Implementing genomic selection into a routine nucleus program

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Genomic selection, marker assisted selection, genomic screening, genetically modified organisms (GMO), genome sequencing. These are all terms that are popping up regularly nowadays and are all related to our increased knowledge and utilisation of DNA information.

DNA stands for deoxyribonucleic acid. It is a nucleic acid containing the genetic instructions or code used in the development and functioning of all known living organisms.

The specific DNA segments carrying genetic information about various aspects of an animal are what are called genes.

Animal breeding or genetics is the area of science where experts are trying to influence the frequency of certain genes by combining the most superior (or desired) individuals to be the parents of the next generation. This process is focused on getting improved offspring who in theory should then, on average, be better than the previous generation.

Statistical models

Sophisticated models are used to compute the differences in genetic merit between animals and predict the genetic values/merit of their offspring before they are even born.

Sophisticated statistical models like BLUP (Best Linear Unbiased Prediction) and increasingly better computing capability have made it possible to predict an animal's genetic merit with much higher levels of accuracy compared to years past.

Information and data from all types of measurements can contribute simultaneously to increasingly more reliable breeding values. An example of the genetic improvement that has been achieved via the use of this technology is the worldwide large improvement in litter size in pigs over the latest decades.

This is a trait with low heritability and thus was hard to achieve substantial improvement in prior to the use of BLUP and improved computing technologies. These technologies made it possible to use all relationships between large groups of individuals (animal model).

A relatively new development in the world of animal genetic improvement is the description of the complete DNA maps (called sequencing) of different livestock species, the pig included.

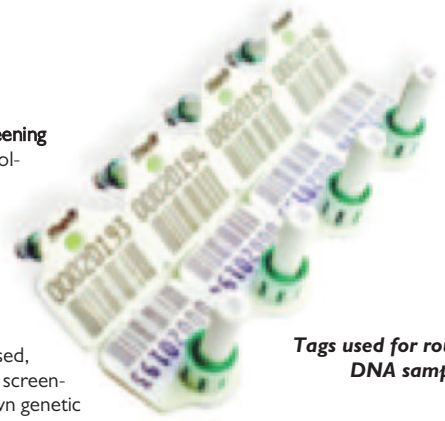
This has, in turn, made it possible for more and more DNA specific information to get used as an added information source to increase the reliability and accuracy of estimated breeding values (genetic merit) of target animals.

SNP	Allele A effect	Allele B effect	Genotype of candidate	Estimated genetic value
1	-0.08	0.12	AA	-0.16
2	0.23	-0.10	AB	0.13
3	-0.15	0.33	BB	0.66
4	-0.01	0.05	BA	0.04
5	-0.02	0.01	AB	-0.01

Table 1. An example of calculation of genomic breeding values out of allele estimates for different SNPs.

● **Marker assisted selection** was one the first applied uses of DNA as an information source. In marker assisted selection, DNA markers linked, or associated with, a trait of interest are used to indirectly increase the frequency of the desired genes, by selecting individuals that carry the identified genetic marker.

On the premise that better performance is associated with the target gene/marker, the trait of interest is consequently improved. Links between desirable genes and markers however can become weaker over time and are strongly breed or population dependent.



Tags used for routine DNA sampling.

● **Genomic screening** is another technology. This is a way to screen for certain genetic markers that determine a specific genotype. It is used, for example, for screening pigs for known genetic defects or off-types in a specific trait, like boar taint in pork. Typically for genomic screening a couple of markers or a small group of markers are used to distinguish the desired from the undesired animals.

● **Genetically modified organisms** (GMO) are organisms whose genetic material has been altered through genetic engineering – this involves the introduction of foreign DNA into the target species. This is frequently applied in bacteria and in plant breeding. It is however certainly not common practice in livestock animal breeding, mainly due to questions of ethics and safety.

● **Genome sequencing** or whole genome sequencing is the laboratory process that determines the complete DNA sequence of an organism's genome. Genome sequencing provides the whole library of base pairs of a species. For most species there are billions of base pairs.

A small part of these can be classified as single nucleotide polymorphisms (SNPs), a situation where the nucleic bases in a certain location of the genome are of different types in some of the individuals within a species. There are several millions of SNPs discovered in most species. These SNPs are the basis of genomic selection.

Table 2. Conventional BLUP breeding values and genomic breeding values for two different litters.

Tattoo	Date of birth (Nov 2011)	GEBV	EBV
D4293	21st	3.00	2.74
D4292	21st	2.61	2.74
D4295	21st	2.76	2.74
D4294	21st	2.58	2.74
D4350	29th	3.18	2.91
D4351	29th	2.89	2.91
D4348	29th	2.73	2.91
D4349	29th	2.69	2.91

● Through **genomic selection** a large number (from 50,000 to several millions) of SNPs are selected across the animal's genome to serve as an information source for breeding value estimation. Linking the differences in these markers to the differences in performance in reference panel animals provides a unique opportunity for a new genomic breeding value (GBV) (see Table 1).

The process of using this technique routinely was fully implemented by Hypor a couple of months ago – to estimate breeding values for all traits in one breed in what is the first-to-market in the pork industry.

