Animal Breeding for Food Security

Opportunities in the genome sequencing era

Prof. dr *ir*. Roel F. Veerkamp

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Inaugural lecture upon taking up the position of Special Professor of
Numerical Genetics and Genomics at Wageningen University
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Esteemed Rector Magnificus,
Dear family, friends, colleagues, collaborators, ladies and gentlemen.

It is an obvious privilege to stand here in front of you all and present my inaugural lecture "Animal Breeding for food security, opportunities in the genome sequence era".

However, it is more than a privilege - it is also a great pleasure to address you today and share with you my ambitions and views in this field. Numerical genetics and genomics is a research area that is thriving. It has witnessed extraordinary developments and had a significant impact on animal breeding over the past decade. For example, the introduction of selection based on genome-wide information is leading to drastic changes in the structure of cattle breeding programmes. These unprecedented changes happening to date demonstrate the impact that numerical genetics can have… and even more changes are expected to come. It is this impact, together with the scientific discoveries, that make it a pleasure for me to work in this area.

In the next 45 minutes I take you on a tour that starts with the external drivers for my research. After that I will explore the developments in the field of numerical genetics and genomics, and my ambitions in this area. Ambitions not only to advance current breeding programmes, but also to better meet the needs of society and disentangle the genetic model underlying quantitative traits even further.

And, to be upfront about it, this tour will end with the following statement:

"In the era where measuring the full DNA sequence of individual animal genomes becomes standard and there is a need to breed animals that fit the needs of society, numerical methods are the key for co-innovation".

External drivers
But let's start first with the external drivers for my research:

Food security
The first external driver is the importance of food security.

Over the past half-century food production tripled and allowed for a doubling of the world population from 3 billion to over 6 billion today. Simultaneously we have seen a dramatic decrease in the proportion of the world's people that are hungry (World Bank, 2008) and an improvement in life expectancy from 46 in the 1950s to around 65 today. Undoubtedly, genetic improvement in animal and plant species has played an important role in increasing this food production.

If I take, for example, milk yield, we see that in the Netherlands milk yield increased annually over the past decades with 84 kg milk per cow per year. If we calculate the genetic trend than 82 kg milk per cow per year could be subscribed to genetic progress (Figure 1). This demonstrates that genetic improvement is probably the major driver to increasing productivity at the animal level (close to a 100%) and it has been making an important positive contribution to the trend in food security over recent years.

Over the next 40 years the growth in the world's population will continue, reaching 9.1 billion by 2050. The global consumption of animal products will increase even faster, especially in Asia and the Pacific (OECD and FAO, 2011).

However, a major difference with the past is that today, for a sustainable future, the growth in food production should come at an acceptable cost to the planet (FAO, 2009, Godfray et al., 2010, Nature, 2010, OECD and FAO, 2012). For example, although food production needs to increase, we have to reduce the carbon foot print associated with this increased production. In addition, fewer resources will be available because of the growing competition for land, water, fuel and energy. Maize is not only grown to feed people and animals, it is grown also to produce electricity or run cars. You just have to follow the recent concerns about the impact of the current draught in the US to realize that food security will be an important issue for another 40 years.

Therefore, the key issue facing global agriculture is how to increase productivity in a more sustainable way: not simply "more", but "more for less" is the challenge… and I believe that animal breeding will be a major contributor to food security, as it has been in the past.
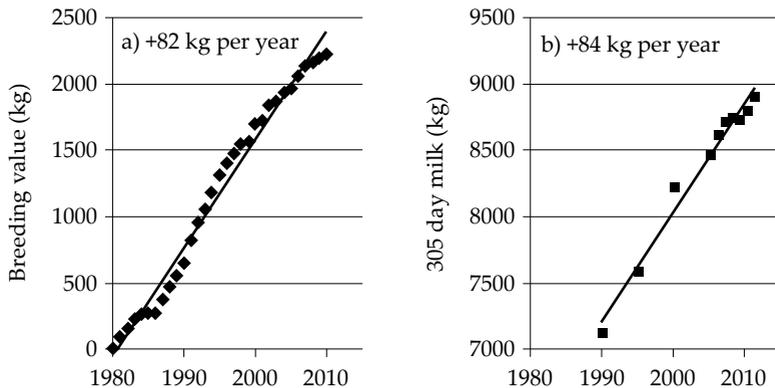
Figure 1 The estimated genetic trend for a 305 day milk production per cow per lactation (a) and the observed phenotypic trend (b) in the Netherlands

Explosion in the amount of genomic data

The second external driver is the development of genome sequencing technology that enables a completely new outlook on the numerical technologies we use today.

