

# Non-genetic variance in pigs

Genetic analysis of reproduction  
and production traits



Ewa Sell-Kubiak

Non-genetic variance in pigs

Ewa Sell-Kubiak



**Non-genetic variance in pigs:  
genetic analysis  
of reproduction and production traits**

**Ewa Sell-Kubiak**

**Thesis committee****Thesis promotor**

Prof. Dr J.A.M. van Arendonk  
Professor of Animal Breeding and Genetics  
Wageningen University

**Thesis co-promotors**

Dr Ir P. Bijma  
Assistant Professor, Animal Breeding and Genomics Center  
Wageningen University

Dr Ir H.A. Mulder  
Assistant Professor, Animal Breeding and Genomics Center  
Wageningen University

**Other members**

Prof. Dr E.N. Stassen, Wageningen University  
Dr S. Janssens, Catholic University Leuven, Belgium  
Prof. Dr J. Szyda, Wroclaw University of Life Sciences, Poland  
Dr A.E. Huisman, Director R&D Hendrix Genetics, The Netherlands

This research was conducted under the auspices of the Graduate School of Wageningen Institute of Animal Sciences (WIAS).

# **Non-genetic variance in pigs:**

**genetic analysis of reproduction and production traits**

Ewa Sell-Kubiak

## **Thesis**

submitted in fulfillment of the requirements for the degree of doctor  
at Wageningen University  
by the authority of the Academic Board,  
in the presence of the  
Thesis Committee appointed by the Academic Board  
to be defended in public  
on Monday 22 June 2015  
at 1.30 p.m. in the Aula.



Sell-Kubiak, E.

Non-genetic variance in pigs: genetic analysis of reproduction and production traits  
186 pages.

PhD thesis, Wageningen University, NL (2015)

With references, with summaries in English and Dutch

ISBN 978-94-6257-329-1

## **Abstract**

Sell-Kubiak, E. (2015). Non-genetic variance in pigs: genetic analysis of reproduction and production traits. PhD thesis, Wageningen University, The Netherlands

The main objective of this thesis was to study the origin of random variance in reproduction and production traits of pigs. In pig breeding for many traits it is important not only to improve the reproduction and production trait itself, but also its variation. The variance of traits can be used to improve pigs' productivity, and potentially also to improve uniformity of traits. Results presented in Chapters 2 and 3 show that the proposed approach to explore the origin of common litter variance was not successful. The impact of various sow features on growth rate and feed intake of grow-finish pigs was very small. More importantly, sow features did not explain the phenotypic variance due to common litter effects found in production traits of pigs. In Chapters 4 and 5 the residual variance of birth weight and litter size were found to have a genetic component. The genetic coefficient of variation at residual standard deviation level ( $GCV_{SDe}$ ) was proposed as a measure of expressing the potential response to selection (Chapter 4). For both traits the estimated  $GCV_{SDe}$  was about 10%, indicating sufficient potential for response to selection. In Chapter 4 it was shown that analyzing variation in traits with Double Hierarchical Generalized Linear model (DHGLM) was highly comparable with the conventional analysis of standard deviation of a trait. The correlation between the additive genetic effects for birth weight and the residual variance was 0.6 (Chapter 4), whereas for litter size (TNB) and its residual variance ( $varTNB$ ) this correlation was 0.5 (Chapter 5). Those moderate correlations are an important indication of the direction of correlated selection response in the mean of those traits. In Chapter 5 in a genome-wide association study for litter size variation, the significant SNPs explained 0.83% of total genetic variance in TNB and 1.44% in  $varTNB$ . The most significant SNP explained 0.4% of genetic variance in TNB (chromosome 11) and 0.5% in  $varTNB$  (chromosome 7). One of the possible candidate genes for  $varTNB$  on chromosome 7 is heat shock protein (*HSPCB*). Studying the residual variance of traits with DHGLM has a great potential to serve as an alternative to conventional analysis to study and to select for improved uniformity of various traits. Lastly, Chapter 6 focuses on discussion of the findings of this thesis and their overall importance for pig breeding, as well as highly relevant topics for breeding uniform and robust pigs (macro-micro sensitivity analysis and application of genomic selection).



***For My Boys***



## **Contents**

5	Abstract
11	1 – General introduction
19	2 – Effect of sow history features on growth and feed intake in grow-finish pigs
41	3 – Effect of gestating sow body-condition, feed refusals and group-housing on growth and feed intake in grow-finish pigs
65	4 – Comparison of methods to study uniformity of traits: application to birth weight in pigs
93	5 – Genome-wide association study reveals novel loci for litter size and its variability in pigs
117	6 – General discussion
135	Summary
141	Samenvatting
147	References
167	Curriculum vitae
171	Publications
175	Training and supervision plan
179	Acknowledgments
185	Colophon





# 1

## **General introduction**



### 1.1 The importance of the environment to breeding

Livestock breeding is focused on the selection of desirable genotypes. The expression of the genes, however, is strongly influenced by the environment in which the animal is born and kept throughout the reproductive and productive lifetime. The success of the selection depends also on interaction between genotype and environmental factors (GxE, Falconer and Mackay, 1996). The environment in which the animal performs can be characterized by a number of known factors, *e.g.*, farming system, management, temperature, or feed quality. Those known factors are defined as macro-environment (Falconer and Mackay, 1996). Yet, not all of environmental effects are already defined (measured) or possible to obtain. In the literature this unknown factors are referred to as micro-environment (Falconer and Mackay, 1996).

Since the environment affects success of selection, the environmental effects are always taken into account in breeding practice. In genetic (animal) models they are included as non-genetic fixed or random effects (Lynch and Walsh, 1998). Non-genetic fixed effects account for the variation between the animals, that is constant over time, not random and affects all the animals in the same manner (Lynch and Walsh, 1998). Fixed effects can be: sex of the animal, farm, or feeding strategy. Non-genetic random effects account for the random variation between the related animals (Lynch and Walsh, 1998). Those effects are in particular useful when repeated measures are made on the same individual or a cluster of related individuals. In pig breeding an example of non-genetic random effect is permanent sow and common litter effect (see section 1.2). Most of the non-genetic effects can be quantified, because their source is known. They are called then macro-environmental effects. The macro-environmental effects can be included directly in the animal model, which allows breeders to quantify – to some extent – those effects due to information on multiple records. This is done by estimating the contribution of the known effects to the total phenotypic variance of a trait (performance) of an animal. In case the source of environmental effect is not known or difficult to quantify, then such an effect is accounted for in the residual term of the model. The residual gathers all the remaining environmental effects that exist between the animals and cannot be accounted for by any other effects in the model. Those effects represent the micro-environmental factors.

This thesis is focused on the non-genetic random variance found in reproduction traits of sows and production traits of grow-finish pigs. The subsequent sections of this chapter describe in more details the non-genetic effects of permanent sow and common litter as well as residual variance.

## 1. General introduction

---

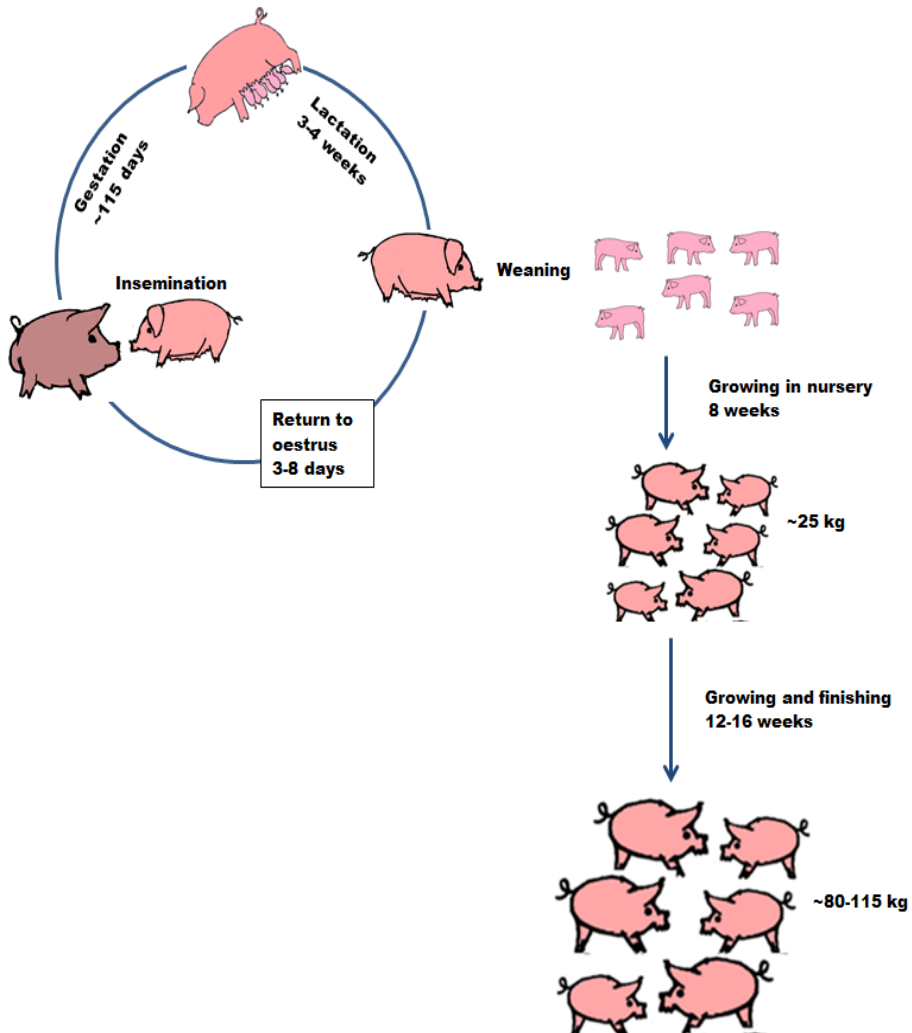


Figure 1.1. Pig production cycle.

### 1.1.1 Common litter and permanent sow effects in pig traits

In pig breeding the permanent sow and common litter effects can be distinguished as known non-genetic random effects. These effects affect productivity of a pig throughout its entire life (Figure 1.1). In pig farming, the sow gives birth to a litter of 12-15 piglets approximately 2.3 times a year. The sow and her piglets commonly stay together for 3-4 weeks until weaning. The full-sibs from one litter share a common environment in prenatal (gestation) and postnatal (nursing/lactation) period. This common environment is captured by the 'common litter effect'. At weaning, the piglets are moved to the nursery to grow till about 25kg. The period from 8 weeks of age till slaughter is generally referred to as the grow-finish phase, where pigs stay till slaughter weight of about 80-115 kg. As the sow farrows several times during her production life, repeated observations on the quality of the offspring – which the sow farrows and weans – are available. The full- and/or half-sibs – offspring from the same sow – share the prenatal and postnatal environment common to all the piglets being born and nursed by one sow during her production lifetime. This shared environment can be captured by the 'permanent sow effect'.

The permanent sow effect is most commonly included in animal models analyzing sow's reproduction traits (*e.g.*, litter size) or piglets' traits (*e.g.*, weaning weight). The permanent sow effects present in traits of offspring decrease over time (Solanes *et al.*, 2004). Even though large permanent sow effects are present in piglets' traits (Solanes *et al.*, 2004; Canario *et al.*, 2010; Kapell *et al.*, 2011), the contribution of these effects to the variance in grow-finish traits is small or even non-existent (Johnson *et al.*, 2002; Chen *et al.*, 2002; Ferraz *et al.*, 1993; Crump *et al.*, 1997). Permanent sow effects are, therefore, often ignored when studying production traits in grow-finish pigs (Chen *et al.*, 2002).

The common litter effect is accounted for when estimating the breeding values of production trait of pigs that originate from the same litter (Bidanel *et al.*, 1996; Johnson *et al.*, 2002; Chen *et al.*, 2002; Kuhlert *et al.*, 2003; Neugebauer *et al.*, 2010). Unlike permanent sow effect, the common litter effect has a substantial contribution to variation in traits recorded on grow-finish pigs, such as growth rate and feed intake. The growth rate usually has the highest estimate of common litter variance, varying from 10% to 25% of total phenotypic variance (Bidanel *et al.*, 1996; Johnson *et al.*, 2002; Van Wijk *et al.*, 2005). The estimates for feed intake are slightly lower: 7% (Neugebauer *et al.*, 2010) and 16% (Bergsma *et al.*, 2008). Although the common litter effect is measurable, its precise origin – in other words relating it to specific characteristics of a sow – is still unknown. Explaining it, could help to decrease the variation of the production traits and to breed more uniform grow-finish pigs through management practices.



### 1.1.2 Residual variance in pig traits

The residual variance gathers the environmental effects – in any trait – that cannot be measured by known factors. In traditional animal breeding it is commonly assumed that the residual variance is homogenous across the observations and has in general non-genetic origin. The residuals are assumed to follow the same distribution, and thus there is no variation between them.

Recent studies, however, indicate that there is evidence for a genetic variation in residual variance, also called in literature micro-environmental sensitivity or genetic heterogeneity of residual variance (Falconer and Mackay, 1996). This means that the residual variance of the traits is not homogenous among the animals, but heterogeneous. Moreover, part of this variance has a genetic component. The empirical evidence for heterogeneity of residual variance has been found for various traits in livestock, *e.g.*: within-family variation in milk yield in dairy cows (Van Vleck, 1968; Clay *et al.*, 1979), fat/protein ratio in milk of goats (SanCristobal-Gaudy *et al.*, 1998), litter size in pigs (Sorensen and Waagepetersen, 2003), body weight in broilers (Rowe *et al.*, 2006; Wolc *et al.*, 2009; Mulder *et al.*, 2009), slaughter weight in pigs (Ibáñez-Escriche *et al.*, 2008), and birth weight in rabbits (Garreau *et al.*, 2008). Different methods are available to estimate the genetic variance in variation of traits as summarized by Hill and Mulder (2010).

