Looking back into the Future

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Introduction

"Looking back into the Future" a quote from Heinz Lohmann (1901-1975) the founder of Lohmann Tierzucht (1956) which today is part of one of the two world wide operating and dominating poultry breeding empires; it is now owned by another German family owned company, the EW Gruppe. While I have never met Mr Lohmann I benefitted from his generosity as I was able to attend an international training course presented in Germany in 1978 by Prof John James (University of New South Wales) entitled "Comparison of theory and experimental results in quantitative genetics".

The course was strongly supported by Lohmann Tierzucht at the time and the two brothers who took over the Lohmann operations have later set up a foundation in his name which is supporting in various ways research into agriculture and food production.

Looking Back

1. Introduction of genetic evaluation

Looking back some 25 years to my first involvements with the Australian pig breeding industry reminds me of a pig workshop in Albury where I was invited to talk about modern genetic evaluation (BLUP). At that meeting a colleague from South Australia talked about the new breeding paradigm genomic selection and he more or less predicted the demise of quantitative genetics. My statistical quantitative expertise wouldn't be needed much longer and in 10 years I would need to find other fields of interest. This might have been expected at the time given the recent discovery of the HAL gene and its impact on many production and meat quality traits which have later been well studied. Today, 25 years later, expertise in quantitative genetics is in demand more than ever; our molecular colleagues can't do without us when it comes to implementing their technology into the next generation of livestock improvement programs which will be selection based on phenotypic information and genomic data. The idea that all we need to do is find those two dozen important genes which we hoped were responsible for the genetic differences between animals for any one trait has now been proven wrong. Nearly all quantitative traits in livestock are impacted on by hundreds or thousands of interacting genes. We will find and already have found a good number of those genes but, with few exceptions, they only explain a small fraction of the total genetic variation.

When, in 1988, we floated the plan to develop genetic evaluation for the Australian pig industry using BLUP models and programs, and went as far as using an early PC which cost around $15,000 to do so, we had opposition from some pig geneticists and a CEO from a large pig breeding company. The first group thought the benefits would be minimal as index selection as practised at the time was thought to be good enough. The CEO, I guess, realised that BLUP on a PC would provide every small breeder access to a technology, which up to then was only available to bigger companies, increasing their ability to compete in an open market.

One of the observations we made later was that there was a lot of data recorded in some pig breeding enterprises, but the data couldn't be used efficiently due to lack of programs that could provide a timely feedback. While the recording exercise might have created a good feeling (we are doing something) it did little in generating genetic change. However with the availability of a genetic evaluation program, in this case PIGBLUP which could provide a selection Index using all the available performance data and the pedigree data before young boars and gilts were sent to the abattoir, genetic change could be generated at a much faster rate. The pigs started to grow faster and became leaner and litter size increased.

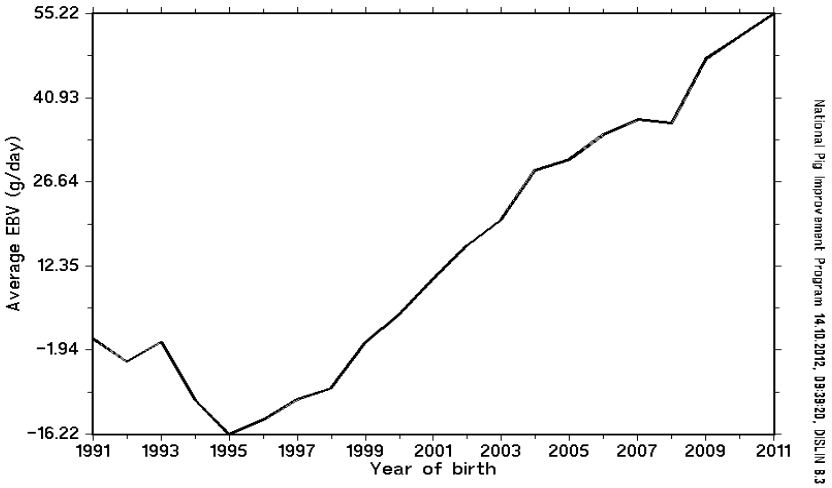
2. Genetic trends achieved

Hermesch (2006) presented at this forum the average genetic change between 2000 and 2005 achieved in some 18 PIGBLUP herds for a number of traits and showed that on average the genetic change was just keeping pace with the deterioration in the environment. Hermesch also presented some results indicating that the 2005 model of pigs would benefit from an increase in the digestible energy (better environment) through higher growth rate and fewer days to market-weight without a reduction in back fat. However the diet was $30 per tonne more expensive than the standard diet at the time and no attempt was made to calculate a cost benefit in the paper.