In this picture (Figure 2) you can see that within each cell the genome is presented on chromosomes. The genome is built from the DNA which is a long string formed by different combinations of four chemical bases. The length of the DNA differs - for the cow and pig there are around 3 billion (or 3 miljard in Dutch) of these bases, for the chicken just over 1 billion.

A relatively small part of the DNA consists of genes. Genes are a specific order of bases that can be translated in amino acids and these form the basis of biology in the body. In the cow there are about 22,000 of these genes. Most of these can also be found in other species.

More than 99% of the DNA is shared between individuals of the same species. As geneticist, we are most interested in the other 1% that creates the genetic variation. In this respect, for the sake of simplicity, I will focus only on the most common source of DNA variation termed "Snip". "Snip" stands for Single Nucleotide Polymorphism (SNP). This is a mutation where one of the single bases is replaced by another base. This is illustrated in the box above Figure 2 where we can identify two SNPs in an animal. For the first SNP the animal is heterozygous, as it received a different base from the sire and dam, and for the second SNP it is homozygous, but both bases are different from the reference genome.

From sire	...CAGTCAG**A**GTAC**C**AGTCT...
From dam	...CAGTCAG**T**GTAC**C**AGTCT...
Common reference	...CAGTCAGAGTAC**G**AGTCT...
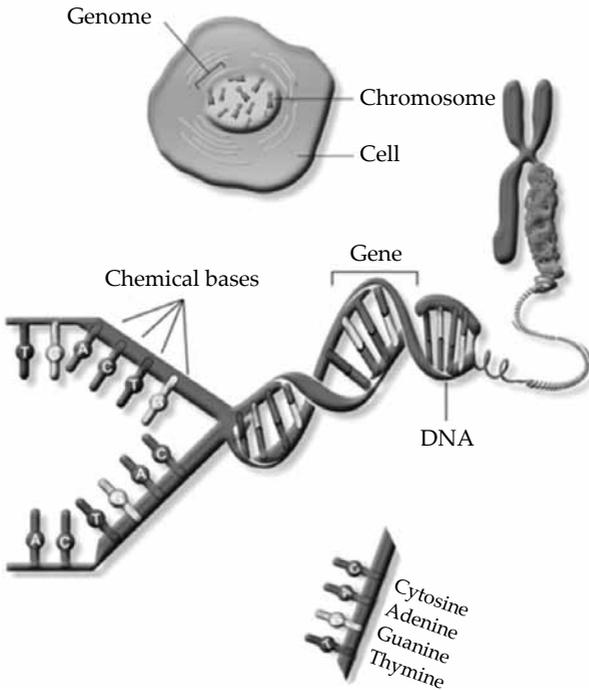
Figure 2 Illustration of a cell with the structure of the genome expanded (from: www.coriell.org)

At genome level there are millions of SNPs and, as you can imagine, it has always been a dream for geneticists and animals breeders to measure these differences at the DNA level on individual animals. Over the past 10 years we have seen tremendous developments in this area, as illustrated in Figure 3. Technological advances have resulted in a 1,000 fold cost reduction in obtaining a full genome sequence of an individual (Wetterstrand, 2012). Initially, the trend was as expected according to Moore's law (the straight line at the top). This law prescribed that for technology advances, for example for computers, you can expect a doubling of capacity every two years. However, recent advances in DNA sequencing technology have outperformed Moore's law considerably. It is for this reason that sequencing the genome of individual animals has become a realistic option and this requires that we re-think the methodology in the area of numerical genetics and genomics.

www.genome.gov/sequencingcosts
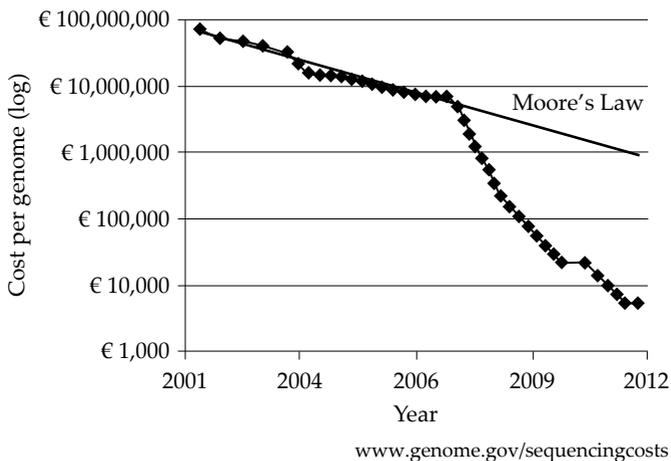
Figure 3 The reduction of the costs of sequencing a whole genome in comparison to Moore's law, that predicts that computers double in power every two years (Wetterstrand, 2012)

Interaction with the other species: human beings

The third external driver for my work might be somewhat of a surprise. It is the interaction with "the other species". No, not cattle, poultry, pigs or horses... no it is the interaction with humans that form an important driver for this research area.