Recently, Rönnegård *et al.* (2010) showed that the Double Hierarchical Generalized Linear model (DHGLM; Lee and Nelder, 2006) could be applied in analysis of the residual variance of a trait. A number of studies already used DHGLM to estimate variance components for the residual variance in: number of teats in pigs (Felleki and Chalkias, 2010), pig litter size (Felleki *et al.*, 2012) and dairy production data (Rönnegård *et al.*, 2013; Vandenplas *et al.*, 2013; Mulder *et al.* 2013a,b; Wijga, 2013). The genetic component in residual variance in these studies was relatively large, as the genetic coefficient of variation on standard deviation level varies from 0.08 to 0.12. This means that the residual variance as a source of variation between the animals can be decreased by genetic selection and potentially used for breeding more uniform pigs.

Unlike permanent sow or common litter effects, the variation between the animals caused by the residual variance is present in every trait. Studying the residual variance as a tool to breed more uniform pigs has much broader application, since it is not limited only to serve the production or reproduction traits of pigs.

### 1.2 The objective

The main objective of this thesis was to study the origin of random variance in reproduction and production traits of pigs. In pig breeding for many traits it is important not only to improve the trait itself, but also to decrease its variation. Obtaining uniform pigs on various production stages is an important goal in pig breeding. Knowledge on variance, can be used to improve pig productivity, and potentially also to improve uniformity of traits. In this thesis the variance was studied with several different approaches. The first approach focused on exploring the effect of sow features – characterizing the sow before the first insemination and during each gestation – on performance of their offspring. The sow features were selected as potentially explaining the background of common litter effects present in grow-finish traits. The second approach was studying the residual variance in sow reproduction traits by application of DHGLM. The residual variance describes the variation of the trait within the population and has potential to be used to obtain more uniform pigs or uniform litter size between sows. Finally, the genetic architecture of residual variance was explored with application of a genome-wide association study (GWAS).

### 1.3 Thesis outline

Chapters 2 and 3 study the background of the common litter effect.

Chapter 2 focuses on sow history features, which are features that characterize the sow (from birth until first insemination), and on their effect on feed intake and growth rate in grow-finish pigs. As the first step, it was tested whether the sow features affect grow-finisher traits. As the second step, significant sow features were simultaneously included into the full animal model to study their impact on common litter and permanent sow effects in production traits.

In Chapter 3 the concept of the sow features affecting production traits is investigated further. Sow features collected on group-housed gestating sows are used to study their effect on performance of grow-finish pig and whether the common litter and permanent sow effects can be explained by the those sow features.

Chapter 4 and 5 study the residual variance.

Chapter 4 studies the application of a Double Hierarchical Generalized Linear model (DHGLM) to analyze variation in birth weight in pigs. A DHGLM is compared with a conventional genetic analysis of the within-litter variation.

In Chapter 5 the genetic architecture of residual variance in litter size is studied by use of DHGLM and genome-wide association study (GWAS). GWAS is performed on

## 1. General introduction

---

deregressed estimated breeding values obtained with the DHGLM to identify genomic regions associated with litter size and its variation in pigs.

Finally, Chapter 6 focuses on discussion of the findings of this thesis and their importance for pig breeding as well as other aspects important for overall improvement of uniformity and robustness of pigs.

# 2

## **Effect of sow history features on growth and feed intake in grow-finish pigs**

E. Sell-Kubiak<sup>1</sup>, E. F. Knol<sup>2</sup>, P. Bijma<sup>1</sup>

<sup>1</sup> Animal Breeding and Genomics Centre, Wageningen University, PO Box 338, 6700 AH Wageningen, The Netherlands; <sup>2</sup> Topigs Norsvin Research Center, P.O. Box 43, 6640 AA Beuningen, The Netherlands

Journal of Animal Science (2012) 90(1):116–126

## **Abstract**

The sow provides a specific environment to her offspring during gestation and lactation. Certain features in the sows' early life (sow history features) may affect her ability to deliver and feed a healthy litter. In genetic analyzes of grow-finish traits these effects are estimated as a common litter or permanent sow effect. The objective of this research was to identify sow history features that affect the growth rate (GR) and feed intake (FI) of her offspring during grow-finish stage. Data from 17,743 grow-finish pigs, coming from 604 sires and 681 crossbred sows, were recorded between May 2001 and February 2010 at the experimental farm of the Topigs Norsvin (Beilen, The Netherlands). The grow-finish stage was divided into two phases (phase one: 26-75 kg and phase two: 75-115 kg). The sow history features were: birth litter size, birth year and season, birth farm, weaning age, age being transferred to experimental farm, and age at 1<sup>st</sup> insemination. The sow features were added to the basic model one at a time to study their effect on grow-finish pigs' traits. Subsequently, significant sow features ( $P < 0.1$ ) were fitted simultaneously in an animal model. With every extra piglet in the sow's birth litter, GR of her offspring decreased by 1 g/day and FI decreased by 4 g/day. Every extra day to the 1<sup>st</sup> insemination increased GR of grow-finish pigs by 0.1 g/day. The heritability estimates for GR and FI (only in the phase two of grow-finish stage) decreased after adding the sow features to the model. No differences were found in estimates of the common litter effects between the basic model and the model with all significant sow features. The estimates of the permanent sow effect changed for FI from 0.03 (basic model) to 0.00 (model with sow features) and for GR in phase one the permanent sow effect decreased from 0.03 (basic model) to 0.01 (model with sow features). In conclusion, selected sow features do affect grow-finish pigs' traits, but their estimates are small and explain only a small proportion of the differences in GR and FI of grow-finish pigs. The sow features partially explained the permanent sow effect of FI related traits and did not explain the common litter effect. Although the sow early life features can affect piglets traits, they do not predict which sows produce better performing offspring in grow-finish stage.

Key words: common litter effect, pigs, production traits, sow permanent effect, sow history

### 2.1 Introduction

The sow has a large genetic and environmental impact on her offspring during gestation (prenatal effect) and from farrowing until weaning (postnatal effect). This environmental impact of a sow can also be seen in permanent sow ( $s^2$ ) and common litter ( $c^2$ ) estimates in genetic studies (Chen *et al.*, 2002; Kuhlert *et al.*, 2003). The common litter effect describes the resemblance between full-sibs due to common environment. This is clearly visible in pigs, where large full-sib litters are carried, delivered and fed by the same sow. The average daily gain in pigs is shown to have the highest  $c^2$  from 0.10 (Van Wijk *et al.*, 2005) to 0.25 (Johnson *et al.*, 2002). Those values suggest that a substantial part of phenotypic variance can be explained by the environmental impact of a sow. Certain features in a sow's life (sow history features) may affect her ability to deliver and feed a healthy litter. Yet, at present the factors underlying  $c^2$  are largely unknown.

The sow history features can be divided into two groups. The first group relates to the sow's early life, *e.g.* birth litter size or weaning age. These features describe sow's life as a gilt and can affect her reproductive performance later in life. The second group relates to the gestation period, *e.g.* feed intake and size of the group during gestation. These features describe the period of gestation, which is common for all the piglets in the litter. Features from both groups could be important for the environment the sow provides to her offspring. Thus the sow features may affect performance of her offspring.

This study focuses on the first group of the sow history features. The first objective is to identify the sow features from her early life that affect her offspring's performance. For this purpose, the effects of sow features on growth rate and feed intake of her offspring will be estimated. The second objective is to investigate whether the sow features can explain  $s^2$  and  $c^2$  estimates in grow-finish pig traits.

### 2.2 Materials

Animal Care and Use Committee approval was not required for this study, because the data were obtained from existing database.

#### 2.2.1 Grow-finish pigs

Data were obtained from the Topigs Norsvin experimental farm (Beilen, The Netherlands). The farm has a farrow-to-finish structure, with 180 crossbred sows and rotational use of 6 sire lines in a 3-week batch management of farrowing. To enable comparison between different line crosses, 2 sire and 2 sow lines are used



## 2. Effect of sow history features on grow-finish pigs

in every batch. The number of grow-finish pigs per cross is presented in Table 2.1. Around 25% of the piglets were cross-fostered to provide additional data on maternal abilities of sows.

Records from 17,743 grow-finish pigs, coming from 604 sires and 681 sows, were collected between May 2001 and February 2010. The grow-finish pigs were housed in pens with 6 – 12 individuals. The pen contained animals of the same sex (female, male or barrow) with a similar start body weight to minimize weight variation.

In each batch, part of the grow-finish pigs was fed *ad libitum*. Their feed intake was recorded using IVOG feeding stations (INSENTEC, Marknesse, The Netherlands).

**Table 2.1.** Number of grow-finish pigs per combination of sire line<sup>1</sup> and sow cross<sup>2</sup> for two feeding strategies.

Sire line	Feeding strategy <sup>3</sup>	Sow cross				For sire line	Total sum
		F	G	H	I		
A	restricted	61	560	1,082	-	1,703	2,670
	<i>ad libitum</i>	109	382	476	-	967	
B	restricted	165	1,248	1,268	6	2,687	4,635
	<i>ad libitum</i>	519	713	527	189	1,948	
C	restricted	143	1,362	719	0	2,224	3,952
	<i>ad libitum</i>	446	802	353	127	1,728	
D	restricted	21	405	379	15	820	1,904
	<i>ad libitum</i>	275	419	285	105	1,084	
E	restricted	217	1,358	727	0	2,302	3,974
	<i>ad libitum</i>	416	686	320	250	1,672	
For sow cross	restricted	607	4,933	4,175	21		
	<i>ad libitum</i>	1,765	3,002	1,961	671		
Total sum		2,372	7,935	6,136	692		17,135 <sup>4</sup>

<sup>1</sup>A to E are different sire lines. <sup>2</sup>F to I are different sow crosses. <sup>3</sup>Grow-finish pigs used in this study were fed *ad libitum* (n=7,727) or restricted (n=10,015) at group level; individual feed intake was not available for restricted fed animals. <sup>4</sup>Total number of grow-finish pigs used in this study was 17,743; 608 grow-finish pigs not included in this table came from lines of low frequency.

Overall 7,728 grow-finish pigs were fed *ad libitum* and the remaining 10,015 were fed restricted at group level; individual feed intake was not available for restricted fed animals. On a group level the grow-finish pigs fed restricted, had feed intake of ~90% of feed intake in grow-finish pigs fed *ad libitum* (Bergsma *et al.*, 2008). Feed for grow-finish pigs fed restricted was transported once per day to the feeder located in a pen. For both groups, feed was provided in a feeding station that allowed only one animal at the time. Above the feeding station water source was provided.

### 2.2.2 Grow-finish pigs' traits

The grow-finish system aimed at a start weight of ~26 kg and a slaughter weight of ~115 kg. Each grow-finish pig was weighted before entering the pen (start weight) and at slaughter. The grow-finish stage in The Netherlands is traditionally divided into two phases; which is used for comparison of the feed conversion ratio in both phases and to optimize the feeding curve. Phase one – from the start to the middle of the grow-finish stage at ~75 kg (mid weight) and phase two – from the middle to the end of the grow-finish stage. The mid weight was recorded only for the grow-finish pigs fed *ad libitum*. Growth rate (g/day) was calculated by subtracting start weight from slaughter weight and dividing by the number of days spent in the pen. Growth rates in phase one and two were calculated based on differences between mid and start weight or slaughter and mid weight.

The study focused on two traits: growth rate and feed intake. Yet, as a result of two phases in the grow-finish stage, 6 traits were distinguished: growth rate (GR), growth rate – during phase one (GR-1), growth rate – during phase two (GR-2), feed intake (FI), feed intake – during phase one (FI-1), and feed intake – during phase two (FI-2).

### 2.2.3 Sow history features

Data on sow history features contained records on 681 crossbred sows. The sows had been transferred as gilts to the experimental farm of Topigs Norsvin, from 5 commercial farms (232, 209, 135, 72, and 21 sows per farm), and were kept at the experimental farm as mothers until their 6<sup>th</sup> parity.

The sow history features were recorded before the sow's 1<sup>st</sup> insemination (Figure 2.1). These features were: size of the litter in which the sow was born (birth litter size), season of birth (birth season), sow's farm of birth (birth farm), weaning age in days, age transferred to the experimental farm in days (age transferred), age at 1<sup>st</sup> insemination in days. Records of sow's birth farm and birth season were combined (birth farm/season) and given unique code. Data were not available for: sex

## 2. Effect of sow history features on grow-finish pigs

composition of birth litter, size of the suckling group, description of the group in which gilts were kept after weaning and before transfer to the experimental farm.

**Table 2.2.** Number of observations and means of grow-finish pig traits.

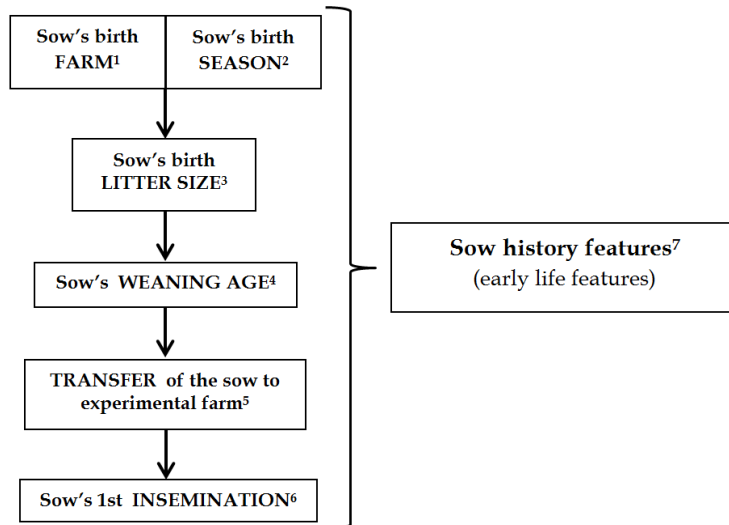
Trait	n	Mean	SD
Start weight, kg	17,678	26.4	5.8
Mid weight, kg	7,315	71.2	11.5
Slaughter weight, kg	17,065	113.6	8.4
GR <sup>1</sup> , g/day	17,025	859	95.3
GR-1 <sup>2</sup> , g/day	7,112	889	125.1
GR-2 <sup>3</sup> , g/day	7,030	868	133.7
FI <sup>4</sup> , kg/day	7,275	2.1	0.31
FI-1 <sup>5</sup> , kg/day	7,175	1.8	0.34
FI-2 <sup>6</sup> , kg/day	7,075	2.5	0.39

<sup>1</sup>GR = growth rate. <sup>2</sup>GR-1 = growth rate in phase one of grow-finish stage (26-75 kg). <sup>3</sup>GR-2 = growth rate in phase two of grow-finish stage (75-115 kg). <sup>4</sup>FI = feed intake. <sup>5</sup>FI-1 = feed intake in phase one of grow-finish stage (26-75 kg). <sup>6</sup>FI-2 = feed intake in phase second of grow-finish stage (75-115 kg).

