



# The use of genetic markers in beef cattle breeding

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*Abstract.* The paper deals with the use of gene markers in beef cattle by first explaining breeding objectives and estimation of breeding values (EBVs). It then explains more generally the genetic control of economically important traits in the beef industry. The search for genes affecting these traits is based on either the candidate gene approach (i.e. a gene is chosen based on knowledge of the physiology of a trait, then look for variable forms of the gene being associated with differences in the trait. The TG5 gene affecting marbling is an example of this). The other approach is gene mapping, where genes for quantitative traits (i.e. QTL) are detected by linkage to genetic markers. In this case the identity of the gene (i.e. the QTL) is not known and its association with the trait may not hold in populations other than the one where it was described. The paper then describes the use of the two types of marker and considers the best way to exploit the technology to select animals with the highest EBVs for profit in the beef business.

## Introduction

A revolution is occurring in biology, driven by human genome projects. A by-product of this revolution is new knowledge and new tools that are useful in cattle breeding. One such new tool is technology that directly detects differences between animals in DNA sequence (the genetic code).

Selection of the bulls and cows that will be the parents of future generations is the basis for the ongoing genetic improvement of cattle herds and breeds. We can now add to our existing tools for making selection decisions, tests that detect differences between animals in DNA sequence.

This paper will describe how DNA information can be used in the selection of bulls and cows. To do this I need first to discuss breeding objectives and the way in which genes control economically important traits such as marbling. I will concentrate on the principles behind the use of DNA tests in general while Bill Barendse in his paper will describe one specific gene test.

## Breeding Objective

I will assume that the objective is to increase the profitability of the commercial descendants of the bulls and cows selected. Therefore all traits that affect profit should be included in the breeding objective. Each trait should be weighted by its effect on profit. These economic weights naturally depend on the market being targetted and the environment and management system in which the cattle will be produced. BREEDOBJECT is a computer program that calculates economic weights according to the inputs of a specific user and several breed societies have used it to calculate general

purpose economic weights for common target markets. It is important to remember that all economically important traits must be considered and not just one trait such as marbling. This applies to single gene tests just as it does to conventional selection.

Since it is the profitability of the offspring and other descendants of the bulls and cows that is important, our aim should be to select bulls and cows with the highest breeding value for profit (breeding value is by definition the value of the genes that an animal passes to its offspring). To do this we need to estimate the breeding value of bulls and cows for the traits in the breeding objective.

## Estimation of breeding value

We cannot directly observe an animal's breeding value so we are forced to estimate it from observable information. The most obvious source of information about an animal's breeding value is its own performance. For instance, an animal's growth rate is a guide to its breeding value for growth rate, but it is an imperfect guide because it depends heavily on environmental effects as well as the animal's breeding value. The accuracy of the estimated breeding value (EBV) can be improved by using information on relatives especially progeny but the accuracy will always be less than 100%. An important feature of BREEDPLAN is that a large amount of information is combined in an optimal manner to produce an EBV for each animal for each trait. Some traits cannot be observed on the animals among whom we are selecting. For instance, milk yield cannot be observed on bulls and eating quality cannot be observed on live cattle. In these cases the EBV must be





based entirely on information from relatives and consequently the accuracy of the EBV for these traits will usually be low for bulls and cows without progeny.

BREEDOBJECT can combine the EBVs for all traits into an EBV for profit or a selection index that is the best predictor of the breeding objective. The accuracy of the EBV for profit depends on which traits have been recorded. If marbling is important to the breeding objective, then recording ultrasonically measured intra-muscular fat will add to the accuracy of the EBV for profit. However there is a cost to recording extra traits, so the cattle breeder should ask 'Is the improvement in the accuracy of the EBV for profit great enough to justify the extra recording cost?' As I will describe below, exactly the same criterion can be applied when deciding whether or not to invest in DNA tests.