Let me explain. You have seen in this little video a prime example that the human species is not only driven by objective rationality, but also by subjective factors, like wanting to belong to a group, looking for own identity, pride, or even maintaining relation. And I think that numerical methods play an important role in balancing between the objective and subjective rationalities.

Let me demonstrate that with some of my earlier work. My first project in the UK was to establish the value of linear type traits for selection. This was like balancing on a knife edge. On the one side a group of traditional breeders who believed that every type trait was very important, and on the other hand were a group of rational breeders that considered every type trait emotion and a waste of time. However, using numerical methods we were able to show the value of a few type traits and developed the first worldwide index that used linear type traits as early predictors for longevity. Most countries have followed this example today. The numerical methods and good communication helped me to stay teetering on that knife.

Another example is my work on the genetics of body condition score in cattle. Pedigree breeders loved the sharp and skinny dairy cows, they even called them the "typical dairy type". At the same time producers tried to maintain body condition

on cows, because it was important for their health and fertility. It was the numerical work establishing the genetics of body condition score that helped start the discussions on this subject and eventually changed the breeders' viewpoint. Today even the World Holstein Association has accepted this trait for their type classification.

For me these are two examples where numerical methods interact with the opinions & emotions of the other species, and in the end we co-innovated together to produce a better system. It was not simply a matter of explaining how it was, but it needed much more two-way interaction for the system to evolve.

I think these are important lessons for the future, but I fully understand these two examples are not convincing enough. However, if I expand "the other species" to society, consumers, and producers, my message maybe becomes clearer.

Consumer demands in Western Europe are not only related to the price of the product, but also to the perception of the product in terms of health, welfare, longevity, production environment and food safety. For example, consumers are concerned about obesity and relate that directly to the food they eat.

At the same time, society puts more and more constraints on the production environment. They question the use of technologies, the size of farms and they want to abandon the use of antibiotics and animal mutilations like beak trimming, tail docking, castration and routine caesarean sections. Just take the current ban of some supermarkets of the fast growing chicken, the so-called "plofkip", or the discussions if cows should be outdoor or not.

Producers have less room to manoeuvre due to financial constraints, scale enlargements and life style changes which are creating difficulties with labour on farms.

For me, these three groups form the other species, and will form an important driver for the future. I see the first signs already in practise: the demand that exists across all species for easy management and robust animals that require low input of labour. Anticipating on the other species is more complex than just measuring another trait, and requires a system approach. Luckily, there is a lot of experience with system innovations within Wageningen Livestock Research. For me this makes "the other species" not the subject of my own research field, but a very important driver for the direction in the future.

Internal drivers

Genetic architecture of quantitative traits

The area of quantitative genetics started well before basic biology was known. Mendel started in the 19th century and demonstrated that offspring peas have similarity with their parents, but also that there is a chance factor involved that causes variation. This chance factor is called Mendelian sampling and determines, in diploid animals, the SNP you will inherit from your grandma or grandpa, obviously through your parents.

At the beginning of the 20th century Fisher (1918) expanded Mendel's calculations to a general concept in which more genes affect a single trait. He introduced the term variance and the genetic correlation between performance of relatives. Furthermore, he developed the general principle that on average I share ½ of the SNP with each of my three brothers, but also ½ with each of my parents or children.

Although this might appear trivial at first sight, using this theoretical expectation, variance components can be estimated from phenotypic records, and these variance components describe the heritability and genetics of traits. Variance components are the basis of animal breeding and quantitative genetics today.

Several statistical procedures were suggested, but Residual Maximum Likelihood Estimation (REML) became the world standard method for the estimation of variance components (Patterson and Thompson, 1971). The development of software (Gilmour et al., 2000, Meyer, 1983) to estimate genetic variance components from large, unbalanced datasets with pedigree information recorded, stimulated a very vibrant research area in the mid-nineties.

Much of my own research, and that of my former PhD students, has been in this area. Initially single traits analysis was used to estimate the heritability of traits, for example the heritability for milk, fat or protein yield. Later multi-trait REML analysis became feasible, such that trade-offs between traits could be investigated. For example, the genetic correlations between fertility and milk yield, or between type traits and longevity.