**Table 2.3.** Number of observations and means of sow history features from sow birth to 1<sup>st</sup> insemination

Sow history features	n	Mean	SD
Weaning age <sup>1</sup> , day	627	28	3.3
Age transferred <sup>2</sup> , day	606	232	28.8
Age at 1 <sup>st</sup> insemination <sup>3</sup> , day	675	257	28.2
Birth litter size <sup>4</sup>	654	13	2.8
Birth farm <sup>5</sup>	669	-	-
Birth season <sup>6</sup>	681	-	-

<sup>1</sup>Sow's weaning age. <sup>2</sup>Age the sow was transferred from birth farm to experimental farm. <sup>3</sup>Age of the sow at 1<sup>st</sup> insemination. <sup>4</sup>Size of the litter in which the sow was born. <sup>5</sup>The commercial farm the sow was born. <sup>6</sup>Season in which the sow was born.



**Figure 2.1.** Sow history features (from sow birth to 1<sup>st</sup> insemination), defined to describe permanent sow and common litter effects in grow-finish pigs' traits.

<sup>1</sup>Sow's birth farm used to account for different management at the farms. <sup>2</sup>Sow's birth season used actually as a combination of a season (4 classes: January to March, April to June, July to September, and October to December). <sup>3</sup>Size of the litter (based on born alive) in which the sow was born. <sup>4</sup>Weaning age of the sow. <sup>5</sup>Age the sow was transferred from commercial farm to the experimental farm. <sup>6</sup>Used as age of the sow at 1<sup>st</sup> insemination. <sup>7</sup>For the purpose of this research sow history (early life) features were defined as events in sow life from birth to age at 1<sup>st</sup> insemination.

## 2.3 Methods

### 2.3.1 Non-genetic model

To investigate the impact of the sow history features on growth rate and feed intake of her offspring, sow features were added to the model applied by Topigs Norsvin (Bergsma *et al.*, 2008).

The fixed effects in the basic model varied depending on the trait analyzed. For GR, fixed effects were: gender of the grow-finish pig (male, female, castrate), line of the grow-finish pig (25 levels), feeding strategy (*ad libitum* and restricted), number of pen mates (7 levels), compartment in which the pen was located (18 levels), and the batch in which the grow-finish pig was born (131 levels). The model for GR-1 and GR-2 did not include the feeding strategy, because these traits included only grow-finish pigs fed *ad libitum*. For FI, the model had an additional fixed effect – start weight (kg) of the grow-finish stage, and did not include feeding strategy, because FI was available only on *ad libitum* fed grow-finish pigs. When analyzing

## 2. Effect of sow history features on grow-finish pigs

---

FI-2, the model included mid weight instead of start weight. The sow history features were added to the basic model (one at the time) as fixed effects: birth litter size, sow's birth farm/season, weaning age, age transferred, age at 1st insemination.

The parity of the sow was also tested, as a possible component of the basic model. The assumption was that there are differences between piglets coming from first and later parities sows. However, that effect was not significant for any of the models for grow-finish pigs' traits and did not change the significance of the other fixed effects in the basic model. Thus parity of the sow was excluded from the model.

To allow inclusion of random effects, the analyses of GR and FI traits were performed using the MIXED procedure (SAS 9.1, 2002). The F-test was used to determine the significance of each fixed effect in the basic model. Also the significance of the sow history features (as addition to basic model) was determined using the MIXED procedure F-test. The addition of sow effects to the model did not affect the significance of the other fixed effects. The random effects in the model were: sow ( $s^2$ ), litter in which a grow-finish pig was born ( $c^2$ ), and group ( $g^2$ ) in which a grow-finish pig was kept during the grow-finish stage. Selecting random effects to the model was made by comparing the log-likelihoods with the  $\chi^2$  – test.

The model for GR was:

$$y = \mu + \text{sow\_feature} + \text{sex} + \text{line} + \text{pen\_size} + \text{compartment} + \text{feeding\_strategy} + \text{batch} + \text{sow} + \text{litter} + \text{group} + e.$$

The model for GR-1 and GR-2 was:

$$y = \mu + \text{sow\_feature} + \text{sex} + \text{line} + \text{pen\_size} + \text{compartment} + \text{batch} + \text{sow} + \text{litter} + \text{group} + e.$$

The model for FI and FI-1 was:

$$y = \mu + \text{sow\_feature} + \text{weight\_start} + \text{sex} + \text{line} + \text{pen\_size} + \text{compartment} + \text{batch} + \text{sow} + \text{litter} + \text{group} + e.$$

The model for FI-2 was:

$$y = \mu + \text{sow\_feature} + \text{weight\_mid} + \text{sex} + \text{line} + \text{pen\_size} + \text{compartment} + \text{batch} + \text{sow} + \text{litter} + \text{group} + e.$$

### 2.3.2 Genetic model

In order to study whether the sow features could explain the common litter ( $c^2$ ) or permanent sow effects ( $s^2$ ) while taking into account the genetics of the grow-finish pigs, the models with significant sow features (based on results from MIXED procedure) were reanalyzed with the REML procedure in ASReml (Gilmour *et al.*, 2006). To estimate the full magnitude of  $c^2$  and  $s^2$ , the basic model did not include fixed effects for the sow history features. Moreover, for each trait with more than one sow feature being significant, a model with all significant sow features (for that trait) was analyzed. The difference of  $c^2$  and  $s^2$  estimates between the model including and the model excluding sow history features shows whether the sow features can explain those effects. The animal model used was:

$$\mathbf{y} = \mathbf{Xb} + \mathbf{Za} + \mathbf{Wc} + \mathbf{Vs} + \mathbf{Ug} + \mathbf{e},$$

where  $\mathbf{y}$  is a vector of observations;  $\mathbf{X}$ ,  $\mathbf{Z}$ ,  $\mathbf{W}$ ,  $\mathbf{V}$ , and  $\mathbf{U}$  are known incidence matrices relating observations to fixed and random effects;  $\mathbf{b}$  is a vector of fixed effects;  $\mathbf{a}$  is a vector of random additive genetic effects, with  $\mathbf{a} \sim N(\mathbf{0}, \mathbf{A}\sigma_A^2)$ ;  $\mathbf{c}$  is a vector of random non-genetic effects common litter effects (litter effect), with  $\mathbf{c} \sim N(\mathbf{0}, \mathbf{I}_c\sigma_c^2)$ ;  $\mathbf{s}$  is a vector of random non-genetic effects common to individuals with the same mother (permanent sow effect), with  $\mathbf{s} \sim N(\mathbf{0}, \mathbf{I}_s\sigma_s^2)$ ;  $\mathbf{g}$  is a vector of random non-genetic effects of individuals kept in the same group (group effect), with  $\mathbf{g} \sim N(\mathbf{0}, \mathbf{I}_g\sigma_g^2)$ ;  $\mathbf{e}$  is a vector of residuals, with  $\mathbf{e} \sim N(\mathbf{0}, \mathbf{I}_e\sigma_e^2)$ .  $\mathbf{I}_c$ ,  $\mathbf{I}_s$ ,  $\mathbf{I}_g$  and  $\mathbf{I}_e$  are identity matrices of the appropriate dimensions and  $\mathbf{A}$  is the numerator relationship matrix. The pedigree contained 34,092 animals over 5 generations.

## 2.4 Results

### 2.4.1 Descriptive statistics

The average start weight, mid weight and the slaughter weight of grow-finish pigs were: 26.4, 71.2, and 113.6 kg, respectively (Table 2.2). The standard deviation of the mid weight was relatively large compared with the start and slaughter weight. The average growth rate of the grow-finish pigs was 859 g/day. Growth rate was higher in phase one than in phase two in grow-finish pigs fed *ad libitum* ( $P < 0.05$ ). The average feed intake was 2.1 kg/day. Feed intake was lower in phase one than in phase two in *ad libitum* fed grow-finish pigs ( $P < 0.05$ ).

The mothers of grow-finish pigs were on average born in litters of 13 piglets and weaned at the age of 28 days (Table 2.3). Transfer of the sows from commercial



## 2. Effect of sow history features on grow-finish pigs

---

farms to the Topigs Norsvin farm on average took place at 232 days of age. The sows were inseminated for the first time at average age of 257 days (Table 2.3).

### 2.4.2 Sow history features

The sow features with significance level of  $P < 0.1$  were considered significant for the trait (Table 2.4). The weaning age as a class variable was significant for GR. The sow's age at 1<sup>st</sup> insemination was significant for: GR and GR-1. Birth litter size as linear variable was significant for: GR, GR-1, FI, and FI-1 ( $P < 0.1$ ). In the model with the sow's birth litter size as a class variable, litter size was significant for GR, FI, and FI-1. When fitted as both linear and quadratic variable in the models, the birth litter size of a sow was significant for all six grow-finish pig traits ( $P < 0.05$ ). The sows' birth farm/season and grow-finish pigs' line interaction was highly significant ( $P < 0.0001$ ) for six grow-finish pig traits. The age transferred was not significant for any of the grow-finish pigs' traits.

Certain similarities were noticeable among models for: FI and FI-1, as well as GR and GR-1. Moreover, in the models for GR-2 and FI-2 the birth litters size (as both linear and quadratic variable) and sow's birth farm/season and grow-finish pig's line interaction were the only significant sow features.

Table 2.5 presents the estimates of significant sow features ( $P < 0.1$ ). Offspring of sows inseminated later grew faster. Every extra day to the 1<sup>st</sup> insemination increased grow-finish pigs' GR by 0.13 g/day and GR-1 by 0.14 g/day. The sows born in larger litters had offspring that grew slower and ate less. With every extra piglet in the sow's birth litter (linear), GR decreased by 1.0 g/day and FI decreased by 4 g/day. Similar change was present for the traits in phase one. Estimates for growth rate had smaller absolute values than estimates for feed intake. In general, however, all estimates of the effect of sow history features on grow-finish pig traits were small, also for highly significant sow features.

Since quadratic relationships are hard to visualize based on the estimated effects, Figures 2-4 show the effect of two sow features - weaning age and litter size (as linear, linear and quadratic and class variables) on GR and FI. The shape of the function for birth litter size as both linear and quadratic variable, for GR and FI, was reasonably similar to the pattern of litter size fitted as class effect (Figure 2.2 and Figure 2.3). The sow's weaning age as a class variable did not show a clear pattern (Figure 2.4).

## 2. Effect of sow history features on grow-finish pigs

**Table 2.4.** Significance (P<0.1) of sow history features for production traits of their offspring as grow-finish pigs (MIXED procedure).

Sow history features	Grow-finish pig traits					
	GR <sup>6</sup>	GR-1 <sup>7</sup>	GR-2 <sup>8</sup>	FI <sup>9</sup>	FI-1 <sup>10</sup>	FI-2 <sup>11</sup>
Weaning age <sup>1</sup> (class)	0.009	n.s. <sup>12</sup>	n.s.	n.s.	n.s.	n.s.
Age at 1 <sup>st</sup> insemination <sup>2</sup> (linear)	0.014	0.088	n.s.	n.s.	n.s.	n.s.
Birth litter size <sup>3</sup> (linear)	0.018	0.084	n.s.	0.011	0.031	n.s.
Birth litter size (class)	0.078	n.s.	n.s.	0.076	0.071	n.s.
Birth litter size (linear)	0.088	0.108	0.015	0.002	0.001	0.043
+ Birth litter size (quadratic)	0.038	0.048	0.014	0.001	0.001	0.023
Sow's farm <sup>4</sup> /season <sup>5</sup> * Grow-finish pig's line	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

<sup>1</sup>Sow's weaning age. <sup>2</sup>Age of the sow at 1<sup>st</sup> insemination. <sup>3</sup>Size of the litter in which the sow was born. <sup>4</sup>The commercial farm the sow was born.

<sup>5</sup>Season in which the sow was born. <sup>6</sup>GR = growth rate. <sup>7</sup>GR-1 = growth rate in phase one of grow-finish stage (26-75 kg). <sup>8</sup>GR-2 = growth rate in phase two of grow-finish stage (75-115 kg). <sup>9</sup>FI = feed intake. <sup>10</sup>FI-1 = feed intake in phase one of grow-finish stage (26-75 kg). <sup>11</sup>FI-2 = feed intake in phase second of grow-finish stage (75-115 kg). <sup>12</sup>n.s. = not significant.

## 2. Effect of sow history features on grow-finish pigs

**Table 2.5.** Estimated effects (with SE) of sow history features on production traits of their offspring as grow-finish pigs (MIXED procedure).

Sow history features	Grow-finish pig traits <sup>3</sup>					
	GR <sup>4</sup>	GR-1 <sup>5</sup>	GR-2 <sup>6</sup>	FI <sup>7</sup>	FI-1 <sup>8</sup>	FI-2 <sup>9</sup>
Age at 1 <sup>st</sup> insemination <sup>1</sup> (g/day)/day (linear)	0.13(0.05)	0.14(0.08)	n.s. <sup>10</sup>	n.s.	n.s.	n.s.
Birth litter size <sup>2</sup> (g/day)/piglet (linear)	-1.0(0.4)	-1.1(0.7)	n.s.	-4.0(0.1)	-3.0(1.0)	n.s.
Birth litter size (linear)	5.0(2.9)	7.01(4.4)	11.07(4.53)	31.1(9.9)	38.6(11.6)	24.8(12.1)
+Birth litter size (g/day)/piglet <sup>2</sup> (quadratic)	-0.24(0.11)	-0.32(0.16)	-0.43(0.17)	-1.3(0.4)	-2.0(0.4)	-1.0(0.4)

<sup>1</sup>Age of the sow at 1<sup>st</sup> insemination. <sup>2</sup>Size of the litter in which the sow was born. <sup>3</sup>Estimated effects for grow-finish pig traits are in g/day. <sup>4</sup>GR = growth rate. <sup>5</sup>GR-1 = growth rate in phase one of grow-finish stage (26-75 kg). <sup>6</sup>GR-2 = growth rate in phase two of grow-finish stage (75-115 kg). <sup>7</sup>FI = feed intake. <sup>8</sup>FI-1 = feed intake in phase one of grow-finish stage (26-75 kg). <sup>9</sup>FI-2 = feed intake in phase second of grow-finish stage (75-115 kg). <sup>10</sup>n.s. = not significant.

