



Genomic breeding programs – a large step forward for low-input dairy cattle breeding?

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About

This technical note gives an overview of the history of dairy cattle breeding, introduces the basic concept and outlines the consequences of genomic breeding strategies especially with regard to functional traits. First results of the LowInputBreeds project in the area of dairy cattle breeding are presented, and limitations and ethical implementations are discussed. Finally, recommendations are given how farmers, especially in the low input sector, should implement the new approach.



Introduction

Milk is a major source for high quality protein in human nutrition, and in many countries milk production with dairy cows is the economically most important sector of the entire livestock production system. The increase of milk production in dairy cattle achieved through breeding in recent decades unfortunately has been accompanied by negative side effects on animal fertility, udder and leg health and metabolic stability. Thus, the increase in productivity has not been associated with a similar improvement in longevity of cows. Developing more 'robust' cows and accounting for traits related to animal welfare in traditional and genomic breeding strategies is thought to be a promising approach to find sustainable solutions for the problems listed above.

Dairy cattle breeding in the pre-genomic era

Dairy cattle breeding requires a greater build up and maintenance of complex infrastructure compared with other livestock species.

Challenges exist on various levels:

- Since cows have a relatively low reproduction rate (only one offspring per year), the majority of genetic progress has to be achieved by selection and high frequency use of the best bulls, either by natural service (with up to 100 offspring per year) or, preferably, via artificial insemination with thousands or even ten thousands of offspring per year.

- Because the most relevant **production traits** centre around milk yield and composition, expressed by cows only, it is not possible to measure a bull's own performance although information on the bull can be retrieved from his daughters (called progeny testing). Besides production traits, a number of other, so-called **functional traits** linked to fertility, health and animal welfare, and product quality need to be recorded and included in the breeding goal.
- All information needs to be collected on a large number of cows (ideally not much less than 100'000) over many farms, usually on a national level or within a **breeding association**.
- All data are combined in a statistically optimal way to obtain so-called **breeding values**. These breeding values reflect the genetic quality of an animal, often expressed relative to a population mean. In the German system, breeding values are expressed with a mean of 100 and a standard deviation of 12. A bull with a breeding value 124 thus is two standard deviations above the average and genetically belongs to the best 2 per cent of a population. Since his offspring inherit on average half of his superiority (the other half comes from its mother), they are expected to have an average breeding value of 112. Other countries use different scales, but the basic principle is the same.

Breeding values are given for different trait complexes (e.g. milk, udder health, calving ease, fertility etc.) separately and condensed in a weighted index of all traits (reflecting the overall value of an animal).

The quality of these estimated values is also published as **reliability of breeding values**, which can vary between 0 and 100% depending on the number of information carriers, family relations, and heritability of each trait. Very high reliabilities (close to 100%) apply to bulls with many performance-tested daughters, while young bulls with only parental information have reliability values of less than 50 %. Highly reliable breeding values remain stable as more information (e.g. performance data of more daughters) accumulates. Breeding values with low reliability may change considerably as more information becomes available. For a bull with a breeding value of 120 and a reliability of 99 %, adding more information may cause a change by a few points, but the final breeding value will lie between 118 and 122. If the breeding value is 120 but reliability is only 50 %, adding information can move the breeding value anywhere between 104 and 136.

The major drawback to established dairy cattle breeding programs is the severe time lag until bulls' progeny can be tested and breeding values are reliable enough (> 50 %) to allow widespread use of the best sires. By then, bulls are usually 7 to 8 years old, although biologically, they could be used as sires with little more than one year of age. Besides the high costs of keeping bulls for many years, this practice also inflates the generation interval, limiting the **genetic progress** per year.

All this in principle is true both for conventional and low input or organic breeding programs. The various types of breeding programs only differ in details, e.g. in the composition of the breeding goal, where organic breeding programs tend to put a higher relative weight on functional traits, e.g.

health and longevity, or the limitation of the use of specific reproduction technologies such as embryo transfer. Apart from these rather marginal differences, the basic structures are comparable as are the shortcomings.