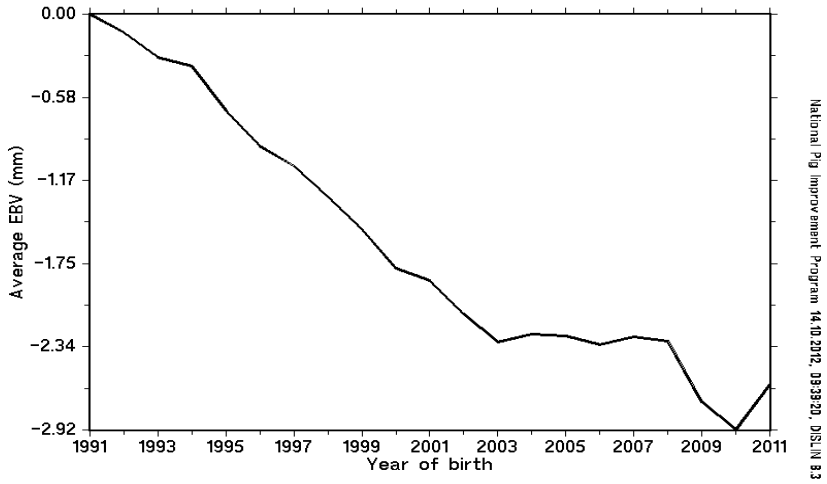
Since then the trend has continued. When looking at the graphs generated from the National Pig Improvement Program regular runs using data submitted by various breeders (Figure 1), we can see that the genetic value for average daily gain is continuously going up and for back fat has decreased further, while number born alive in the first parity is not increasing any more, but it does so in later parities.

Figure 1. Genetic trends in Australian Landrace pigs from the NPIP analysis 14/10/2012

