Chapter 19

Examples of MAS in industry programs

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Introduction

Currently there are few examples of breeding programs where marker assisted selection is applied. Some pig and dairy breeding programs claim to actively use marker genotype information for selection purposes. Industries are usually not extremely open about their MAS strategies, as they usually have invested significantly in obtaining marker profiles on their breeding animals, and prefer to keep information for themselves.

In this Chapter I will discuss some results from simulation studies and discuss some implementation issues regarding marker-assisted selection in different breeding program scenario's. The distinction typically made her is between marker for traits that can be measured on animals before selection and measurements on traits that cannot be easily measured on both sexes and before selection. The first exercise is therefore to look at the value added by marker genotype information to predicted levels of genetic improvement. We can distinguish here between purebreeding programs and crossbreeding programs. Realizing that profits from new technologies can sometimes be better reaped when the design of the breeding program is changed, I will also talk about some new suggestions to redesigning breeding programs in case marker data is available. In general, there will be a lot of 'implementation issues, and currently these are still open for discussion. I will discuss some of the issues that have to be considered by breeders that want to apply marker-assisted selection.

Possible gains from marker assisted selection in existing breeding programs

Progeny testing in dairy

The first MAS simulation studies dealt with dairy cattle and single QTL (Kashi et al., 1990; Meuwissen and Van Arendonk, 1992). Marker effects were accurately known within a grandsire family because sons of the grandsire were progeny tested, indicated as granddaughter design (Weller et al., 1990). As an outbred population was considered, there was no LD assumed over families, i.e. marker-phase had to be established within each grandsire family. Established marker associations can be exploited by selecting only grandprogeny of the sons for entrance in the progeny testing team. In spite of this long pedigree, the gains can be reasonable in dairy populations because of \

1) Widespread progeny testing with generally large progeny groups
2) Intensive use of the tope bulls worldwide, such that investments can easier be earned back
3) Relatively large grandsire families (sons of one grandsire) due to widespread use of some bull-sires
4) Trait not measurable on bulls such that selection for entrance into a progeny test is based on pedigree only. MAS helps to distinguish between you bulls within families.

Meuwissen and Van Arendonk (1992) found addition genetic gains from MAS equal to 10-20%, depending on the size of the QTL. Additional gains were mostly explained by additional accuracy because markers explain some of the information, within full-sib families of young bulls. Kashi et al (1990) found gains of 20-30% in the selection pre-selection of young bulls by pre-selecting from a larger group of young bull candidates, therefore increasing selection differentials.

The last study refers to only to gains in one of the selection paths and gains in the commercial cow population are likely lower (Spelman and Garrick, 1997). Last authors used two strategies: 1) selecting young bulls based on EBV, using QTL as well as polygenic information and 2) only testing young bulls with at least a Q-allele. The last strategy quickly increases Q-frequency, but there is less gain for the polygenic component. The second strategy was therefore only competitive for very large QTL effects (1-2 σ_p). Spelman and Garrick found additional gains not higher than 2.5%. They suggested higher gains may be obtained in a breeding nucleus where MOET and OPU techniques are used.

Mackinnon and Georges (1998) suggested an alternative approach for a dairy program with progeny testing: the “bottom-up approach”. Rather than basing genotype selections based on segregation within a grand-sire family, they proposed to marker genotype the tested daughters of the best progeny tested bulls. Based on a marker contrast in this group, they inferred whether the young promising sire was heterozygous, and if so, only his sons carrying the Q-allele would be progeny tested. This procedure would be convenient when a young bull would be from an unmarked grand-sire family, and actually gave more profit than the usual ‘top down’ approach. In an ongoing breeding program, probably a combination of the two schemes would be optimal.