Towards the genomic era

Dairy cattle breeding programs based on progeny testing and artificial insemination were introduced in the 1960s (Skjervold and Langholz, 1964) and in principle have remained unchanged. Attempts to improve breeding programs by incorporating information on single genes, the so-called marker-assisted selection, were widely discussed in the 1990s but did not prove efficient, partly because the number of available genetic markers (~300) was too low.

A simulation study in 2001 by Meuwissen, Hayes and Goddard showed this could change if many more markers are used and novel statistical techniques are applied. It is noteworthy that this study was conducted long before such marker densities were practically available.

Knowing that marker densities need to be increased considerably, the scientific community, led by the US Department of Agriculture (USDA), made a joint effort together with the private company Illumina Inc. to fulfill the requirements outlined by Meuwissen and colleagues. For this, a new marker class, **single nucleotide polymorphisms** (abbreviated as **SNPs**, pronounced as 'snips') was introduced. A panel of 54'001 SNPs was selected to regularly cover the whole cattle genome. These SNPs were put on one array, and genotyping one individual for the complete set of 54'001 SNPs today costs less than 100 Euro. Note this technological innovation increased the amount of information by a factor of ~100 whilst costs were less than half the pre-SNP times.



Blood samples are taken from which DNS is extracted and applied to a SNP array for genetic analysis. (Photo: Anna Bieber, FiBL)

Having both the statistical concept and the new genotyping tools in place, it was possible to practically implement the 'genomic prediction' of breeding values. The underlying idea is: with a given set of animals (the so-called training set, originally around thousand progeny tested bulls with highly reliable conventional breeding values) effects are estimated for all SNPs. Some SNPs may have small and others large effects, but all are considered simultaneously. Then for a new animal (a newborn bull, say) the SNP genotype is assessed and its estimated (genomic) breeding value is just the sum of all effects of the SNP genotypes this animal carries. In most cases these genomic breeding values (often termed 'direct genomic values') are blended with conventional breeding values, so the resulting combined genomic value encompasses the complete information available for the respective animal at this point of time.

It can be shown that resulting breeding values can be predicted with more than 50 % reliability, regardless of the animal's age. Remember that the reliability of conventional breeding values of young bulls, with only parental information, is far below 50 %. Genomic breeding values thus allow more reliable and earlier selection of young bulls.

Genomic selection as the new paradigm in dairy cattle breeding

How can this advantage in genomic prediction be transformed into greater genetic progress or **genomic selection**? This was first described by Larry Schaeffer (2006) from the University of Guelph (Canada) in a very simple model calculation. He took the conventional Canadian dairy cattle breeding program as a basis, where progeny-tested bulls are at least 6 years of age before they can be widely used. Selected based on genomic breeding values, young bulls can already be used with one year of age, and the reduction in reliability of breeding values (from 98 % to 56 %) is more than outweighed by the shortening of the generation interval (from 6.5 years to 21 months). Altogether, Schaeffer could show that using genomic prediction can double the genetic progress per year, and at the same time breeding costs can be substantially reduced by waiving the costs for keeping unproductive bulls until their progeny information is available.

Starting in 2009, genomic selection was practically implemented in large dairy cattle breeding programs around the world. A major modification from the original ideas was that with larger training sets, more reliable genomic breeding values can be obtained. This was achieved through collaborations between the major breeding programs in the respective breed blocks (e.g. Holstein or Brown Swiss). Today training sets comprise up to 20'000 progeny tested bulls, allowing reliabilities of ~75 %, comparable with performance data of around 50 daughters of a bull. The use of a second generation SNP array with more than 700'000 SNPs did not lead to a significant increase in reliabilities, though. Today, all relevant dairy cattle breeding programs have – partly or completely – switched to genomic breeding programs with an increasing number of dairy bulls genotyped and having genomic breeding values.

Advantages of genomic selection for functional traits

Which advantages has the genomic approach to offer besides speeding up genetic progress in major production traits? Or do we have to fear that existing problems of dairy cattle breeding are also accelerated by this novel technology?