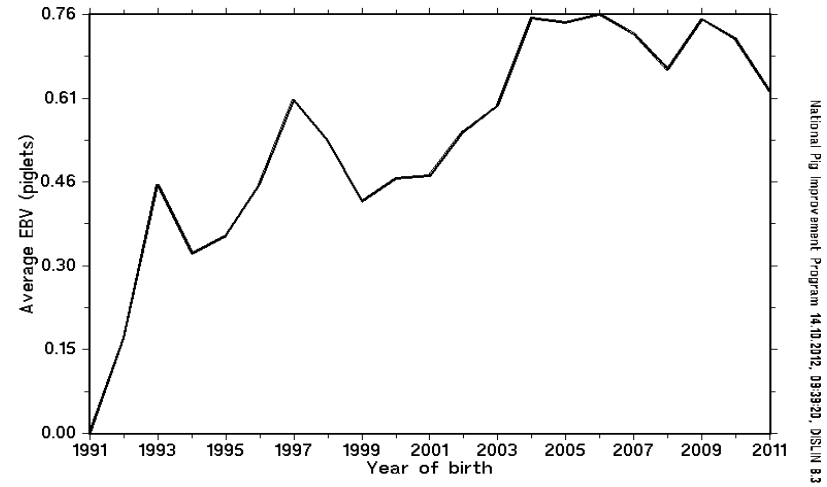
a) Trend in Average Daily Gain



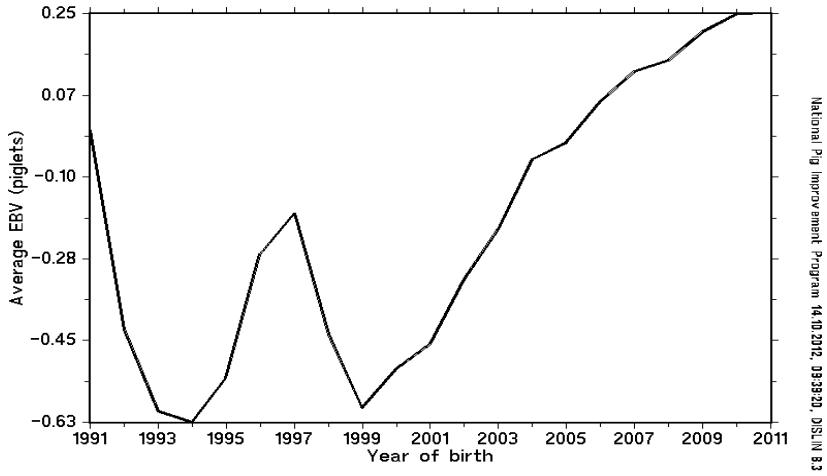
b) Trend in Back Fat



c) Trend in Number Born Alive first parity



d) Trend in Number Born Alive second and later parities



From these results, and the many papers we had to read in the course with Prof James 35 years ago, I conclude like others, that we can change, although commonly slowly, any trait for which we observe phenotypic variation within a group of animals managed together. If we should or want to do this depends on the economic importance of the trait or other considerations we might have e.g. animal welfare, genetic diversity or pure pleasure to breed something which looks different.

Looking into the future

Genomic selection is finally upon us, a decade or two later than previously predicted. All major dairy cattle breeding programs in the developed world use DNA information to select unproven young bulls and cows. This was made possible because they have access to a huge amount of phenotypic data recorded on daughters of 10,000 plus sires over the last four decades. Large sums of money have been spent during the last 10 years to drive the genotyping technology and increase its power and reduce the costs. The reduction in cost per single genotype is spectacular and easily matches the increase in computing power at lower and lower costs we have seen during the last 50 years.

In cattle we get today a single nucleotide polymorphism, if we do them with the 800,000 SNP chip, at around 0.02 cent or 50 for a cent, and every company along the way providing this service makes a profit. Ten years ago we budgeted multiple $$ per SNP. We can also get the full sequence of some 9 billion or so base pairs for around $1,000. These single nuclei polymorphisms are linking chromosome segments and sometimes genes to performance differences for all traits recorded in dairy populations. However it is quite clear that many of these linkages are breed specific and work better in generations close to the discovery population.

As pig breeding is mostly done with lines of Large White, Landrace and Duroc and many of the lines are a number of generations apart from the lines of other breeding enterprises, prediction equations cannot simply be transferred with great success from one line (breeder) to another one of the same breed. Does this mean smaller pig breeders cannot use the technology? Are we at a similar point as 25 years ago with the application of BLUP to small breeding companies? I believe the answer to the first question is NO and to the second one is YES.

BLUP evaluation and DNA data

The BLUP model we are using for genetic evaluation relies on two key components: the phenotypic data recorded and the pedigree of the animals which also needs to be recorded. From this pedigree we construct a relationship matrix (and its inverse) which links past generations to the current one in an average way. Every animal is related exactly the same way to its ancestors, e.g. 0.25 with every one of the four grandparents. This method of course does not recognise any pedigree errors in the database, but uses them linking the performance data of animals to incorrect relatives. For some beef cattle populations up to 10% of calves have either dam or sires or both recorded incorrectly. I would not be surprised if this is of the same magnitude in less well controlled and recorded pig breeding operations.

However using SNP-chip data changes all this. A genomic relationship matrix which calculates the relationship between animals on the basis of the similarity of the SNP profile across a couple of hundred SNPs per chromosome not only avoids the obvious errors in the pedigree but also overcomes the averaging of relationship we perform with our so called Numerator Relation Matrix (NRM). We can identify differences in the genomic relationship of piglets even within a litter which will vary around the average 0.5. Genotyped piglets in litters produced using more than one boar for mating or mixed semen can easily be allocated their “correct family” using the

genomic relationship. Of course genotype sample ID and phenotype ID must match correctly, otherwise we still have errors.

By modifying our BLUP programs we can now utilise genomic information. We replace the NRM calculated from the pedigree with the observed genomic relationship (GRM) based on 10,000 or more SNPs. The more SNP we can use the more accurate that calculated relationship will become. While this is not a trivial computing exercise as some adjustments are required and no easy way exists to invert the genomic relationship matrix (other than strong arm) the methods are now well understood and computer programs have been developed to manage this. It will however require the storage of all the genotypes and the genomic relationship between all animals as we don't want to recalculate those every time we do an analysis.