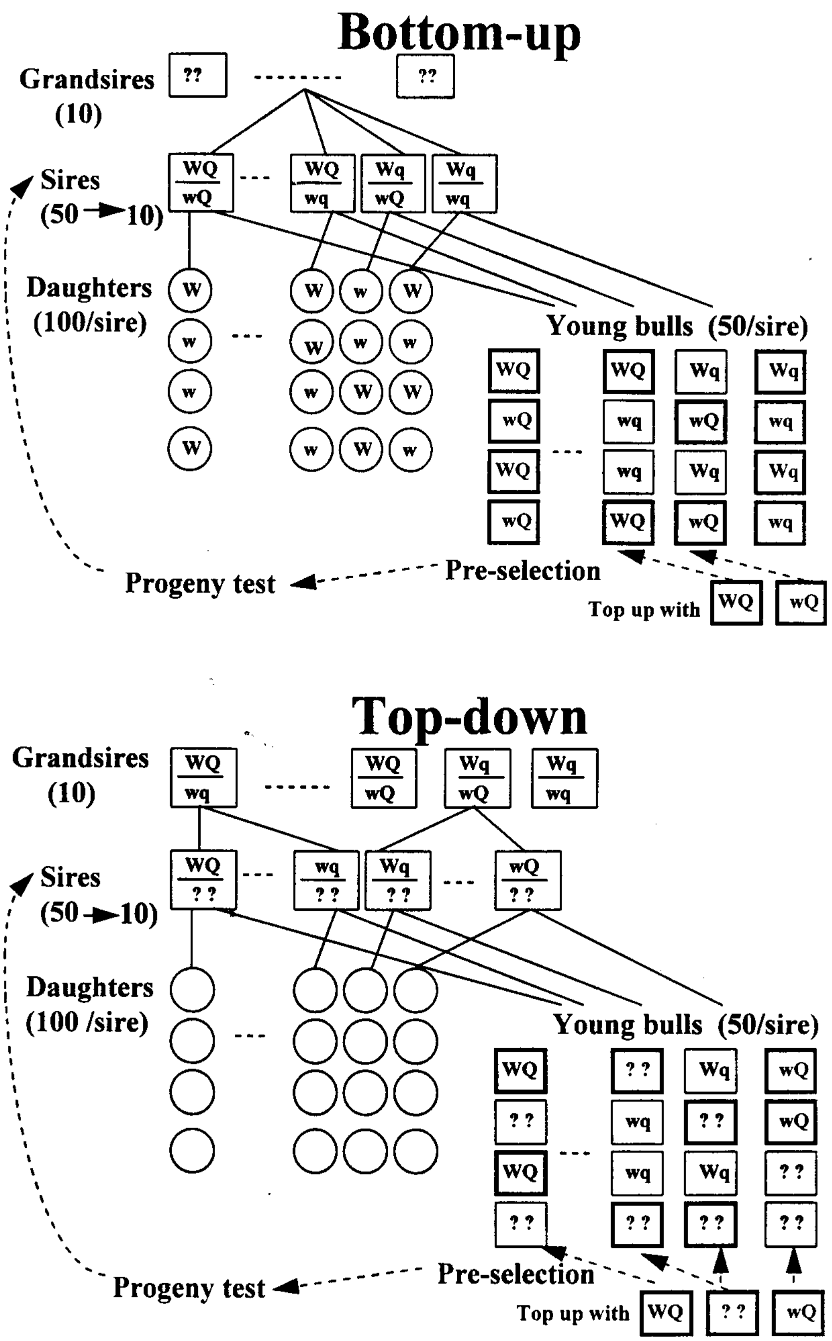

Figure 1. Schematic diagram of the bottom-up and top-down schemes. Sires of young candidate bulls are evaluated for their QTL genotype using marker information from their daughters (bottom-up) or their sires (top-down).

Marker assisted introgression in crossbreeding programs

Visscher and Haley (1995) reviewed application of MAS in pig breeding programs. They particularly discussed implementation of introgressing a desired allele from on otherwise undesirable genotype into a commercial line. Marker brackets should be used with close markers, to minimize the risk of loosing the valuable alleles. Several markers on either side of the QTL are desired as QTL positions may be estimated with some errors and double crossovers may otherwise lead to loosing the desired a QTL-allele.
An example of introgression in pigs breeding is the introduction of litter size genes from the Meishan breed into Western pig breeds. The possible gains from such strategies depend heavily on the gene effect and the frequency in the commercial lines. Introgression is expensive, as it involves several generations of backcrossing to the desired genotype, while keeping a desired haplotype from the introgressed QTL. At the same time markers can be used to select against haplotypes for background genes from the imported line. This generally speeds up the introgression process and reduces the number of generations needed to arrive at the desired genotype (possibly in two generations).

Marker assisted selection can also be used in crosses of lines of about equal economic value. In that case, population wide linkage disequilibrium can be exploited, giving potentially large increases in response (Lande and Thompson, 1990). Genetic evaluation models can have a significant effect on the achieved genetic response, models with random marker(haplotype) effects being superior (Zhang and Smith, 1993), because the approach takes better account of the uncertainty of certain haplotype effects.

Other examples of MAS

Meuwissen and Goddard, 1997 simulated a breeding nucleus and varied the following situations

- Whether selection was before or after trait recording
- The size of the QTL effect
- Moderate and low heritability
- Sex-limited and carcass traits

They also looked at several generations of selection, comparing shoer and medium/long term response.