A well-known problem of intensive dairy cattle breeding is that traits related to health and fertility (often summarized as 'functional traits') are not improved at the same rate as production traits. In many populations the longevity of cows is stagnating or even slightly decreasing; involuntary culling of cows after only two or three lactations occurs more often. Major reasons for early culling are udder infections (mastitis), infertility, claw disorders and feet and leg problems as well as metabolic diseases like milk fever and ketosis.

The reason for genetic progress in functional traits falling behind performance traits primarily lies in their low **heritability**. Genetics only account for a small proportion (often less than 10 per cent) of variability in functional traits as they are influenced more by environmental factors like management, feeding or infection pressure. As a consequence, conventional breeding values for functional traits have low reliabilities and selection is inefficient, despite the fact that, in recent years, most breeding programs have more than 50 % of the breeding goal assigned to functional trait complexes.



Functional traits might benefit from genomic selection. Evaluating body score condition within the LowInputBreeds project. (Photo: Thomas Alföldi, FiBL)

In contrast, genomic breeding values (regardless of an animal's sex or age) are immediately available with similar reliability for all traits; hence the relative efficiency of genomic selection for functional traits is much greater than for conventional traits. Beyond that, we have the potential to change breeding goals by giving greater weight emphasis to functional traits, so part of the additional genetic progress offered by genomic selection for production traits can be invested into health and fertility.

Can genomic selection help to reduce the problems caused by inbreeding?

Another undesired consequence of conventional dairy cattle breeding is an increase in **inbreeding** from heavy reliance on a few highly selected bulls. High levels of inbreeding will exacerbate health and fertility problems, as well as increasing the risk of novel genetic defects, which can be spread in the population by a single heavily used bull, who happens to be an undetected defect carrier.

Since genomic breeding values for young bulls have a lower reliability, it is recommended to spread the risk by mating cows to a wide range of bulls with high genomic breeding values, rather than relying on a few. This is possible because many more excellent young bulls with high genomic breeding values are available. In April 2013 only 11 German Holstein Friesian bulls have progeny-based breeding values over 140, while 246 young bulls have a genomic breeding value above this limit.

Using a set of these bulls is equivalent to not putting all eggs in the same basket and has the added advantage of reducing paternal half-sib family sizes, creating a more diverse population with less inbreeding. However, while this applies to inbreeding per generation, it is not necessarily true for the average increase in inbreeding per year (due to the shortening of the generation interval) or per unit of genetic progress (due to the increase of genetic progress).

Although genomic information offers a new perspective for active management of inbreeding in dairy cattle populations it appears that the problem will not automatically be solved with genomic selection.

Limitations of genomic selection and its ethical implications

On a global scale, the influence and use of genomic selection focuses on high input systems with established, conventional breeding programs, large target populations of cattle and therefore greater financial implications. Little attention has been paid to variation seen in animals farmed in *different* environments (genotype by environment interactions = GxE).

Until now, genomic breeding value estimation has not been applied to smaller dairy or dual purpose cattle breeds, such as Original Braunvieh in Switzerland, or crossbred animals, although these breeds/animals may be highly relevant for low input systems, due to their ability to adapt to local environments.

There are concerns that genomic breeding might not only improve traits related to animal health and welfare, but may also imply a greater risk of accelerating unwanted side-effects. Among these are detrimental genetic trends for non-measured welfare traits and the increased risk of spreading unfavorable mutations. Moreover, worries over patents may reduce the willingness to share genotypic and phenotypic data.

The active involvement of farmers could also be suppressed (Mark and Sandøe, 2010). For example, the present implementation of genomic selection in Switzerland has reduced the number of progeny tested bulls, therewith excluding smaller farms from provision with test bulls. This development reinforced concerns that genomic breeding programs may have a negative impact on farmer's socio-cultural contribution in cattle breeding.

