny testing, or if the trait is highly heritable and accurately measured before selection), extra genetic gains are considerably lower (<10%) (Meuwissen and Van Arendonk, 1992; Ruane and Colleau, 1995; Meuwissen and Goddard, 1996).

An alternative, and more exploitative way of improving genetic gains in dairy breeding schemes using marker information is to employ pre-selection (Kashi et al.,

1990; Mackinnon and Georges, 1996). This entails screening the population of young bulls which are destined for progeny testing for inheritance of marked QTL alleles: bulls which have received favourable QTL alleles are retained in the progeny test team, and those without favourable alleles are precluded from the subsequent progeny test. Thus pre-selection raises the genetic value of the progeny testing team before progeny tests are carried out and therefore produces a gain which is additional to conventional genetic gains. Kashi et al. (1990) predict increases in genetic gain of 15% to 30%, while Mackinnon and Georges predict gains of 9% to 24%. The major extra cost of this scheme is the generation of extra young bulls to replace those precluded from progeny test: marker genotyping costs are relatively small compared with overall breeding costs as in marker-BLUP schemes. When any of these schemes are evaluated in economic terms, the financial benefits far outweigh the costs whether evaluated at the national herd level, or at the level of the breeding companies through increased market share of semen sales (Brascamp et al. 1993; Mackinnon and Georges, 1996).

Applying MAS to a synthetic population derived from crossing two breeds, through the utilization of linkage disequilibrium across the whole population (Lande and Thompson, 1990), is likely to give even larger benefits, because the additional genetic gain relative to conventional BLUP selection is about 10 to 20% (Zhang and Smith, 1992).

Finally, it should be mentioned that the benefits of MAS in animal breeding are not always perceived as favourable. Doubt has been raised as to whether genetic gains in the long-term will be increased by MAS because gains due to increasing the frequency of the favourable QTL alleles may compromise the improvement in polygenic value (Gibson, 1994; Ruane and Colleau, 1995). Also, any pleiotropic effects of QTL

on other traits are largely unexplored to date. Thus while the immediate economic benefits can clearly be substantial, only time will tell whether practising MAS is sustainably useful.

In conclusion, the effect of an allele in an introgression programme should be worth between 1 and 3 generations of genetic gain for profit, and MAS is profitable if markers can be found which explain a significant proportion of the genetic variance. However, the optimum usage of the explosion of genomic information that will soon be upon us has yet to be determined and its value estimated. It is almost unnecessary to state that if we have more information and use it well then we will make more progress. We should now be looking to the future and asking 'If we had the complete sequence of all individuals in this population, how would we use it in a breeding programme?'. The challenge remains to evaluate such information and use it wisely.

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