### 2.4.3 Random effects and heritability estimates

Based on significance level (MIXED procedure), for every grow-finish pig trait the significant sow history features were selected for further analysis using the REML procedure. For each trait two additional models were analyzed; the first with no sow features (basic model) and the second with all significant sow features (Table 2.6).

It was not possible to estimate the  $s^2$  for FI-2 and GR-2; in the basic model this parameter did not converge and in the model with all sow features it was equal to 0 (Table 2.7). For growth related traits almost no differences were found between estimates of  $s^2$ ,  $c^2$  and  $g^2$  in the basic model and the model with all sow features. That was not the case, however, for feed intake related traits, where both  $s^2$  and  $c^2$  decreased in comparison to basic model when including all sow features.

The estimates of  $h^2$  for GR and GR-1 were similar and higher than for GR-2 (Table 2.7). For feed intake related traits, the  $h^2$  estimates were higher for FI and FI-2 than for FI-1. Models with significant sow features for GR-2 and FI-2 showed a drop in  $h^2$  estimates compared with the basic model. Opposite results were found for FI and FI-1, where basic models had lower  $h^2$  estimates than the model with sow features.

## 2.5 Discussion

The sow provides a specific environment to her offspring during gestation and from farrowing to weaning. Feed compositions and amounts during gestation impact piglet's muscle development (Dwyer *et al.*, 1994; Nissen *et al.*, 2003; Musser *et al.*, 2006). The body condition of the sows during lactation has an impact on piglets' growth (Yang *et al.*, 1989; Grandinson *et al.*, 2005). In addition, relatively large common litter effects found in grow-finish pigs indicated a substantial non-genetic effect of the sow on offspring performance after weaning. To investigate this effect we fitted sow history features as explanatory variables in the model for performance of her offspring, and investigated whether fitting such effects decreases the magnitude of permanent sow and common litter effects. To our knowledge, this is a first study that investigates factors affecting the common litter effect in grow-finish pigs' traits as potential explanation for differences in performance between pigs.

## 2. Effect of sow history features on grow-finish pigs

**Table 2.6.** Significant sow history features, used as fixed effects in the REML procedure models, for their offspring production traits as grow-finish pigs (significance level based on MIXED procedure).

Sow history features	Grow-finish pig traits					
	GR <sup>4</sup>	GR-1 <sup>5</sup>	GR-2 <sup>6</sup>	FI <sup>7</sup>	FI-1 <sup>8</sup>	FI-2 <sup>9</sup>
Weaning age <sup>1</sup> (class)	x					
Age at 1 <sup>st</sup> insemination <sup>2</sup> (linear)	x	x				
Birth litter size <sup>3</sup> (linear)						
+ Birth litter size (quadratic)	x	x	x	x	x	x

<sup>1</sup>Sow's weaning age. <sup>2</sup>Age of the sow at 1<sup>st</sup> insemination. <sup>3</sup>Size of the litter in which the sow was born. <sup>4</sup>GR = growth rate. <sup>5</sup>GR-1 = growth rate in phase one of grow-finish stage (26-75 kg). <sup>6</sup>GR-2 = growth rate in phase two of grow-finish stage (75-115 kg). <sup>7</sup>FI = feed intake. <sup>8</sup>FI-1 = feed intake in phase one of grow-finish stage (26-75 kg). <sup>9</sup>FI-2 = feed intake in phase second of grow-finish stage (75-115 kg).

### 2.5.1 Identification of sow history features

The first objective was to identify the relevant sow history features. Indeed, a number of sow early life features affected grow-finish pigs' production traits. Growth rate seems to be more dependent on sow history features, since four different sow features were significant for GR and three for GR-1. Differences in significance level for sow features between GR and other traits are probably related to the differences in number of records. As a result of management, growth rate analyses were based on 17,065 grow-finish pigs, whereas for the other traits only ~7,100 observations were available (only animals fed *ad libitum*). Moreover, more sow features was significant for the traits in phase one than in phase two. This could be expected since the animals in phase one are younger and it could be assume that the sow effects are more likely to still affect them. The sow effects decrease with life of the offspring (Solanes *et al.*, 2004).

## 2. Effect of sow history features on grow-finish pigs

**Table 2.7.** Estimates (with SE) of parameters<sup>1</sup> for base model (no sow's feature) and model with significant sow features<sup>2</sup> for grow-finish pig traits.

Trait <sup>3</sup>	Model	$\sigma_A^2$	$s^2$	$c^2$	$g^2$	$\sigma_e^2$	$\sigma_P^2$	$h^2$
<b>GR</b>	Base model	1440 (183)	0.015 (0.01)	0.052 (0.01)	0.164 (0.01)	3515 (133)	6444 (97)	0.224 (0.03)
	All sow features	1373 (198)	0.015 (0.01)	0.051 (0.01)	0.165 (0.01)	3534 (113)	6373 (102)	0.216 (0.03)
<b>GR-1</b>	Base model	2435 (447)	0.022 (0.01)	0.049 (0.01)	0.169 (0.01)	5339 (120)	10230 (236)	0.238 (0.04)
	All sow features	2325 (488)	0.023 (0.01)	0.053 (0.01)	0.176 (0.01)	5328 (282)	10220 (252)	0.228 (0.05)
<b>GR-2</b>	Base model	2506 (425)	<sup>-4</sup>	0.067 (0.01)	0.201 (0.06)	7374 (126)	13490 (312)	0.186 (0.03)
	All sow features	1949 (440)	0	0.074 (0.01)	0.203 (0.02)	7559 (285)	13150 (316)	0.148 (0.03)
<b>FI</b>	Base model	0.010 (0.002)	0.028 (0.01)	0.043 (0.01)	0.334 (0.02)	0.023 (0.001)	0.056 (0.002)	0.178 (0.04)
	All sow features	0.011 (0.002)	0.005 (0.01)	0.035 (0.01)	0.335 (0.02)	0.024 (0.002)	0.056 (0.002)	0.203 (0.04)
<b>FI-1</b>	Base model	0.008 (0.002)	0.030 (0.01)	0.061 (0.01)	0.414 (0.02)	0.023 (0.001)	0.070 (0.002)	0.121 (0.04)
	All sow features	0.012 (0.003)	0.008 (0.01)	0.047 (0.01)	0.404 (0.02)	0.027 (0.002)	0.071 (0.002)	0.166 (0.04)
<b>FI-2</b>	Base model	0.016 (0.003)	<sup>-4</sup>	0.044 (0.01)	0.308 (0.02)	0.023 (0.001)	0.088 (0.003)	0.178 (0.03)
	All sow features	0.014 (0.003)	0	0.037 (0.01)	0.312 (0.02)	0.044 (0.002)	0.089 (0.002)	0.157 (0.04)

<sup>1</sup>Sow effect:  $s^2 = \sigma_s^2 / \sigma_P^2$ ; litter effect:  $c^2 = \sigma_c^2 / \sigma_P^2$ ; heritability:  $h^2 = \sigma_A^2 / \sigma_P^2$ . <sup>2</sup>Sow history features were: size of the litter in which the sow was born, sow's birth farm and season, weaning age, age transferred to the experimental farm, age at 1<sup>st</sup> insemination in days. <sup>3</sup>GR = growth rate. <sup>5</sup>GR-1 = growth rate in phase one of grow-finish stage (26-75 kg). <sup>6</sup>GR-2 = growth rate in phase two of grow-finish stage (75-115 kg). <sup>7</sup>FI = feed intake. <sup>8</sup>FI-1 = feed intake in phase one of grow-finish stage (26-75 kg). <sup>9</sup>FI-2 = feed intake in phase second of grow-finish stage (75-115 kg). <sup>4</sup>Parameter did not converge.

## 2. Effect of sow history features on grow-finish pigs



**Figure 2.2.** The effect of sow's birth litter size as class variable (■), starting from the class with most observations, 14 piglets, ( $P=0.08$ )<sup>1</sup> for growth rate – GR (g/day) of grow-finish pigs. ▲ – as linear variable ( $P=0.02$ ); ● – as linear and quadratic variable ( $P=0.03$ ). SD of GR is  $\sigma_{GR} = 95.3$ .

<sup>1</sup>Significance level based on the MIXED procedure (SAS 9.1, 2002).

Although the sow history features used in this study were significant for grow-finish pigs' traits, the estimates of the sow features for these traits were small (Table 2.5) and explained only a minor proportion of the differences in growth rate (for GR, *e.g.* sow's age at 1st insemination explained 6% of the difference in growth) and feed intake (for FI, *e.g.* sow's birth litter size explained 2% of the difference in feed intake) between grow-finish pigs. In literature, however, age at 1st insemination and birth litter size are often mentioned as affecting the reproductive performance of the sow and piglets' birth traits (*e.g.* Schukken *et al.* 1994; Sterning *et al.* 1998; Tummaruk *et al.* 2001). Parity of the sow is also known to affect piglet traits (Koketsu and Dial, 1997; Tummaruk *et al.* 2001), however, it was found not significant for grow-finish pig traits investigated in this study. The standard error of the parity estimates on average explained 5% of standard deviation of growth and 8% of standard deviation of feed intake. Therefore, the parity effect on grow-finish pig traits was estimated correctly, but it was very small.

The sow early life features, investigated in this study, have little impact on offspring performance in later stages of life. It means the sow features do not predict which sows produce better performing offspring in grow-finish stage.

The impact of sow history features (e.g. birth litter size of the sow, age at 1<sup>st</sup> insemination and sow parity) on performance of their offspring is also of interest in epigenetic studies. While this study does not provide information on the molecular mechanisms underlying such epigenetic effects, it gives an indication of their magnitude, based on large numbers of observations. Based on the results presented in this study, it can be concluded that any existing epigenetic effects of the sow features would have rather small impact on the growth and feed intake in grow-finish pigs.

### 2.5.2 Sow features in the models

During the analyses, confounding was observed between a sow's birth farm/season and the line of the grow-finish pig. The farms provided sows of a single cross, thus all grow-finish pigs of a certain cross had mothers coming from a single farm only. Moreover, each year different lines were used, thus some sow's birth seasons were present for a single line only. Since the line effects could not be separated from the sow's farm/season effect; the effects were fitted as interaction between sow's farm/season and grow-finish pigs' line. It indicates that the actual confounding was between sows' and grow-finish pigs' lines. Moreover, sow's farm/season interaction with grow-finish pig's line was highly significant ( $P < 0.0001$ ) for all grow-finish pig's traits. This can be easily explained by the relation between the line of the mother and her offspring, since the line of the offspring directly depends on the mother's line.

When analyzing other sow features no confounding was found based on SAS output files.

### 2.5.3 Data structure

In this study, the additive genetic effects, common litter effects and permanent sow effects were estimated simultaneously, which is statistically challenging. However, the data structure allowed clear separation of those effects. Additive genetic effects could be separated from litter and permanent effects because sires were mated to multiple dams (on average 4.2), which provided both full and half-sibs. First, because half-sibs have different dams, the covariance between records of half-sibs provides information only on the additive genetic effects, which allows estimation of the additive genetic variance. Second, common litter and permanent sow effects could be separated, because sows produced multiple litters (on



## 2. Effect of sow history features on grow-finish pigs

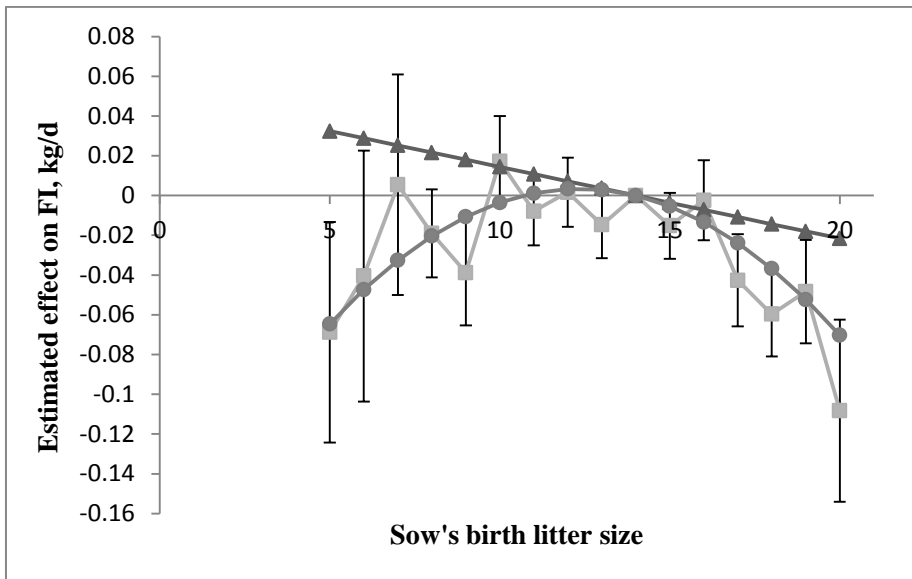
---

average 3.7). Records of maternal half-sibs born in different litters include the same permanent sow effect, allowing estimation of the permanent sow variance. Finally, records from full-sibs born in the same litter provide information on the common litter variance.