Finally, more parsimonious descriptions of the multidimensional space describing genetic variances across traits, environments and time were introduced in the last decade.

At the same time the use of DNA information became increasingly popular. Either through genome-wide associated studies or the candidate gene approach, where

mutations in known genes were investigated. This became a large research area at the turn of the century. Markers linked to functional mutations (also called QTL) were expected to dissect the genetic architecture of traits (Mackay, 2001) and molecular genetics would finally detect the true genetic model underlying quantitative traits. However, identification of causative mutations has proven to be time consuming and costly, and single QTL tend to explain only a limited part of the genetic variation, meaning that impact on animal breeding has been relatively limited so far.

As nicely described by Bruce Walsh (Walsh, 2001), two paradigms have grown: the molecular geneticist (who is convinced that we need to investigate the fine details and mechanistic framework before we make progress) and the quantitative geneticist who has benefitted from ignoring the underlying genetic details using the robust Fisher approach.

This difference in paradigms can be illustrated with our own results. In Figure 4 for nearly 40,000 SNPs on the 30 cattle chromosomes, the statistical significance is given for the effects on feed intake in dairy cattle. A molecular geneticist would take the significant SNPs (above the dashed line) and identify, for example, the SNP with the highest blue dot on chromosome 27. This SNP is highly significant and is located in the middle of a tryptophan gene. This is, clearly, a feel good result for molecular geneticists. Tryptophan is involved in many processes related to feed intake and metabolic processes, and these are very well described in several species. However, a quantitative geneticist would derive that the significant SNP explains only a little of the total genetic variance, and therefore knowing the biology of this gene will contribute little to animal breeding.

I believe that this gap between the paradigms of the molecular geneticist and the quantitative geneticist will be closed in the next decade. Molecular geneticists will focus increasingly on genomic prediction rather than significant single gene effects. Quantitative genetics will get the tools to not only focus on Fisher relationships as a source of variation, but also try to explain genetic variation with the functional mutations measured at DNA level. This is important because using the functional mutations improves the applicability of genomic predictions across unrelated animals. So I believe that there is an exciting period ahead in which the genetic architecture of traits in the human being, plants and animal genetics will be dissected, and it will be an important internal driver for me to bridge the gap between these two paradigms using numerical methods.
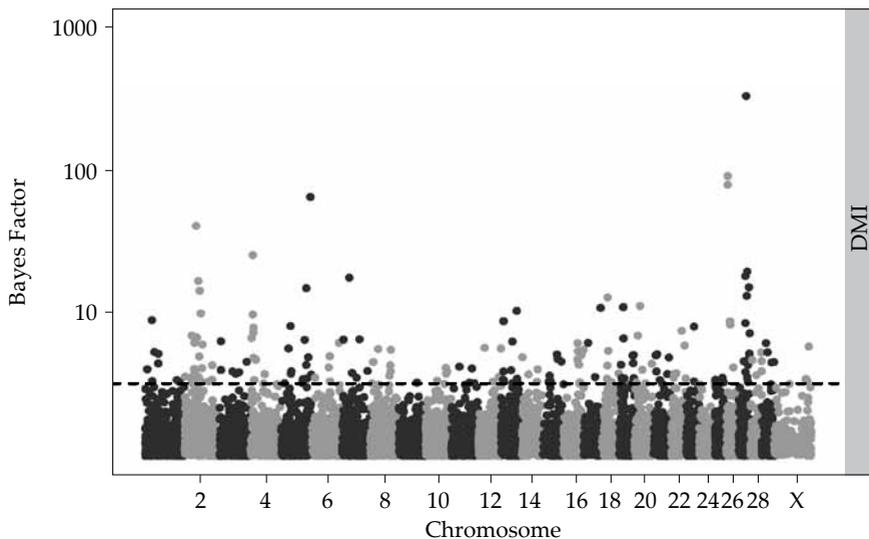
Figure 4 Significant SNP effects (above dashed line) on feed intake in Holstein heifers using RobustMilk datasets

Application in animal breeding

The application of numerical methods in animal breeding is the second important internal driver of my field. Robert Blackwell in the 18th century (1725-1795) has been documented as one of the first to practise performance recording (growth and feed intake), line breeding and a form of progeny testing (Simm, 2002).