In this approach all data, new and old, will be used in what has been termed the single step approach which is different to the commonly used two or three step approach. We do not distinguish between discovery population from which prediction equations for all traits of interest are derived and the application population were the prediction equations are applied to (or commercialised). In the single step approach prediction equations are not explicitly calculated (but they can be extracted) and then applied to other animals which have been genotyped. Newly genotyped animals are linked through the GRM to other animals with records and their EBVs are calculated directly (one step). This also means that the internal prediction equations are updated as new phenotypic information is collected. We can even go one step further and pick out for each trait the dozen or so SNPs which have the largest estimated effect and treat them slightly differently. You can't do much better than that.

Recently Danish scientists (Christensen *et al*. 2012) applied this one step approach to a large pig dataset with more than 330,000 pigs which had been recorded for daily gain. 25,000 of them also had a feed intake record to calculate FCR. Pedigree and performance data recording started in 1992. They genotyped 2668 animals born between 1996 and 2010, using the Illumina PorcineSNP60 Bead Chip and could use 25,720 SNP markers for their work. Using the latest data of animals born after 1 October 2008 and comparing various models of utilising the phenotypic and genomic data they came to the following conclusions.

- Single-step methods provide more accurate predictions than the pedigree-based method for both genotyped and non-genotyped animals.
- For genotyped animals the accuracies were similar between the one-step and the GBLUP method
- The single-step multi-trait model increased the accuracy of the sparsely observed trait FCR compared to a single step single trait model.

The improvement in accuracy varied between models, traits and groups of animals. Using traditional BLUP (only phenotypes and pedigree) compared to one-step (all phenotypes and a GRM for genotyped animals) they observed that the accuracy increased more for genotyped animals (0.18 to 0.35) than for non genotyped animals (0.19 to 0.22) but about the same for daily gain and 0.20 to 0.23 and 0.09 to 0.12 for FCR respectively.

When compared across all animals and with a multi-trait model the improvement in accuracy for daily gain was from 0.193 to 0.228 or 18% whereas the improvement for the less well recorded trait FCR was from 0.106 to 0.166 or a big 56%. Of course this one-step doesn't allow any predictions for traits which are not recorded.

We expect that the price for genotyping will decrease further and there is now a real possibility that medium size breeding companies and smaller breeders if they work together could utilise this technology. It would be feasible if funds are made available to genotype all AI boars used in

the Landrace, Large White and Duroc breed during the last five years and make the genotypes available for genetic evaluation to NPIP, Cefn, Rivalea, PIC or Myora. The breeding program might not have necessarily used the boar but would still receive a prediction based on the relationship with its own breeding program. One might find an interesting boar which one would have otherwise never discovered. Obviously such a project requires a good deal of cooperation and the willingness to share genotypes (not phenotypes) and fund the genotyping together. (It wouldn't be the first time that I'm accused of dreaming.) For less than A$ 50 per boar we can have our boars genotyped by GeneSeek in the US which will return 8,500 SNP. If you are then interested in some already identified gene e.g. for litter size you only need to pay extra for those boars which you might be really interested in.

I think it would be worth approaching APL or the Pork CRC to fund the first 1000 boars. Breeders would only need to contribute semen or hair samples to the project.

I trust that similar to the introduction of PIGBLUP 25 years ago my colleagues at AGBU will work on the enhancement of PIGBLUP and NPIP software to accommodate such data by the end of next year.

Such projects will mean that, using old well known technology - BLUP derived breeding values – which will have increased accuracy, our Australian pig breeding companies will be able to generate faster genetic progress and contribute through better genetics to the competitiveness of the Australian pork industry.

One warning however, genotyping animals cannot replace solid performance recording in the grandparent stock of our production system, but it will allow with some additional software, which I understand is already in use in some breeding/ production programs, for targeted mating in grandparent to produce F1 sows and further planned mating to produce the best combination of genotypes in the slaughter stock (Kinghorn 2011).

References

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Kinghorn, B.P. (2011). "An algorithm for efficient constrained mate selection" Genetics Selection Evolution. 43:4