### 2.5.4 Sow features effect on $s^2$ and $c^2$

The estimates of  $s^2$  for grow-finish pigs' traits were small (Table 2.7), however, in line with the literature. Johnson *et al.* (2002) showed estimates of  $s^2$  for average daily gain around 0.05 (for Landrace, Yorkshire and Duroc) and 0.10 (for Hampshire). Chen *et al.* (2002) showed low estimates for  $s^2$  ranging from 0.01 to 0.04 (depending on the breed). Based on these results, Chen *et al.* (2002) concluded that  $s^2$  can be ignored for production traits in pigs. They supported this conclusion with the results of two other studies (Ferraz *et al.*, 1993; Crump *et al.*, 1997), which indeed indicated no practical use of  $s^2$  in models for production traits in pigs. In fact, more studies focused on  $s^2$  for early life traits of piglets, rather than for grow-finish pigs' traits (Solanes *et al.*, 2004; Canario *et al.*, 2010; Kapell *et al.*, 2011). Moreover, the sow effect on traits of her offspring decreases in time (Solanes *et al.*, 2004). The near-zero  $s^2$  estimates for FI and FI-1 in models including sow features, suggests that the sow effect is fully explained by the significant sow features for those traits. Nevertheless, when omitting the sow features,  $s^2$  estimates were small and did not explain a substantial part of phenotypic variance among grow-finish pigs.

Many studies have reported common litter estimates for various production traits in pigs: growth rate (Bidanel *et al.*, 1996; Johnson *et al.*, 2002), backfat (Chen *et al.*, 2002), and feed conversion (Kuhlers *et al.*, 2003; Neugebauer *et al.*, 2010). Among the production traits, the growth rate usually has the highest estimate of  $c^2$ , varying from 0.10 to 0.25 (Bidanel *et al.*, 1996; Johnson *et al.*, 2002; Van Wijk *et al.*, 2005). The estimate of  $c^2$  for feed intake was reported as 0.07 (Neugebauer *et al.*, 2010) and 0.16 (Bergsma *et al.*, 2008) in the model without group effect. Those high estimates suggest great impact of  $c^2$  on grow-finish pigs' traits. The estimates found in this study, however, are significantly lower than the estimates reported in literature. Moreover, the decrease in  $c^2$  estimates for feed intake related traits in models with sow features was small.



**Figure 2.3.** The effect of sow's birth litter size as class variable (■), starting from the class with most observations, 14 piglets, ( $P=0.08$ )<sup>1</sup> for feed intake – FI (kg/day) of grow-finish pigs. ▲ – as linear variable ( $P=0.01$ ); ● – as linear and quadratic variable ( $P=0.01$ ). SD of FI is  $\sigma_{FI} = 0.31$ .

<sup>1</sup>Significance level based on the MIXED procedure (SAS 9.1, 2002).

The estimates for  $c^2$  and  $h^2$  in the basic model are in line with those reported by Bergsma *et al.* (2008) in the model including group effects; Bergsma's study was partly based on the same data as used in this study. In Bergsma's study several models for grow-finish pigs' traits were compared; a substantial drop in  $c^2$  and  $h^2$  was found when fitting a random group effect to account for similarities among grow-finish pigs kept in the same group. For growth rate,  $c^2$  dropped from 0.12 to 0.04, and for feed intake,  $c^2$  dropped from 0.16 to 0.03 (Table 2.3 vs. Table 2.4 in Bergsma *et al.*, 2008). Those values are clearly below the level of  $c^2$  found in literature, suggesting that confounding of common litter and group effects may occur more often. This confounding is caused by the grow-finish pig group composition, which often contains full-sibs, therefore, group is confounded with common litter. This leads to overestimation of  $c^2$ , which can lower accuracy of selection and with this lower genetic gain. To avoid these problems, grow-finish pig groups should ideally be composed without full-sibs.

Based on the estimates of random effects found in this study, it is clear that  $g^2$  has greater impact on the grow-finish pigs traits than  $s^2$  and  $c^2$  (Table 2.7). Random group effects are often not included in the genetic analysis of grow-finish pigs'

## 2. Effect of sow history features on grow-finish pigs

data, because physical differences among pens are minor after accounting for systematic differences, for example, the feeding strategy (Bergsma *et al.*, 2008). Results of this study and Bergsma *et al.* (2008), however, suggest that group effects may originate from the individuals within the pen, rather than from physical differences among pens, suggesting social effects. Accounting for such group effects in the statistical model should help to avoid biased genetic and common litter parameters estimates.

### 2.5.5 Sow and common litter vs. foster sow and litter

About 25% of piglets at the experimental farm of Topigs Norsvin in Beilen were cross-fostered. The sow and common litter effect describe both the gestation and suckling period in grow-finish pigs' life. In contrast, foster sow and foster litter refer only to the suckling stage in grow-finish pigs' early life. Since the permanent sow effect did either not converge or was equal to 0 in the analysis, it was tested whether fitting foster sow ( $s_f^2$ ) and foster litter ( $c_f^2$ ) effects would be more suitable. Comparison was based on four variants of the basic model using:  $s^2$  and  $c^2$ ,  $s_f^2$  and  $c^2$ ,  $s^2$  and  $c_f^2$ , or  $s_f^2$  and  $c_f^2$ .



**Figure 2.4.** The effect of sow's weaning age as class variable (■), starting from the class with most observations, 28 days, ( $P=0.01$ )<sup>1</sup> for growth rate – GR (g/day) of grow-finish pigs. ▲ – as linear variable ( $P=0.36$ ); ● – as linear and quadratic variable (0.43). SD of GR is  $\sigma_{GR} = 95.3$ .

<sup>1</sup>Significance level based on the MIXED procedure (SAS 9.1, 2002).

For feed intake related traits, log-likelihoods indicated that the basic model was best (with  $s^2$  and  $c^2$ ). For FI-2 the log-likelihoods did not differ among the four models and all estimates of  $s^2$  and  $s_f^2$  were equal to 0. This indicates small effect of both the mother and the foster sow on FI-2. In contrast, for GR and GR-1 the model with  $s^2$  and  $c_f^2$  fitted the best, whereas for GR-2 the model  $s_f^2$  and  $c^2$  fitted best. The postnatal environment provided by the litter and sow appears to have greater effect on growth of grow-finish pigs than prenatal environment. Since for feed intake related traits the basic model fitted best, additional analyses were performed only for the growth related traits. Those analyses did not yield significant changes in sow or common litter estimates ( $s^2$  vs.  $s_f^2$  and  $c^2$  vs.  $c_f^2$ ); all estimates were on the same level as in the original analyses and did not provide more insight into the identification of the sow history features and their effect on  $s^2$  and  $c^2$ .

### 2.6 Conclusions

To conclude, selected sow history features do significantly affect grow-finish pigs' traits, but their estimates are small and explained only a minor proportion of the differences in growth rate and feed intake among grow-finish pigs. For FI related traits, selected sow features almost entirely explained permanent sow effect. Nevertheless, their contribution to phenotypic variance was small. Even though the sow early life features can affect piglets traits, they do not predict which sows produce better performing offspring in grow-finish stage.

### 2.7 Acknowledgments

This research was financially supported by the Dutch Science Council (NWO) and part of the study was co-ordinated by the Dutch Technology Foundation (STW). The authors would like to thank Topigs Norsvin (Beuningen, The Netherlands) for providing the data and also to Rob Bergsma and Naomi Duijvesteijn from Topigs Norsvin (Beuningen, The Netherlands) for valuable comments and explanations. Ewa Sell-Kubiak would like to thank fellow PhD students, especially Katrijn Peeters, for interesting discussions during writing this manuscript.



# 3

## **Effect of gestating sow body-condition, feed refusals and group-housing on growth and feed intake in grow-finish pigs**

E. Sell-Kubiak, E. H. van der Waaij, P. Bijma

Animal Breeding and Genomics Centre, Wageningen University,  
PO Box 338, 6700 AH Wageningen, The Netherlands

J. Anim. Sci. (2013) 91(8):3538-3548

## Abstract

The main focus of this study was to identify sow gestation features that affect growth rate (GR) and feed intake (FI) of their offspring during grow-finish stage. Since the sow provides a specific environment to her offspring during gestation, certain features, *e.g.*, sow's weight, feed refusals or gestation group may affect her ability to deliver and feed a healthy litter. Data on 17,743 grow-finish pigs, coming from 604 sires and 681 crossbred sows, were obtained from the Topigs Norsvin (Beuningen, The Netherlands). Sow gestation features were collected during multiple gestations and divided into three clusters describing: *i.* sow body-condition, *i.e.*, weight, backfat, gestation length; *ii.* sow feed refusals (FR), difference between offered and eaten feed during three periods of gestation: 1-28, 25-50, 45-80 days; *iii.* sow group features, *i.e.*, number of sows, average parity. Sow gestation features were added to the base model one at a time to study their effect on GR and FI. Significant gestation features ( $P < 0.1$ ) were fitted simultaneously in animal model to investigate whether they could explain common litter and permanent sow effects. Gestation length had effect on GR ( $1.4 \text{ [g/day]}/\text{day}$ ,  $P = 0.04$ ) and FI ( $6.8 \text{ [g/day]}/\text{day}$ ,  $P = 0.007$ ). Sow's weights at insemination ( $0.07 \text{ [g/day]}/\text{kg}$ ,  $P = 0.08$ ), at farrowing ( $0.14 \text{ [g/day]}/\text{kg}$ ,  $P < 0.0001$ ) and after lactation ( $0.1 \text{ [g/day]}/\text{kg}$ ,  $P = 0.003$ ) had effect on GR. Sow parturition-lactation loss in backfat thickness and weight were not significant for GR and FI. Days with FR during 25-50 and 45-80 days of gestation and average FR during 45-80 days of gestation had negative effect on GR and when substantially increased had also a positive effect on FI. Sow FR from 1-28 days of gestation were not significant. Number of sows in gestation group had effect on FI ( $-9 \text{ [g/day]}/\text{group\_member}$ ,  $P = 0.04$ ) and day sow entered group had an effect on GR ( $-0.9 \text{ [g/day]}/\text{day}$ ,  $P = 0.04$ ). Sow gestation features explained 1% to 3% of the total variance in grow-finish pigs. Gestation features did explain phenotypic variance due to permanent sow and part of phenotypic variance due to common litter effects for FI, but not for GR.

Key words: common litter effect, production traits, gestation features, sow permanent effect

#### 3.1 Introduction

In genetic studies, the environmental effects of a sow on her piglets are known as permanent sow and common litter effects (Chen *et al.*, 2002; Kuhlert *et al.*, 2003). Those effects indicate the non-genetic effect of a sow on performance of her offspring (*e.g.* Kaufmann *et al.* 2000). Causal mechanisms underlying those effects are largely unknown. Thus far, Sell-Kubiak *et al.* (2012) used features from sow's life before the first insemination (history features), which can affect her entire reproductive performance and therefore the offspring, to explain those mechanisms. Results showed, that sow history features had a small effect on grow-finish pig traits and explained part of permanent sow effect in feed intake, but not common litter effect.

In this work, we aim to further investigate the mechanisms underlying the observed permanent sow and common litter effects, focusing on the gestation period. During gestation, a sow has environmental and genetic effects on her offspring. To describe the environment that the sow provided to her offspring during each gestation, we defined three clusters of sow gestation features. The clusters describe: *i.* body-condition of a sow in gestation, *i.e.* weight, backfat, gestation length, *ii.* sow feed refusals, *i.e.* difference among feed offered and eaten, and *iii.* sow group features, *i.e.* number of sows, average parity.

The first objective of this study is to identify gestation features of individually and group-housed sows that affect offspring performance as grow-finish pigs. These features will be identified by estimating their effect on growth rate and feed intake of grow-finish pigs. The second objective is to investigate whether those gestation features can explain the permanent sow and common litter effects in grow-finish pig traits.

#### 3.2 Materials

Under Dutch law, Animal Care and Use Committee approval was not required for this study, because the data were obtained from the pre-existing database of Topigs Norsvin (The Netherlands), which contains the data collected routinely for breeding value estimation.

##### 3.2.1 Grow-finish pigs

Data on grow-finish pigs were obtained from the research farm of the Topigs Norsvin (Beuningen, The Netherlands). These are the same data that were previously used by Sell-Kubiak *et al.* (2012); note that the sow data differs from



### 3. Effect of gestating sow features on grow-finish pigs

that study. The farm has a farrow-to-finish structure, with 180 crossbred sows and rotational use of 6 sire lines in a 3-week batch management of farrowing. The number of grow-finish pigs per cross is presented in Table 3.1.

Records from 17,743 grow-finish pigs, coming from 604 sires and 681 sows, were collected between May 2001 and February 2010. In each batch, part of the grow-finish pigs was fed *ad libitum*. Their feed intake was recorded using IVOG feeding stations (INSENTEC, Marknesse, The Netherlands). Overall 7,529 grow-finish pigs were fed *ad libitum*, whereas the remaining 10,214 were fed restricted at group level. Individual feed intake was not available for restricted fed animals. The barn in which the grow-finish pigs were kept contained 18 compartments (7 for *ad libitum* and 11 for restricted fed animals) with six pens in each compartment. Further details on feed and farm management can be found in Sell-Kubiak *et al.* (2012).

**Table 3.1.** Number of grow-finish pigs per combination of sire line<sup>1</sup> and sow cross<sup>2</sup> for two feeding strategies.

Sire line	Feeding strategy <sup>3</sup>	Sow cross				For sire line	Total sum
		F	G	H	I		
A	Restricted	68	567	1,096	-	1,731	2,670
	<i>ad libitum</i>	102	375	462	-	939	
B	Restricted	176	1,269	1,283	12	2,740	4,635
	<i>ad libitum</i>	508	692	512	183	1,895	
C	Restricted	156	1,390	752	-	2,298	3,951
	<i>ad libitum</i>	433	774	320	126	1,653	
D	Restricted	21	415	379	15	830	1,904
	<i>ad libitum</i>	275	409	285	105	1,074	
E	Restricted	228	1,360	736	-	2,324	3,971
	<i>ad libitum</i>	405	684	311	247	1,647	
For sow cross	Restricted	649	5,001	4,246	27		
	<i>ad libitum</i>	1,723	2,934	1,890	661		
Total sum		2,372	7,935	6,136	688		17,131 <sup>4</sup>

<sup>1</sup>A to E are different sire lines. <sup>2</sup>F to I are different sow crosses. <sup>3</sup>Grow-finish pigs were fed *ad libitum* (n=7,529) or restricted (n=10,214) at group level; individual feed intake was not available for restricted fed animals. <sup>4</sup>Total number of grow-finish pigs was 17,743; 612 grow-finish pigs not included in this table came from lines of low frequency.