It was only in the last century that animal breeding became increasingly acknowledged and numerically driven. First of all because of the theory developed by people like Fisher and secondly because of the development of computing power and computer algorithms that enabled the implementation of this theory. I have mentioned the importance of REML already, but in terms of the application of breeding value estimation, Henderson's (1953, 1975) Best Linear Unbiased Prediction or BLUP methodology became the world standard in the seventies.

The application of numerical methodology moved selection from phenotypic eyeballing of selection candidates towards selection on objectively measured traits. Initially focus was on production only, but gradually selection moved toward more extensive breeding goals with more and more traits. Currently in the Dutch-Flemish breeding goal for dairy cows not only productivity, but also many other traits, receive attention, for example, longevity is important (Figure 5). Similar lists can be produced for pigs and poultry breeders.

Several of my PhD students are working on important improvements in this area. For example, Margherita Caccamo utilizes these models to give farmers in Sicily better nutritional advice, John McCarthy is working on across breed evaluations, and soon a PhD student will start to improve the longevity evaluation in the Netherlands and Flanders.

Trait		Response (5 years)	Relative archievements
Milk	Kg	272	40%
Fat	Kg	13.0	47%
Protein	Kg	8.7	46%
% fat	%	0.01	
% protein	%	-0.01	
Longevity	Days	200	74%
Udder health	Pnt	2.3	50%
Udder	Pnt	1.8	39%
Feet and legs	Pnt	2.2	48%
Calving interval	Pnt	0.8	18%
interval 1^e-last insemination	Pnt	1.0	21%
Ease of birth	Pnt	1.4	30%
Ease of calving	Pnt	1.1	21%
Survival birth	Pnt	0.7	16%
Survival calving	Pnt	0.9	21%
Claw health	Pnt	1.9	43%

Figure 5 Traits in the NVI, the Dutch-Flemish breeding goal as guided by the expected response and the gain as a percentage of the genetic standard deviation for each trait

However, the use of DNA technology in animal breeding also became popular in the 1990s and although the dissection of the genetic architecture was difficult, several QTL were found. As simulation had revealed, higher genetic gains could be achieved using molecular information for traits that can only be recorded in one of the sexes (e.g., fertility) or phenotypic recording of traits is only possible late in life or even too late (e.g., slaughter traits, longevity) (Meuwissen and Van Arendonk, 1992).

The major breakthrough using DNA information came with the introduction of genomic selection in the last decade (Meuwissen et al., 2001). In genomic selection a large group of reference animals is phenotyped and genotyped with a large number of SNPs. Initially a few thousand, but currently 50,000 or even 800,000 SNP are used. Using numerical methods a value is put on each SNP, and a calibration equation is developed from combining both phenotypes and genotypes. The calibration equation can then be used to predict the breeding value of selection candidates. This methodology of genomic selection has improved the rate of genetic gain considerably especially in dairy cattle, up to 100% (Pryce and Daetwyler, 2012).

However, there are several factors that affect the accuracy of this calibration equation and large reference populations are required of well phenotyped animals (Daetwyler et al., 2008, Goddard, 2009). Also, predictions do not work very well across populations or breeds. Together with Mario Calus, we work on improving the efficiency of genomic selection. For example, Marcin Pszczola, a PhD student together with Poznan University, has done valuable work on the design of the reference population. Yvonne Wientjes is investigating the factors that determine the accuracy of genomic predictions across breeds and populations.

Research ambitions within the field of numerical genetics

You have heard the external drivers - food security, genome sequence data and "the other species". You have also heard the internal drivers:

i) dissecting the genetic architecture of complex traits; and

ii) the application of numerical methods in animal breeding.

So now it is time to zoom in on my ambitions. What are the areas where I, and obviously several of my colleagues and PhD students, will focus on in the coming years? We will:

- develop methodology and investigate the optimal use of sequence information in plant and animal breeding;
- enable selection for new traits: improving resource efficiency (feed efficiency and methane emission) in dairy cattle;
- investigate the genetic architecture of the correlation between traits.

Utilizing DNA sequence information in breeding

To date the full genome of about 39 Dutch born bulls have already been sequenced (some by other countries). Many important founders of the Holstein breed will be recognized by the cattle breeders. Similar more and more plants have been sequenced. However, sequence information on its own does not contain functional information and it just takes up a lot of space on our computers.

Therefore, together with Prof. Fred van Eeuwijk in the Plant Science Group and the PhD student Rianne van Binsbergen, we will investigate the statistical techniques required to make sequence data functional in plant and animal breeding, for example through genomic selection.