## The genetics of economic traits

Most economically important traits, such as marbling, are controlled by many genes and by environmental effects. Consequently these traits usually show a continuous distribution from low to high with many animals in the middle around the average. Since the effect of most genes is small relative to other sources of variation, it is not possible to follow the inheritance of individual genes, as it is for instance with red vs black coat colour. In fact, until recently almost none of the genes that cause variation in economic traits of beef cattle were known. Fortunately, we only need to know the cumulative effect of all genes on the breeding value of an animal in order to select those with the highest breeding value. That is why conventional genetic selection has been so successful. However, the new technology provides us with an opportunity to use information on differences between animals in the genes they carry to improve the accuracy with which we can estimate breeding values.

The number of genes that play a role in the growth of cattle is huge, but a gene can only cause variation between animals if there is variation in the gene between animals. For instance, we know that growth hormone is important in growth of cattle but there may be no variation in the growth hormone gene in our cattle that affects the function of the gene. Variation between genes means differences in DNA sequence and these come about through mutation. For instance, the double muscling gene is one of the genes affecting eye muscle area in cattle. A mutation occurred in breeds such as the Belgium Blue in the myostatin gene whose normal function is to inhibit muscle growth. The mutation inactivated the gene, leading to an increase in muscle growth. In nature this mutation is selected against because it causes an increase in calving difficulty and other problems. However, when selection for muscularity was applied in the Belgium Blue the frequency of this gene increased until it almost totally replaced the normal allele in this breed. All Belgium Blue cattle examined have the same mutation indicating that all the double muscle alleles trace back to a single original mutation. The same allele is also found in the Asturiana breed indicating that the double muscle gene arrived in the Asturiana by crossing with Belgium Blue or vice

versa. However, some breeds have a different mutation at the myostatin gene indicating that it occurred independently of the mutation in Belgium Blue. The myostatin gene is not the only gene affecting muscularity in cattle. Even in breeds with only the normal version of the gene there is genetic variation in eye muscle area, presumably caused by variation at other genes.

The double muscling gene is unusual because its effect is very big relative to other variation in muscling. In marbling we know of no single gene with a huge effect such as myostatin has on muscling. A more typical situation is that of milk yield in dairy cows where over 20 genes that affect this trait have now been mapped. These genes vary from a few of largish effect, more of medium effect and even more whose effects are too small for them to have been discovered.

Thus for marbling (and most economic traits) we should not talk of the gene for marbling, but of many genes, some of which have been discovered and some of which have not.

## Finding genes for economic traits

Two broad approaches are used to find genes for quantitative traits. In the candidate gene approach, knowledge of the physiology of the trait is used to suggest (candidate) genes that might affect the trait. The strategy is then to look for differences between alleles in DNA sequence and then to determine if these differences are associated with differences in the trait. This approach has proved successful in some cases such as the effect of the thyroglobulin gene on marbling. However it is often unsuccessful, perhaps because many genes, although involved in the physiology of the trait, show no variation which greatly affects their function. When the candidate gene approach is successful it is very useful because it should identify the actual gene that affects the quantitative trait. This is not the case in the gene mapping approach.

In the gene mapping approach, genes for quantitative traits (i.e. QTL) are detected by linkage to genetic markers. If markers covering all the chromosomes are used, called a genome screen, genes for quantitative traits throughout the genome can be detected. Thus this method is less likely to be a complete failure than the candidate gene approach but it has two disadvantages. Firstly, large and costly experiments are necessary. Secondly, the outcome is that a gene for a trait of interest is known to map to a particular region of one chromosome but the identity of this gene is still not known. It is known that the gene is linked to one or more markers and these markers can be used for marker assisted selection, but this is not a simple matter if the marker(s) and the gene are in linkage equilibrium.

## Linkage equilibrium and disequilibrium

Linkage equilibrium means that chromosomes, which carry the favourable allele at the QTL, do not all carry the same allele at the marker. In fact, across the population, the association between marker alleles and QTL alleles is random. Within the offspring of one bull, one marker allele will be associated with the favourable QTL allele. This fact can be exploited by marker assisted selection but only after determining for each



family which marker allele is associated with the favourable QTL allele.

Linkage equilibrium is likely unless the marker and the QTL are very close together on the chromosome, i.e. very closely linked. Linkage disequilibrium means that the association between marker alleles and QTL alleles across the population is non-random. If the linkage disequilibrium is complete, one marker allele is always on the same chromosome as the favourable QTL allele. In that case marker assisted selection is easy to apply and in practice it is almost as good as having identified the QTL itself.