### 3. Effect of gestating sow features on grow-finish pigs

**Table 3.2.** Characteristics of studied grower-finishing traits.

Trait <sup>1</sup>	n	Mean	SD
Start weight, kg	17,678	26.4	5.8
Mid weight, kg	7,284	71.2	11.4
Slaughter weight, kg	17,064	113.6	8.4
GR, g/day	17,025	859	95.4
GR-restr, g/day	9,668	844	91.7
GR-adlib <sup>2</sup> , g/day	7,357	879	96.3
FI <sup>2</sup> , kg/day	7,251	2.2	0.31

<sup>1</sup>GR = growth rate; GR-restr = growth rate of grow-finish pigs fed restricted; GR-adlib = growth rate of grow-finish pigs fed *ad libitum*; FI = feed intake. <sup>2</sup>Trait was available on *ad libitum* fed grow-finish pigs only.

**Table 3.3.** Characteristics of studied sow gestation features describing sow body-condition<sup>1</sup>.

Sow gestation features <sup>2</sup>	n	Mean	SD
Gestation length, d	2,517	115.7	1.5
Weight at insemination, kg	1,653 <sup>3</sup>	208.4	34.7
Weight at farrowing, kg	2,138	249.9	35.9
Backfat at farrowing, mm	2,135	18.2	4.0
Weight after lactation, kg	2,120	213.3	37.4
Backfat after lactation, mm	2,111	14.7	3.6
Parturition-lactation weight loss, kg	2,102	36.6	15.0
Parturition-lactation backfat loss, mm	2,111	3.4	2.1
Previous lactation weight loss, kg	1,644 <sup>3</sup>	36.8	14.2

<sup>1</sup>In total, 681 sows produced 2,521 litters. <sup>2</sup>Gestation length = length of gestation; Weight at insemination = weight of the sow at insemination; Weight at farrowing = weight of the sow at farrowing; Backfat at farrowing = backfat thickness of the sow at farrowing; Weight after lactation = weight of the sow after lactation; Backfat after lactation = backfat thickness of the sow after lactation; Parturition-lactation weight loss = weight loss of the sow during lactation; Parturition-lactation backfat loss = backfat thickness loss of the sow during lactation; Previous parturition-lactation weight loss = weight loss of the sow during lactation prior to next insemination. <sup>3</sup>Without the first parity sows.

### 3. Effect of gestating sow features on grow-finish pigs

---

This study focused on two grow-finish pig traits: growth rate and feed intake. Those traits were chosen based on preliminary analyzes, which indicated high estimates of common litter effect (~10% of phenotypic variance). As a result of two feeding strategies and to investigate if the grow-finish pigs fed restricted or *ad libitum* are affected in the same way by the sow gestation features, in total four traits were distinguished: growth rate (GR), growth rate of grow-finish pigs fed restricted (GR-restr), growth rate of grow-finish pigs fed *ad libitum* (GR-adlib), feed intake (FI). The descriptive statistics of grow-finish pig traits are presented in Table 3.2. Further details on the grow-finish pig traits can be found in Sell-Kubiak *et al.* (2012).

#### 3.2.2 Sow gestation features

Data on sow gestation features contained records on 681 crossbred sows and were not previously used. The sows had been transferred as gilts to the research farm from 5 commercial Topigs Norsvin farms, and were kept at the research farm as mothers until their 6<sup>th</sup> parity. During gestation, the sows were fed restricted based on the Topigs Norsvin feeding curve; the amount of feed was assigned to a sow according to her parity and body weight. The IVOG feeding stations (INSENTEC, Marknesse, The Netherlands) located in gestation pens recorded the actual amount of feed eaten by each sow on each day of gestation (up to a maximum amount of feed assigned to that sow). The sows produced 2,521 litters, from which 988 came from the sows kept in individual crates and remaining 1,533 from group-housed sows. For better overview of sow gestation features, this study defines three clusters of gestation features which are described below.

The first cluster includes sow gestation features describing sow body-condition during gestation (Table 3.3). All sows had gestation length recorded, as well as weight and backfat thickness measured at the entrance to farrowing crate and after lactation. At the research farm, weight at insemination is not routinely recorded. Thus, weight after the preceding lactation was used as a proxy for weight at insemination. This left the first parity sows without a record on insemination weight.

The second cluster includes sow gestation features describing the sow feed refusals (Table 3.4). The focus in current study was on the effect of sow average amount (kg) of feed refusals (FR), so the difference between offered feed and feed eaten by the sow, rather than on overall feed intake of a sow. The feed refusals were available only for group-housed sows and were subdivided into three periods of gestation: 1-28 days, 25-50 days, and 45-80 days. The first gestation period covers successful insemination and embryo implementation (Mwanza *et al.* 2000; Razdan *et al.* 2004a;b), so it is responsible for the sow reproductive performance. The

second gestation period covers the formation of the primary muscle fibers and the third period covers the formation of secondary muscle fibers in the two-phase-process of myogenesis in fetuses (McNamara *et al.* 2011), so are responsible for the fetus development. The process of myogenesis doesn't have completely fixed time boundaries and the two phases may overlap. FR observations from a gestation period were used in the analyses if at least 70% of days had FR recorded.

The third cluster includes sow gestation features describing sow gestation group (Table 3.5). Gestation groups (n=81) were created from the sows inseminated within the similar period of time and contained information on: gestation day sow entered group, number of sows, group average parity, and group average FR. During the first 28 days of gestation the group composition was stable. With time, the group composition changed; sows were removed from a group (because of return to estrus) or were mixed with another group. Therefore, this cluster included only observation on the first 28 days of gestation.

## 3.3 Methods

### 3.3.1 Non-genetic model

The first step in the analysis was to identify the sow gestation features that significantly affected grow-finish pig traits. The impact of the sow gestation features on growth rate and feed intake of her offspring was investigated using adjusted model for grow-finish pig traits as applied routinely by Topigs Norsvin (Bergsma *et al.* 2008). The fixed effects in the model varied depending on the analyzed trait (see models below). To quantify the effect of sow gestation features, they were added to the base model one at the time as a fixed effect. The significance of the sow gestation features (as addition to the base model) was determined using the MIXED procedure F-test (SAS Inst. Inc., Cary, NC). Addition of gestation features to the model did not affect the significance of the other fixed effects. The MIXED procedure was used to allow inclusion of random effects (given in italic in the models below). Selection of random effects to the model was made by comparing the log-likelihoods with the  $\chi^2$  – test. Effect “sow\_feature” in the models refers to the sow gestation features fitted into the model as: linear, linear and quadratic or class.

The model for GR, GR-restr, GR-adlib was:

$$y = \mu + \text{sow\_feature} + \text{sex} + \text{line} + \text{npen\_mates} + \text{compartment} \\ + \text{sow} + \text{litter} + \text{group} + \text{batch\_compartment} + e$$

### 3. Effect of gestating sow features on grow-finish pigs

**Table 3.4.** Characteristics of studied sow gestation features describing sow feed refusals during three stages of gestation<sup>1</sup>.

Gestation features <sup>2</sup>	1-28 day <sup>3</sup>			25-50 day <sup>3</sup>			45-80 day <sup>3</sup>		
	n <sup>4</sup>	Mean	SD	n <sup>4</sup>	Mean	SD	n <sup>4</sup>	Mean	SD
Days with records	1,562	25.1	1.7	1,648	25.4	1.3	1,664	35.1	1.5
Days with FR	1,562	2.3	3.5	1,648	1.3	2.6	1,664	2.3	3.6
Ratio of days with FR	1,562	0.09	0.14	1,648	0.05	0.1	1,664	0.07	0.1
Average FR, kg	1,562	0.13	0.21	1,648	0.05	0.1	1,664	0.06	0.1
Ratio of FR	1,562	0.05	0.09	1,648	0.02	0.1	1,664	0.02	0.04

<sup>1</sup>In total, 500 group-housed sows produced 1,735 litters. <sup>2</sup>Days with records = number of days the sow had feed refusals recorded; Days with FR = number of days the sow had feed refusals; Average FR = sow's average amount of feed refusals; Ratio of FR = sow's ratio of feed refusals to offered feed. <sup>3</sup>Based on observations during 1-28 days = from 1<sup>st</sup> to 28<sup>th</sup> day of gestation; 25-50 days = from 25<sup>th</sup> to 50<sup>th</sup> day of gestation; 45-80 days = from 45<sup>th</sup> to 80<sup>th</sup> day of gestation. <sup>4</sup>If >30% of records from the observed stages of gestation were missing, the gestation was not included in the analyses.

### 3. Effect of gestating sow features on grow-finish pigs

**Table 3.5.** Characteristics of studied sow gestation features describing group-housed sows<sup>1</sup>.

Sow gestation features <sup>2</sup>	n	Mean	SD
Gestation day sow entered group	1,533	4.0	3.0
Average group parity	1,533	3.8	1.1
Deviation from group parity	1,533	0.003	1.802
Number of sows in group, n	1,533	22.5	3.2
Number of sows with FR, n	1,533	14.2	6.0
Ratio of sows with FR	1,533	0.62	0.23
Average group FR, kg	1,533	0.13	0.09
Group ratio of FR	1,533	0.05	0.04

<sup>1</sup>In total, 494 sows were assigned to 81 gestation groups and produced 1,533 litters. <sup>2</sup>Gestation day sow entered group = gestation day when the sow is moved from individual crate to gestation group pen, counted from the day of insemination; Average group parity = average parity in gestation group; Deviation from group parity = difference between sow's parity and the group mean; Number of sows in group = number of the sows in gestation group; Number of sows with FR = number of sows in gestation group with feed refusals; Ratio of sows with FR = ratio of sows in gestation group with feed refusals to total number of sows in a group; Average group FR = average feed refusals in gestation group (from 1<sup>st</sup> to 28<sup>th</sup> day of gestation); Group ratio of FR = gestation group ratio of feed refusals to offered feed (from 1<sup>st</sup> to 28<sup>th</sup> day of gestation).

The model for FI was:

$$y = \mu + \text{sow\_feature} + \text{weight\_start} + \text{sex} + \text{line} + \text{npen\_mates} + \text{compartment} + \text{sow} + \text{litter} + \text{group} + \text{batch\_compartment} + e$$

For GR, GR-restr, GR-adlib fixed effects were: sex of the grow-finish pig (male, female, castrate), line of the grow-finish pig (25 levels), number of pen mates (7 levels), and compartment of the barn in which the pen was located (18 levels). For FI, the model had an additional fixed effect of start weight (kg); weight of the grow-finish pig at the beginning of finishing stage. The random effects in the model were: sow (*i.e.*, biological dam), litter in which a grow-finish pig was born, group in which grow-finish pig was kept during finishing stage, and the interaction of the batch in which the grow-finish pig was born and the compartment in which the pen was located.

### 3. Effect of gestating sow features on grow-finish pigs

---

Based on the results of the first step of the analyses, significant ( $P < 0.1$ ) sow gestation features were selected to be used in the second step.

#### 3.3.2 Genetic model

The second step of the analyses was to investigate whether the significant sow gestation features could explain the observed common litter and/or permanent sow effects while taking into account the genetics of the grow-finish pigs. For this purpose, the grow-finish pig traits were reanalyzed using an animal model in ASReml (Gilmour *et al.* 2006). To estimate the full magnitude of permanent sow and common litter effects, the initial model did not include sow gestation features (base model). Subsequently, the second model simultaneously included all significant gestation features for a trait ('all sow features' model). As common practice in animal breeding, the variances of common litter and permanent sow effects were expressed as fractions of phenotypic variance ( $\sigma_p^2$ ). Thus the magnitude of common litter effects was expressed as  $c^2 = \sigma_c^2 / \sigma_p^2$ , where  $\sigma_c^2$  is the common litter variance, and the magnitude of permanent sow effects as  $s^2 = \sigma_s^2 / \sigma_p^2$ , where  $\sigma_s^2$  is the variance of permanent sow effects. The difference in  $c^2$  and  $s^2$  estimates between the model including and the model excluding sow gestation features reveals whether all significant gestation features together can explain those effects. The animal model was:

$$\mathbf{y} = \mathbf{Xb} + \mathbf{Za} + \mathbf{Wc} + \mathbf{Vs} + \mathbf{Ug} + \mathbf{Tbc} + \mathbf{e},$$

where  $\mathbf{y}$  is a vector of observations on a grow-finish pig trait;  $\mathbf{X}$ ,  $\mathbf{Z}$ ,  $\mathbf{W}$ ,  $\mathbf{V}$ ,  $\mathbf{U}$  and  $\mathbf{T}$  are known incidence matrices relating observations to fixed or random effects;  $\mathbf{b}$  is a vector of fixed effects;  $\mathbf{a}$  is a vector of random additive genetic effects, with  $\mathbf{a} \sim N(\mathbf{0}, \mathbf{A}\sigma_a^2)$ ;  $\mathbf{c}$  is a vector of random non-genetic common litter effects (litter effect), with  $\mathbf{c} \sim N(\mathbf{0}, \mathbf{I}_c\sigma_c^2)$ ;  $\mathbf{s}$  is a vector of random non-genetic effects common to individuals with the same mother (permanent sow effect), with  $\mathbf{s} \sim N(\mathbf{0}, \mathbf{I}_s\sigma_s^2)$ ;  $\mathbf{g}$  is a vector of random non-genetic effects of individuals kept in the same group (group effect), with  $\mathbf{g} \sim N(\mathbf{0}, \mathbf{I}_g\sigma_g^2)$ ;  $\mathbf{bc}$  is a vector of random non-genetic effects of batch of birth by compartment of finishing stage (batch\_compartment effect), with  $\mathbf{bc} \sim N(\mathbf{0}, \mathbf{I}_{bc}\sigma_{bc}^2)$ ;  $\mathbf{e}$  is a vector of residuals, with  $\mathbf{e} \sim N(\mathbf{0}, \mathbf{I}_e\sigma_e^2)$ .  $\mathbf{I}_c$ ,  $\mathbf{I}_s$ ,  $\mathbf{I}_g$ ,  $\mathbf{I}_{bc}$  and  $\mathbf{I}_e$  are identity matrices of the appropriate dimensions, and  $\mathbf{A}$  is the numerator

relationship matrix calculated from a pedigree containing 34,092 animals over 5 generations.