As a first step we have teamed up with the 1,000 bull genome consortium, coordinated by Ben Hayes in Melbourne, and brought together the full sequence of hundreds of bulls. In the first run there were a 150 bulls present and 15 million SNPs were identified for these animals. These form the base for our further work.

Many direct research questions exist like:
- How can we handle such a large volume of data (15,000,000 times 150 sires is already a lot of data-points, and have to use at least 20,000 sires) and still predict breeding value and estimate variance component weekly?
- Can we estimate genetic effects from limited phenotypic data with so many SNPs (statistical P>N problem) and/or do we need to do pre-selection utilizing functional information?
- Do we need to sequence all animals in the population or can we infer the full sequence for animals that have been genotyped and their sire sequenced?

These are research questions with practical relevance that need to be addressed, however, the most fundamental question is: are we going to select more accurately in animal breeding using this detailed information on the genome and what should our statistical model assume?

My initial presumption is, yes, animal breeding is going to benefit because with sequence data we get more accurate prediction equation that would last across populations, breeds or unrelated animals. This is because we no longer rely on the non-random associations between QTL and functional SNP. It is well-known that the current SNP chips we use have an ascertainment bias: they do not contain SNP with a low minor allele frequency. These differences in allele frequency reduce the association between QTL and SNP considerable, and leads to a strong bias found in QTL detected in several species (Figure 6). In many species they only find the SNP with a very strong effect or with a very large minor allele frequency. With sequence information the causative SNP are included and therefore we should identify QTL more accurately.

If we are going to be better off with sequence data, there are however a few uncertainties. The first questions is if our numerical methods can handle so many SNPs compared to the number of available phenotypes. Our current methods might

not be able to sufficiently separate noise from true QTL effects and this noise might lead to inaccuracy of selection. The second questions is if we can improve the accuracy of the breeding values, since in livestock species we have a lot of relationships between animals. These relationships cause associations between SNP and QTL that might be hindering the detection of functional SNP. These relationships might also provide such a high accuracy that it will be difficult to increase the accuracy of the genomic predictions. Still the persistency across several generations and breeds night improve.
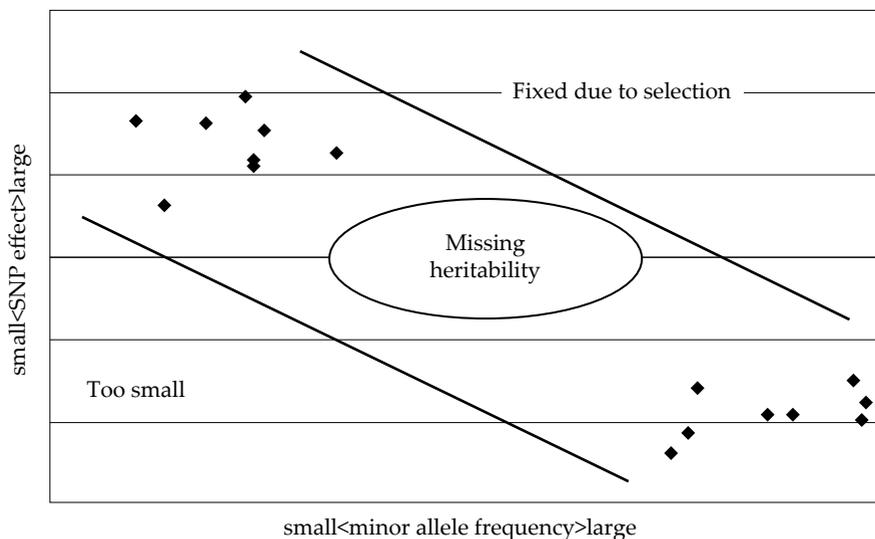
Figure 6 The graphical illustration of the QTL (green dots) that have generally be found in different species

To work out where the advantage in utilizing sequence data lies (none, accuracy or persistency) is an important research question for my future work. Eventually, the outcome of this research will also affect the best method for applying genomic predictions with extreme high density genotypes. I would hypothesis that we need the models that include the individual SNP effects specifically, like the method used in routine evaluations of dairy cattle in the Netherlands (Calus et al., 2008), rather than the easier implementable methods based on the genomic relationship matrix.

New traits: resource efficient dairy cows
Food security is important drivers for my research. What is lacking, however, in dairy cattle breeding, is information on resource efficiency and ecological footprint. Resource efficiency is important for animal production systems because:

i) ruminant animals account for up to 20% of worldwide methane production; and
ii) ibecause of the shortage of energy supplies: the food, fuel, forest and fibre
discussion mentioned before.