Collecting DNA samples of pigs has been common procedure in our nucleus farms for quite some time. Routine sampling, shipping and processing of samples has been further professionalised through the use of DNA sample tags that catch an ear notch sample in a small tube. All samples are shipped and processed in the genomics laboratory of Hendrix Genetics in France.

Our ability to run genomic breeding values will change the way we run our programs. After the DNA ear-notch samples are received at the genomics laboratory, DNA is extracted and samples readied for routine genomic analysis. On average it takes about 14 weeks to complete the full cycle from sampling to having a genomic breeding value.

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The main benefits with genomic selection will come from selecting our most superior high impact breeding animals with higher accuracy than before. It is common knowledge that the males in a pig breeding program have the most impact.

Since on average fewer males than females are needed, selection room (intensity of selection) for males is bigger at all levels of the pyramid – GGP, GP and PS.

In all these levels analyses of a small number of samples from males only will have a relatively large impact on the average accuracy of breeding values used at the moment of selection.

Higher accuracy translates to faster genetic progress! What is critical is that the higher accuracy information is available in time to be used in the selection process.

This means that males should be still intact males at the moment their genomic breeding values become available.

Accurate breeding values of females have less 'value' when they get selected anyway if they meet certain basic criteria.

Genomic index

The genomic index will be one BLUP index combining conventional and genomic information in one value. As with the regular index the highest ranking animals will be the preferred ones for selection. Ranking will not change dramatically, when the traits involved and breeding goal do not change. It is possible that the odd animal might rise or drop significantly.

Many animals will tend to have the bulk of their relevant information at around the same moment now (using genomics), while with traditional parameters and measurements it takes a much longer time spread and additionally this information would be available much later in their life time.

With the use of genomics animals with incorrect pedigrees will also be determined at an earlier age.

As we move into the future with the use of genomics more drastic changes are foreseen. New traits which can be more easily exploited with genomic selection will be added to the breeding goals, for example health traits.

Depending on the importance of a trait, this will affect the ranking of individuals in a breed. Typically, genomic selection is much more effective when used for those traits with a low heritability, traits that are sex-linked, or those that can only be measured at slaughter.

Other potential traits are those that are measured on crossbred market progeny (CCPS traits), genetic defects, piglet losses or health related traits.

In the coming decade we expect to regularly add new traits to the breeding goals. DNA-based information will be the main driving force in the process to further improve our breeding stock towards our clients' requirements.

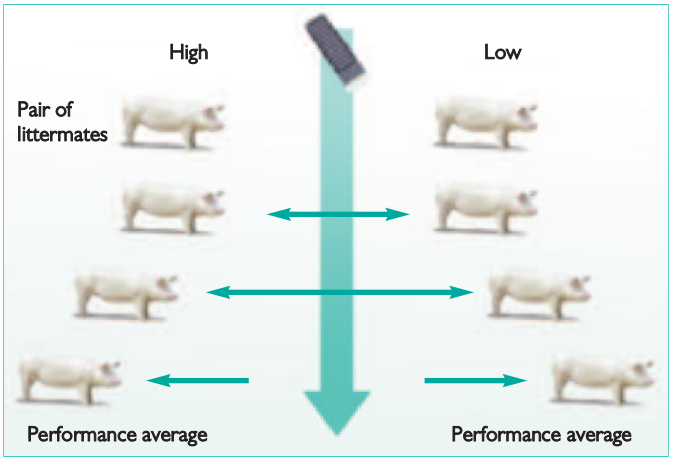

Fig. 1. Proof of principle setup – assigning high and low genomic breeding value animals to a high and low group and comparing real performance figures.

Proof of principle

A proof of principle was conducted to calibrate existing software packages and confirm that we are able to read DNA based on SNP-marker information.

This proof of principle was used to evaluate if early predictions of performance, based on DNA-markers, were effectively reflected in later differences in actual performance. This was a very exciting process.

Based on SNP-marker information we assigned littermates to groups of high or low predicted future performance in reproduction traits. This was later on confirmed through real production differences. Several hundreds of litters were used in this proof of principle exercise. Gilts assigned to the high category outperformed their full sib sisters in the low category with an average of 0.4 piglets total born.

This number was very similar to what was predicted by our genomic models. Additionally, in two other traits, percentage stillborn and preweaning mortality, we were able to distinguish littermates, which had less losses (1.86% and 2.28%, respectively) in the group with the desired genotype. One can imagine the excitement about exploiting this in a practical breeding program.

Being able to utilise the within litter genetic variation in reproductive traits in our selection process will be an enormous step forward in genetic progress. Depending on heritabilities it will mean about a 10-40% increase in accuracy for traits with heritabilities of 0.4 and 0.1, respectively.

Now littermates will no longer be anonymous piglets with the same expected breeding value. Randomly picking one or picking an average pig based on its looks will no longer be the way to go.

Future GGP pigs will have their own genomic breeding values based on their own unique pattern of DNA markers, which will be strong predictor of their future production.

This genomic breeding value will predict with relative high accuracy what these pigs' genes are worth in the breeding program. This opens up a complete new era in pig breeding. It will potentially change the structure of breeding pyramids and it will enhance the limits for future pig performance. ■