## 3.4 Results and discussion

In total, the effect of 32 different sow gestation features divided into three clusters, *i.e.*, body-condition, feed refusals and group features, on the sow's offspring as grow-finish pigs was studied. The significant sow gestation features and their effects are described in Table 3.6 and Table 3.7.

This section will be divided into two parts. First, identification of gestation features that affect grow-finish pig traits. Second, investigation of the impact of gestation features on permanent sow and common litter effects in grow-finish pig traits.

### 3.4.1 Identification of significant sow gestation features

#### ***Sow body-condition***

In current study, the sow body-condition during gestation was described by gestation length as well as weight and backfat thickness measured at the entrance to the farrowing crate and after lactation. Gestation length affected both GR and FI of grow-finish pigs, whereas weight of a sow (at insemination, farrowing and after lactation) affected the growth related traits (Table 3.6).

Figure 3.1 shows the relation between traits of grow-finish pigs and gestation length. According to the linear estimate, grow-finish pigs (based on *ad libitum* fed animals) grow and eat more when their mother's gestation length increases (Table 3.6). Gestation length has a positive phenotypic correlation with individual/average birth weight of the piglets (Omtvedt *et al.* 1965; Rydhmer *et al.* 2008) and piglet birth weight has a large effect on overall performance of the pigs (Bee 2004; Gondret *et al.* 2005; Foxcroft *et al.*, 2006; Rehfeldt *et al.* 2008; Fix *et al.* 2010; Schinckel *et al.* 2010). To better understand this effect, we performed an additional analysis, in which gestation length and birth weight were simultaneously included in the model for grow-finish pig traits, and showed that the effect of gestation length was no longer significant. This suggests that the observed relationship between gestation length and growth rate of grow-finish pig may work via effect of birth weight, which is related to longer gestation. Sows that were heavier at insemination, at farrowing, and after lactation, produced offspring that grew faster in the finishing stage (Table 3.6). As body weight is a highly heritable trait, heavier sows on average produce heavier offspring. Thus the observed relationship between body weight of sows and growth rate of offspring may be a combination of genetic effects and effects originating from the body-condition of a sow.



### 3. Effect of gestating sow features on grow-finish pigs

**Table 3.6.** Estimated effect of significant sow gestation features describing sow body-condition (with SE), on production traits of grow-finish pigs (MIXED procedure)<sup>1</sup>.

Sow gestation features <sup>3</sup>		Grower-finishing traits <sup>2</sup>			
		GR	GR_restr	GR_adlib	FI
Gestation length, (g/day)/day	linear	1.4(0.7) <sup>**,4</sup>	n.s.	n.s.	6.8(2.5) <sup>***,4</sup>
Gestation length (g/day)/day <sup>2</sup>	linear+ quadratic	106(61) <sup>*</sup> -0.45(0.26) <sup>*</sup>	n.s.	237(84) <sup>***,4</sup> -1.0(0.4) <sup>***,4</sup>	n.s.
Weight at insemination, (g/day)/kg	linear	0.07(0.04) <sup>*,4</sup>	0.09(0.05) <sup>**,4</sup>	n.s.	n.s.
Weight at farrowing, (g/day)/kg	linear	0.14(0.03) <sup>***,4</sup>	0.14(0.04) <sup>***,4</sup>	0.16(0.05) <sup>***,4</sup>	n.s.
Weight after lactation, (g/day)/kg	linear	0.10(0.03) <sup>***,4</sup>	0.12(0.04) <sup>***,4</sup>	0.10(0.05) <sup>**,4</sup>	n.s.

\*\*\*P<0.01, \*\*P<0.05, \*P<0.1. <sup>1</sup>Estimated effects for grower-finishing traits are in g/day. <sup>2</sup>GR = growth rate; GR-restr = growth rate of grow-finish pigs fed restricted; GR-adlib = growth rate of grow-finish pigs fed *ad libitum*; FI = feed intake. <sup>3</sup>Weight at insemination = weight of the sow at insemination; Weight at farrowing = weight of the sow at farrowing; Weight after lactation = weight of the sow after lactation; Weight loss during lactation = weight loss of the sow during lactation. <sup>4</sup>Sow gestation features selected for the second step of analysis in model with all (significant) sow features per grow-finish pig trait. <sup>5</sup>n.s. = not significant.

### 3. Effect of gestating sow features on grow-finish pigs

**Table 3.7.** Estimated effect of significant sow gestation features describing feed refusals during 25-50 and 45-80 days of gestation (with SE), on production traits of grow-finish pigs (MIXED procedure)<sup>1</sup>.

Sow gestation features <sup>3</sup>		Grower-finishing traits <sup>2</sup>			
		GR	GR_restr	GR_adlib	FI
Days with FR (25-50), (g/day)/day	Linear class <sup>6</sup>	-1.1(0.5) <sup>**</sup>	-1.0(0.5) <sup>**</sup> n.s.	n.s. <sup>5</sup> <sup>**</sup>	n.s. n.s.
Ratio of days with FR (25-50), (g/day)/day	Linear Class	-32(11) <sup>***</sup> <sup>**</sup>	-31(13) <sup>**</sup> n.s.	-33(18) <sup>*</sup> <sup>**</sup>	n.s. <sup>**</sup>
Days with FR (45-80), (g/day)/day (g/day)/day <sup>2</sup>	Linear linear+ quadratic	-1.2(0.3) <sup>***</sup> n.s. n.s.	-1.2(0.4) <sup>***</sup> n.s. n.s.	-1.1(0.5) <sup>**</sup> -3.2(1.0) <sup>***</sup> 0.1(0.1) <sup>**</sup>	n.s. -5.7(2.7) <sup>**</sup> 0.4(0.1) <sup>**</sup>
Ratio of days with FR (45-80), (g/day)/day (g/day)/day <sup>2</sup>	Linear linear+ quadratic	-46(11) <sup>***</sup> n.s. n.s.	-46(12) <sup>***</sup> n.s. n.s.	-49(17) <sup>***</sup> -102(36) <sup>***</sup> 140(83) <sup>*</sup>	n.s. -189(94) <sup>**</sup> 393(215) <sup>*</sup>
Average FR (45-80), (g/day)/kg (g/day)/kg <sup>2</sup>	Linear linear+ quadratic	-24(11) <sup>**</sup> n.s. n.s.	n.s. n.s. n.s.	-44(17) <sup>**</sup> n.s. n.s.	n.s. -274(103) <sup>***</sup> 689(236) <sup>***</sup>
Ratio of FR (45-80), (g/day)/kg	Linear	-51(24) <sup>**</sup>	-52(27) <sup>**</sup>	n.s.	n.s.

<sup>\*\*\*</sup>P<0.01, <sup>\*\*</sup>P<0.05, <sup>\*</sup>P<0.1. <sup>1</sup>Estimated effects for grower-finishing traits are in g/day. <sup>2</sup>GR = growth rate; GR-restr = growth rate of grow-finish pigs fed restricted; GR-adlib = growth rate of grow-finish pigs fed *ad libitum*; FI = feed intake. <sup>3</sup>Days with FR = number of days the sow had feed refusals; Ratio of days with FR = sow's ratio of days with feed refusals to all days from the gestation period; Average FR = sow's average amount of feed refusals; Ratio of FR = sow's ratio of feed refusals to offered feed. Sow individual feed refusals were based on 25-50 or 45-80 days of gestation.

### 3. Effect of gestating sow features on grow-finish pigs

**Table 3.8.** Estimates (with SE) of parameters<sup>1</sup> for base model (no gestation features) and model with significant gestation features for grow-finish traits.

Trait <sup>2</sup>	Model	$\sigma_A^2$	$s^2$	$c^2$	$g^2$	$\sigma_e^2$	$\sigma_P^2$	$h^2$
<b>GR</b>	Base	1519 (187)	0.013 (0.008)	0.057 (0.007)	0.12 (0.007)	3614 (109)	6284 (95)	0.24 (0.03)
	All sow features	1576 (263)	0.009 (0.012)	0.056 (0.010)	0.11 (0.009)	3617 (150)	6273 (126)	0.25 (0.04)
<b>GR-restr</b>	Base	1382 (222)	0.01 (0.01)	0.066 (0.011)	0.11 (0.01)	3606 (132)	6127 (115)	0.23 (0.03)
	All sow features	1387 (288)	0.0004 (0.01)	0.071 (0.014)	0.12 (0.01)	3560 (169)	6091 (142)	0.23 (0.04)
<b>GR-adlib</b>	Base	1812 (295)	0.021 (0.014)	0.053 (0.013)	0.11 (0.01)	3460 (173)	6478 (144)	0.28 (0.04)
	All sow features	1988 (438)	0.019 (0.022)	0.052 (0.019)	0.10 (0.02)	3412 (250)	6525 (200)	0.31 (0.06)
<b>FI</b>	Base	0.012 (0.002)	0.02 (0.01)	0.04 (0.01)	0.31 (0.02)	0.023 (0.001)	0.056 (0.002)	0.22 (0.04)
	All sow features	0.016 (0.003)	0.004 (0.01)	0.01 (0.01)	0.33 (0.02)	0.019 (0.002)	0.055 (0.002)	0.30 (0.05)

<sup>1</sup>Sow effect:  $s^2 = \sigma_s^2 / \sigma_P^2$ ; litter effect:  $c^2 = \sigma_c^2 / \sigma_P^2$ ; group effect:  $g^2 = \sigma_g^2 / \sigma_P^2$ ; heritability:  $h^2 = \sigma_A^2 / \sigma_P^2$ . Batch\_compartment variance was not included into phenotypic variance. <sup>2</sup>GR = growth rate; GR-restr = growth rate of grow-finish pigs fed restricted; GR-adlib = growth rate of grow-finish pigs fed *ad libitum*; FI = feed intake.

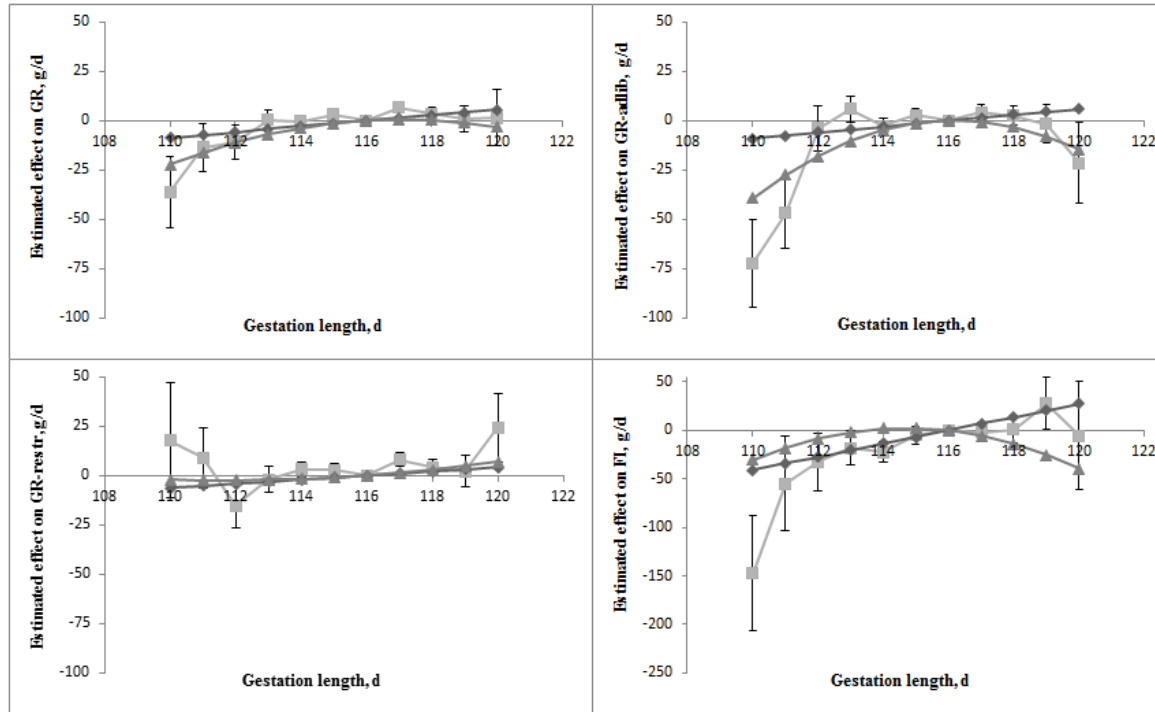
It is a common practice to use lactation loss of weight and/or backfat to describe sow body-condition. In current study, however, sow parturition-lactation weight and backfat loss had no effect on grow-finish pig traits (results not shown). No effect of the weight/backfat loss could be caused by the fact that in the current study the sow's weight/backfat at parturition and after lactation was used instead of the actual lactation weight/backfat loss.

#### ***Sow feed refusals***

Sow feed refusals data, collected under regular commercial circumstance, showed that sows did not eat the whole amount of offered feed during gestation. During 1-28 days of gestation 47% of the sows had at least one day with FR. During 25-50 days of gestation it was 26% and during 45-80 days of gestation it was 36% of the sows. The data used in the current study did not allow to investigate the reason the sow had feed refusals. Sow average FR during the first period of gestation did not significantly affected grow-finish pig traits. During 25-50 days of gestation, days with FR and the ratio of days with FR affected grow-finish pig traits (Table 3.7). During the last period of gestation (45-80 days) all FR related gestation features affected grow-finish pig traits (Table 3.7).