Although there has been a lot of research into the genetics of feed intake and feed efficiency, not the least my own work, the application has been hindered by the difficulty and the cost of recording feed intake on individual cows.

I think genomics and pooling of data from breeding and research herds across the world might be a way out of this bottleneck. If we can bring datasets together for these new traits, to develop genomic prediction equations, I can envisage that even in dairy cattle breeding programmes we can start selection for these difficult traits such as dry matter intake (DMI) and greenhouse gas (GHG) emissions (de Haas et al., 2011).

Recently, by international collaboration, we have made an important step by pooling feed intake records in the global dry matter initiative, that I coordinate. More than 10,000 lactations with feed intake recorded on 7,000 animals have been put together, and all these animals have been genotyped. Now we can investigate if it will work to deliver accurate genomic predictions for feed intake for each partner. But, the numerical challenges are large, for example, how to combine the different phenotypes, measured in different systems, and how to deal with stratification of genotypes and phenotypes. Together, we have split to work, and are addressing these research questions. Later this year the Mexican PhD student Coralia Manzanilla will start her PhD project in this area under my supervision.

Genetic architecture of trade-offs

The third interest I have is to quantify the genetic associations between traits in a more accurate way than with genetic correlations. For example, to describe trade-offs between yield and fertility or describe the genetic association between traits like liveweight, body condition score, feed intake and milk yield (Figure 7). From variance components we know that all these traits are correlated, but what is the underlying genetic architecture for the genetic correlation? Has selection for milk yield an equal effect on feed intake, as selection for feed intake has on milk yield?

What makes the genetic correlation particularly interesting is that it is relatively sensitive to the underlying genetic model (Bohren et al., 1966), in contrast to the heritability. Also, the genetic correlations are more likely to be affected by (genomic) selection. I think, with the use of sequencing data and the more precise detection of causative SNP, we might be able to test alternative models to describe the genetic co-variation between traits, and allow for genetic associations between traits that are

nonlinear and asymmetric; this will also allow us to separate the effects of linkage disequilibrium and pleiotropic effects. This might then enable more accurate prediction of trade-offs in animal breeding, which is important to stay teetering on the edge of the knife in order to co-innovate with the other species.
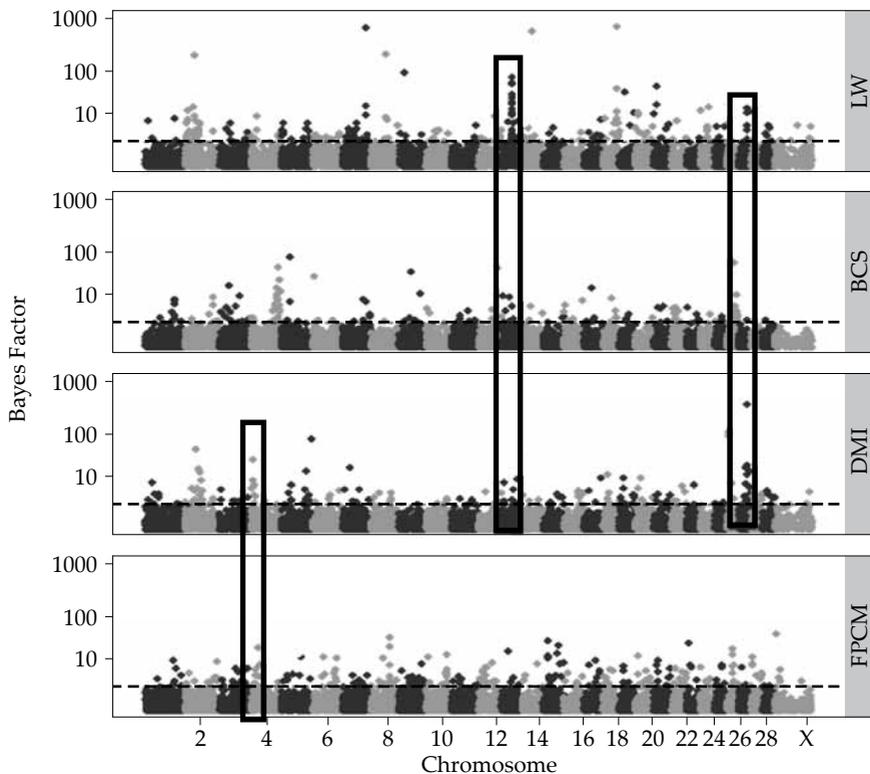
Figure 7 Significant SNP effects (above dashed line) on traits in the feed intake complex of Holstein heifers: liveweight, body condition score, feed intake and fat-protein corrected milk production

In conclusion

In this address I have taken you on route through the external and internal drivers of the field of numerical genetics and genomics. Together these formed my ambitions in the field of numerical genetic and genomics. Collaboration in many different directions, is a key to achieve these ambitions. I believe that if the impact and importance is large enough, traditional boundaries dissappear.