Table 1: Additional gain from MAS in a nucleus breeding program, depending on the moment of trait recording. QTL explains 33% of genetic variance. (Meuwissen and Goddard, 1996)

	Selection *after* trait recording	Selection *before* trait recording
Heritability = 0.27		
Generation 1	+ 9%	+38%
Generation 5	+ 2.3%	+15%
Heritability = 0.11		
Gen 1	+ 21%	+ 45%
Gen 5	+ 6%	+ 23%

Table 2: Additional gain from MAS in a nucleus breeding program, depending on the size of the QTL effect (heritability = 27%). (Meuwissen and Goddard, 1996)

	Selection *after* trait recording	Selection *before* trait recording
QTL explains 33% of genetic variance		
Generation 1	+9%	+38%
Generation 5	+2.3%	+15%
QTL explains 11% of genetic variance		
Generation 1	+1.3%	+8%
Generation 5	+1.3%	+6%

Beef and sheep

Marker assisted selection is starting to be implemented in nucleus breeding programs. In pyramidal breeding structures the investments can be easier recouped due to the ability to spread additional gains over many descendants. However, it is not only investments that breeders need to consider, but also risk. Selecting on marker information is not fully reliable, due to possible overestimation of QTL effects, error in QTL position, uncertainty about background effects, etc.

Breeders in more flat breeding structures like beef cattle or sheep have less advantages of being able to spread investments over a large group of animals. In addition, such industries are often less well organised, in terms of systematic progeny testing, or even common breeding goals in the major part of the (dispersed) nucleus, and the use of reproductive technology (even AI) is not widespread. However, genetic markers are being found for these species, and some progressive breeders are starting to look at MAS. Typically, marker profiles (TM-Genetic Solutions, Brisbane) should be developed within sire families. Such families should first be marker-phase tested (e.g. a bull with 30-50 progeny), and subsequently, progeny could be selected based on marker information. In beef and sheep, many traits are measured before selection, making MAS less worthwhile. On the other hand, carcase traits are becoming very important in beef and meat sheep. Such traits are typically suited for MAS, as they are expensive to measure, and some specific single locus effects have already been found (and may be more likely). Meuwissen and Goddard found that MAS gave an additional gain of 24% when half of the selection candidates were slaughtered to measure phenotypes on carcasses. When the non-selected half were slaughtered, the marker-phenotype information could be used to select in the next generation, giving 64% additional gain.

Finally

Although the type of additional information that can be obtained from using genetic markers in selection programs is reasonably well understood, it does not yet seem to be totally clear how such information can be optimally utilized. A proper genetic evaluation program can optimally combine information on phenotype and marker genotype, and account for uncertainty. However, such methods are generally not designed to optimize the amount and the place of where information should be collected. Which animals should be genotyped, how often does a marker phase have to be re-estimated, where should the design be changed in order t find a new optimum? These are questions that are not full answered. Soller (1999) uses the concept of ‘creating selection space’. The terms refers to strategies like generating additional young bull candidates such that selection differentials can be increased based on MAS, or reducing generation intervals, such that the possible loss of accuracy can be partly avoided using MAS.

Further studies that include uncertainty about inheritance state, missing marker genotypes, inaccuracy of QTL information, inbreeding, loss of polygenic selection response, etc. should be useful to generate more insight in the issue of optimal use of MAS.

References

Kashi, Y., E. Hallerman and M. Soller. 1990. Marker assisted selection of candidate bulls for progeny testing programs. Anim. Prod. 52:21-31.
Mackinnon, M.J. and M.A.J. Georges. 1998. Marker-assisted preselection of young dairy sires prior to progeny testing. Livest. Prod. Sci. 54:229-250.
Meuwissen, T.H.E. and J.A.M. van Arendonk. 1992. Potential improvements in rate of genetic gain from marker assisted selection in dairy cattle breeding programs. J. Dairy Sci. 75:1651-1659.
Meuwissen, T.H.E. and M.E. Goddard. 1996. The use of marker haplotypes in animal breeding schemes. Genet. Sel. Evol. 28:161-176.
Spelman, R. and D. garrick. 1997. Utilization of marker assisted selection in a commercial dairy cow population. Livest. Prod. Sci. 47:139-147.
Soller, M. and I. Medjugorac, 1999. A successful marriage: making the transition from QTL mapping to marker assisted selection. Dekkers et al.)Eds.) Proc. of the Conf. “From Jay L. Lush to genomics: visions for animal breeding and genetics.
Visscher, P.M. and C.S. Haley.1995. Utilizing genetic markers in pig breeding programmes. Animal Breed. Abstracts. 63:1-8.
Weller, J.I. Y. Kashi and M. Soller. 1990. Power of daughter and granddaughter designs for determining linkage between marker loci and quantitative trait loci in dairy cattle. J. Dairy Sci. 73:2525-2537.
Zhang, W and C. Smith. 19923. Simulation of marker assisted selection utilizing linkage disequilibrium. Theor. Appl. Genet. 86:492-496.