Incorporating novel traits in the genomic selection program

Another often discussed challenge is to add novel traits into dairy cattle breeding programs. Likely trait complexes to be included in breeding goal might be:

- **Resource use efficiency**, like the feed conversion rate;
- **Behaviour and welfare**, encompassing general behaviour as well as behaviour towards humans, herd mates, or during milking, especially aggressive tendencies;
- **Health**, especially detailed health records like clinical mastitis or claw disorders;
- **Environmental impact**, since ruminants are a major source of the greenhouse gases methane and nitrous oxide, a minimization of emission of is desirable.

A common feature of all novel traits is that recording is difficult, expensive, and not (yet) routinely collected on a population wide scale (with some exceptions, e.g. health trait recording in most Scandinavian countries).

In conventional dairy cattle breeding programs, establishing estimated breeding values for novel traits is highly demanding, since population-wide performance testing for the respective trait has to be established. In genomic selection, though, it might be sufficient to record the trait in a training set of limited size, then to train the model with this respective data and subsequently have the possibility to estimate moderately reliable genomic breeding values for genotyped selection candidates.

One objective of the LowInputBreeds project was to validate promise in this strategy. For this, around 1800 cows on 40 Swiss dairy herds, operating under organic or low input conditions, were recorded for: General temperament, Milking temperament, Aggressiveness, Rank order in herd, Milking speed, Udder depth, Position of Labia, and Days to first heat. At the same time all cows and their sires were genotyped with a 777k SNP array. First results indicate it is possible to derive genomic breeding values that are more reliable than conventional breeding values for most of these traits. This provides a good basis for early selection; it will be possible to obtain greater genetic progress in these functional traits which are highly relevant for the low input sector.

Recommendations

Since the implementation and publication of direct and composite genomic breeding values, farmers have a larger choice of sires, but should also be aware of the implications these different breeding values have, especially with regard to their reliability. When using young bulls with genomic breeding values, it is recommended to use a diverse set of these bulls, to spread the risk (Berweger, 2011). The proportion of cows inseminated with genomically selected young bulls in a herd will be an individual decision of each farmer, which should reflect a balance of the chances (higher genetic merit of young bulls in production and functional traits) and the risks (less reliable breeding values, thus possible positive or negative deviations from realized values) associated with this decision.

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Glossary

Breeding value: Genetic value of an animal relative to the population mean. A parent passes half its breeding value over to offspring.

Functional traits: Traits related to fitness, health and fertility which are important for an animal well-being and an essential pre-condition for productivity. Other than for production traits, the economic potential of functional traits lies in the avoidance of costs, e.g. of veterinary treatments.

Genetic progress: Rate of improvement of the average breeding value for any trait in a population per year. Often, the genetic progress per year is 1 per cent or less.

Genomic prediction: Prediction of breeding values based on SNP information and phenotypes of a reference population.

Genomic selection: A breeding program where young animals are selected based on their genomic breeding values.

Genotype x Environment interaction (GxE): Describes the phenomenon that the performance of the same genotype differs with changing environment because genes interact with the environment.

Heritability (h^2): Proportion of trait variation due to genetics. It is easier to make genetic progress for traits with high heritability, such as milk yield. While h^2 takes moderate to high values (~0.3) for most production traits, it is low (< 0.1) for most functional traits.

Inbreeding: Related parents give inbred offspring. A high level and fast increase in inbreeding is undesirable as it can lead to health problems, but is sometimes hard to avoid in small populations

Production traits: Primary traits linked to the quantity and quality of the product that is sold to generate income, in dairy cattle the main production traits are milk yield and fat and protein contents.

Reliability of breeding values: Measure for the accuracy of an estimated breeding value ranging from 0 (completely inaccurate) to 100 % (perfectly known).

Single nucleotide polymorphism (SNP): SNPs are point mutations that appear almost everywhere in the genome. In the cattle genome, millions of SNPs have been found and selected subsets of these SNPs are combined on a SNP array for efficient genotyping.

Imprint

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LowInputBreeds

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Review

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Cover picture

Evaluation of new functional traits in cows with a farmer within the EU-funded LowInputBreeds project. Photo by Thomas Alföldi, Research Institute of Organic Agriculture (FiBL), Switzerland

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