To students I would like to say, these are very exiting areas, with very good job opportunities and huge potential impact in practise and science. Four of my former PhD students gave a major invited presentations at the last EAAP. All smiling and

enjoying their successful international careers. As a special professor, you will not encounter me during many courses, but that should not stop you to get in touch with me. If you are interested in pursuing a career in this area, you are very welcome to do a thesis.

And, as promised, I end the tour with the take-home message:
"In the era where measuring the full DNA sequence of individual animal genomes becomes standard and there is a need to breed animals that fit the needs of society, numerical methods are the key for co-innovation"

But before closing, I would like to share some words of gratitude with you.

First of all I would like to thank Mr. Rector Magnificus, for the trust in me and accepting me as new Professor at this university. Furthermore, I would like to thank Martin Scholten, Paul Vriesekoop and Johan van Arendonk for their trust and involvement in my appointment. Wageningen Livestock Research provides the finance for this position, and the freedom to pursue this path.

There are many people who have had a positive influence on me during my training. First at the Agricultural College in Deventer and later at Wageningen University. Some people I am particularly grateful to are Prof. Pim Brascamp who sent me to Edinburgh for my M.Sc. thesis and Prof. Chris Haley who awoke my numerical interests during that visit. After that I started my first job in Edinburgh at SAC, and simultaneously undertook a Ph.D, with three special people: Prof. Geoff Simm at SAC, Prof. Bill Hill at the University of Edinburgh and Prof. Robin Thompson at the Roslin Institute. Undoubtedly these people and the seven years in Edinburgh have been very influential on me. After seven years in Edinburgh I moved to Lelystad, Kor Oldenbroek and Sierk Spoelstra were my superiors. I am very thankful for the opportunities they gave me and the many skills I learned during those years.

Also, I want to express my appreciation to all the colleagues that form and have formed the research teams I have been part of. Some of these teams are institutional, but others are more virtual. For example, the RobustMilk team. The interaction with all of you is probably the biggest stimuli for my work.

Four important colleagues I would like to name specifically - because they are very directly involved in fulfilling the ambitions presented here: Mario Calus who has become a world player in the area of genomic prediction and selection, and Yvette de Haas who is leading the work on resources efficiency in dairy cattle. Prof. Mari Smits and Prof. martien Groenen as leading genomics expert in our group.

I would also like to express words of gratitude to Johan van Arendonk and his group. I am very pleased to become a Professor in your group. As managers we also joined forces and formed the Animal Breeding and Genomics Centre. We were committed to becoming a cohesive force and made ABGC the place to be. Lucia Kaal has now taken over my management responsibility and I trust her to strengthen ABGC even further. With our collaborators in Breed4Food, CRV, Topigs, Hendrix Genetics and Cobb we are now taking the next step.

The cooperation with the breeding industry has been a major stimulus throughout my career. During my period in the UK, the work for ICBF in Ireland, CRV, the AI organizations grouped together in GES, and more recently the collaboration with the Breed4Food partners. These collaborations convince me that science and impact go hand-in-hand, even in a field such as numerical genetics and genomics.

The Hammink family in Almelo awoke my interest in animal breeding. Although there are no genetic relationships, our friendship is deeply rooted in our pedigree.

Charles and Mieke. It is the clear mindedness of my father, together with the creativity of my mother, that formed me. But both of you have been a great support during my career, but also for the family over the past years.

Then to my three brothers, Harm, Bert and Wouter. You have now learned that Mendelian sampling makes us unique, but I am pleased that in real life we share more than half the genetic variation.

Finally, I would like to thank Gerlien and our children Kirsten, Tim and Jorik. To you children - you brighten our lives with your presence as unique persons, but also collectively as a family.
Gerlien, what you have given me over the past 27 years is indispensable and so unique that it is not for sale or even makeable: love, support and happiness. Thank you.

I have said,

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'Producing more food from less inputs, whilst maintaining health and welfare of animals, is the major challenge for animal production systems. Numerical methods applied in animal breeding have made a major contribution already. Genome information will provide even greater opportunities to select for new and important traits, and also to investigate the genetics underlying these complex traits. At least, when numerical methods allow us to draw inferences from these large amounts of data.'