### **A logical strategy for mapping, using and identifying QTL is as follows:**

- map QTL using a genome screen
- find markers in linkage disequilibrium with the QTL. This provides more useful markers for marker assisted selection and maps the QTL more precisely, which is beneficial in the next step
- search the cattle gene map in the region to which the QTL has been mapped, and the homologous region of the human gene map, for possible candidate genes
- test these (positional) candidate genes to determine if they affect the trait.

This is the strategy used by the CRC for Cattle and Beef Quality to find genes for meat quality and other traits.

### **Using identified genes or markers**

Whether we know the genes responsible for variation in a trait or not, it is still the breeding value of an animal that best describes the value of those genes to his or her progeny. Thus our aim is still to estimate the breeding value of each animal as accurately as possible. The value of knowing which genes contribute to variation in a trait is that we can use tests for differences in those genes to improve the accuracy with which we estimate breeding value. The increase in accuracy that can be achieved was quantified by Goddard (1999). Here I will summarise the main factors that determine the gain in accuracy in EBVs from using tests for individual genes.

The proportion of variance in profit that is explained by the gene or genes is important. If a gene explains little variation in a trait, tests for it cannot improve the accuracy of the EBV greatly. It doesn't matter how many genes are used, it is the total variance explained by them that is important. In the future I expect many more genes will be discovered and so their collective value in selection decisions will increase.

If the accuracy of the EBV is already high then tests for specific genes cannot improve it much. For instance, if a bull has been progeny tested with many progeny then his EBV will be highly accurate and gene tests will be of little use. Conversely, if the existing EBV is a lowly accurate, the benefit from the gene test is greater. For instance, young bulls without progeny inevitably have lowly accurate EBVs for traits that cannot be recorded on the bull himself such as daughter fertility or eating quality.

DNA tests for a gene that effects the trait of interest are more useful than tests for a marker linked to the gene and in linkage equilibrium with it. If the gene itself is known, the difference between the alleles segregating in the population can be measured in large experiments and this value used in other herds. However if only a marker linked to the gene is available, then the marker allele on the same chromosome as the desirable allele of the gene must be determined for each family in which the test is to be used. This means that for each family an experiment must be performed in which the trait is measured and the marker is typed. This is expensive and usually the size of the experiment limits the accuracy with which the effect is measured.

Whether the DNA test is for the gene itself or a linked marker, the logical way to use the information is to combine it with the phenotypic data to produce an overall EBV for the trait. In this way the EBV combines the DNA, pedigree and performance data just as conventional EBVs combine pedigree and performance data. Selection on that EBV will maximise the genetic merit of the next generation. An exception to this policy occurs when there is no performance data on a trait. For instance, DNA tests for carriers of genetic abnormalities do not need to be used in EBV calculations because if there is no phenotypic data on the disease.

If genes show non-additive inheritance such as dominance, the gene test results could be used in mate allocation and design of crossbreeding programs as well as selection. For instance, it has been found that the IGF-2 gene in pigs affects muscling, but only the allele inherited from the sire is active, while the maternally derived allele is turned off. This is called imprinting. A DNA test could be used to select for the high muscling allele in a sire line but against it in a dam line. The crossbred offspring would get the full benefit of the high muscling allele because they would always inherit it from their sire.

The cost of performing the DNA test must be considered. The same principle applies as to the cost of recording additional traits. That is, does the DNA test increase the accuracy of the EBV for profit sufficiently to warrant the cost of the test?

### **Conclusions**

New technology is allowing us to identify genes that control variation in economically important traits. Tests for differences in DNA sequence between copies of the genes carried by different animals can be used in the selection of bulls and cows for breeding. However the aim is still to select the animals with the highest EBV for profit. Thus the role of DNA tests is to increase the accuracy of EBVs. The increase in EBV accuracy will be greatest when the existing EBV is of low accuracy and when the DNA tests explain a large proportion of the variation in breeding value.

### **References**

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