All significant gestation features related to FR had a negative effect on growth rate of grow-finish pigs (Table 3.7). That was the case for both restricted and *ad libitum* fed grow-finish pigs . Figure 3.2 shows the relation between GR traits of grow-finish pigs and sow FR during 45-80 days of gestation. Increasing sow FR from that period of gestation decreased the growth rate of grow-finish pigs , which may indicate an effect on grow-finish pig muscle development during prenatal life. During myogenesis the fixed number of muscle fibers is created (Rehfeldt *et al.* 2008; McNamara *et al.* 2011), and restrictive maternal nutrition during the fetus myogenesis can negatively affect this number (Ravelli *et al.*, 1999; Bee 2004). The lower number of muscle fibers is responsible for limiting the growth potential of the individual (Rehfeldt *et al.* 2006). It is known that myogenesis in pigs has two phases, the first one takes place around 25-50 days of gestation, and the second around 45-80 days of gestation (McNamara *et al.* 2011). From literature it is unclear in which of the two phases of myogenesis feed intake of a sow is most crucial for growth of her offspring. In studies applying dietary treatments to sows in gestation, Nissen *et al.* (2003) and Bee (2004) found a negative effect of increased sow feed intake during early stages of gestation on the smallest piglets muscle development and growth. However, also a positive effect of increased feed intake during later stage of gestation on offspring growth was reported

### 3. Effect of gestating sow features on grow-finish pigs



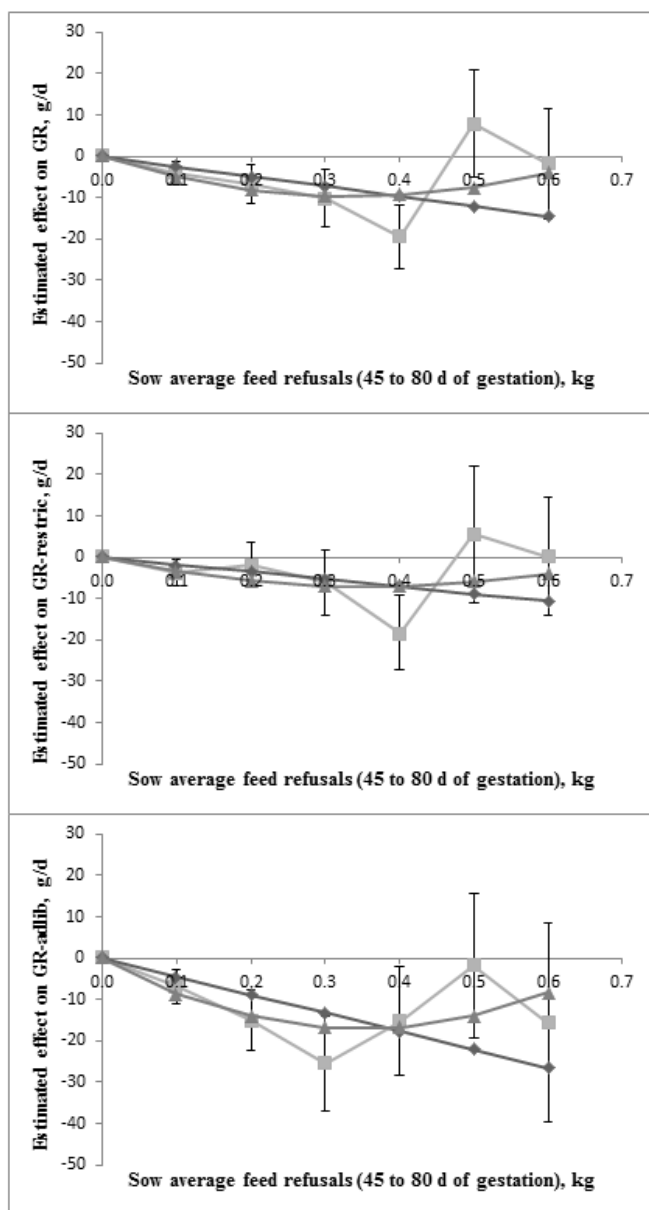
**Figure 3.1.** The effect of gestation length as class variable (■), as a deviation from the class with most observations, 116 days, for: growth rate of grow-finish pigs ( $P=0.1$ ) – GR (g/day), growth rate of grow-finish pigs fed restricted ( $P=0.3$ ) – GR-restr (g/day), growth rate of grow-finish pigs fed *ad libitum* ( $P=0.01$ ) – GR-adlib (g/day), and feed intake of grow-finish pigs ( $P=0.2$ ) – FI (g/day). ▲ – as linear variable (GR –  $P=0.04$ , GR-restr –  $P=0.2$ , GR-adlib –  $P=0.1$ , FI –  $P=0.007$ ); ● – as linear and quadratic variable (GR –  $P=0.09$ , GR-restr –  $P=0.7$ , GR-adlib –  $P=0.005$ , FI –  $P=0.1$ ). SD of GR is  $\sigma_{GR} = 95.4$  and SD of FI is  $\sigma_{FI} = 310$ . Significance level based on the MIXED procedure (SAS Inst. Inc., Cary, NC).

(Dwyer *et al.*, 1994; Musser *et al.*, 2006; McNamara *et al.*, 2011); while Heyer *et al.* (2004) and Lawlor *et al.* (2005) found no effect. In contrast to those studies, in the current study only the effect of sow FR (collected in commercial circumstances) rather than the effect of dietary treatments was investigated. Therefore, it is not possible to fully compare the current results with literature.

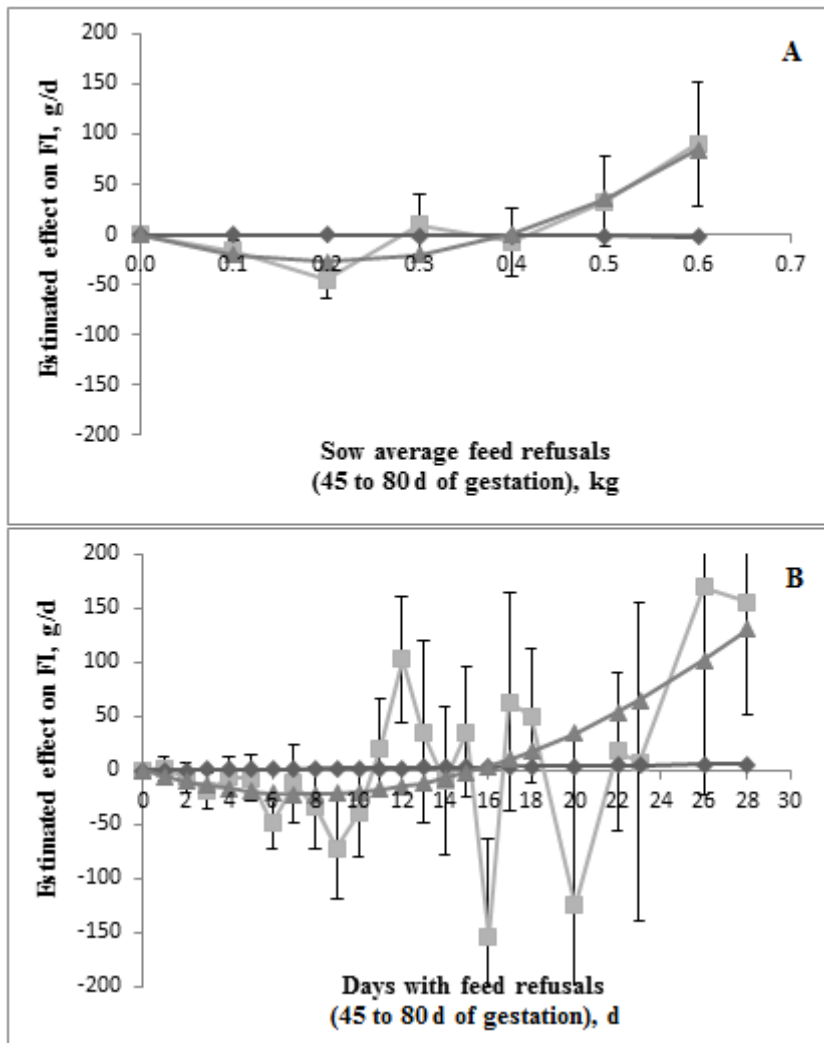
For FI an interesting pattern was observed in the relation with average FR (Figure 3.3, A) as well as days with FR (Figure 3.3, B) during 45-80 days of gestation. Sows that had substantially increased number of days with FR and average FR, had offspring with increased feed intake. This was also observed for FR during 1-28 and 25-50 days of gestation (results not shown). This could suggest a phenomena, called metabolic programming, which was investigated in studies on pigs (Bee 2004; Rehfeldt *et al.* 2006), sheep (Fahey *et al.* 2005; Costello *et al.* 2008) and human (Ravelli *et al.* 1999) and showed that offspring of mothers that experienced feed deficiency during gestation have decreased muscle mass and a tendency to obesity in adult life. Such offspring have increased feed intake that does not stimulate muscle growth, but leads to increase in adipose tissue (Ravelli *et al.*, 1999; Bee 2004; Kind *et al.* 2005). Additionally, in current study the effect of sow average FR and days with FR on grow-finish pig backfat thickness was investigated, but it was not significant. Also in current study, the feed deficiency that the sow experienced was smaller than in the studies where metabolic programming was found. Still, the sows with the highest average FR and number of days with FR produced offspring with increased FI and decreased GR. This would indicate the undesirable feed conversion ratio and to avoid it, FR during gestation should be limited.

Although, sow FR during 1-28 days of gestation did not have a significant effect on grow-finish pig traits (results not shown), this still requires a discussion. Results shown here indicate that even if sows do not eat the full amount of offered feed during 1-28 days of gestation (average ratio of FR was 5%, Table 3.4), on average their offspring's GR and FI in finishing stage is not affected. The FR during 1-28 days of gestation were most probably caused by introducing sows to a new gestation group, which is a stressful moment for sows (discussed in the next section). Previous studies showed that the early gestation feed deficiency is the most crucial for the sow's reproductive performance rather than offspring performance. Feed deficiency during the first 21 days of gestation affects sows' hormones levels, development and transport of embryos, as well as placenta size (Mwanza *et al.* 2000; Razdan *et al.* 2004a;b). In current study, sows with FR during 1-28 days of gestation, were still able to produce a regular litter.

### 3. Effect of gestating sow features on grow-finish pigs



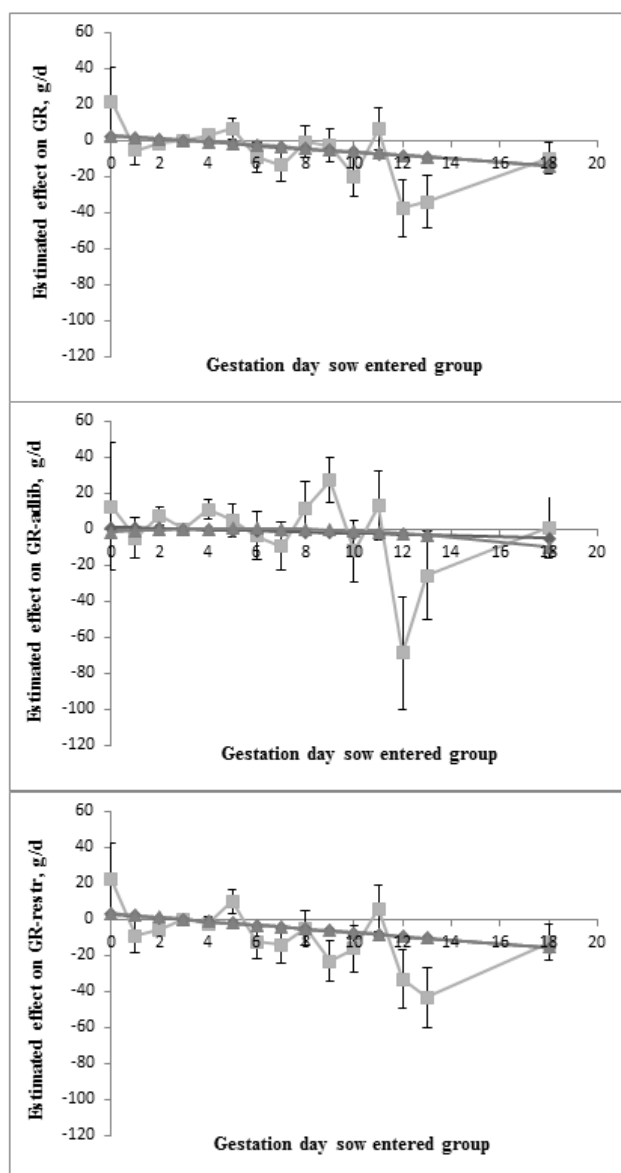
**Figure 3.2.** The effect of sow average feed refusals during 45-80 days of gestation as class variable (■), as deviation from the class with most observations, 0 kg of feed refusals, for: growth rate of grow-finish pigs ( $P=0.1$ ) – GR (g/d), growth rate of grow-finish pigs fed restricted ( $P=0.5$ ) – GR-restr (g/d) and growth rate of grow-finish pigs fed *ad libitum* ( $P=0.1$ ) – GR-adlib (g/d). ▲ – as linear variable (GR –  $P=0.03$ , GR-restr –  $P=0.2$ , GR-adlib –  $P=0.01$ ); ● – as linear and quadratic variable (GR –  $P=0.1$ , GR-restr –  $P=0.4$ , GR-adlib –  $P=0.1$ ). SD of GR is  $\sigma_{GR} = 95.4$ . Significance level based on MIXED procedure (SAS Inst. Inc., Cary, NC).



**Figure 3.3.** A – The effect of sow average feed refusals during 45-80 days of gestation as class variable (■), as a deviation from the class with most observations, 0 kg of feed refusals, for feed intake of grow-finish pigs ( $P=0.09$ ) – FI (g/day). ▲ – as linear variable ( $P=0.9$ ); ● – as linear and quadratic variable ( $P=0.004$ ). B – The effect of sow days with feed refusals during 45-80 days of gestation as class variable (■), starting from the class with most observations, 0 days with feed refusals, for feed intake of grow-finish pigs ( $P=0.5$ ). ▲ – as linear variable ( $P=0.9$ ); ● – as linear and quadratic variable ( $P=0.01$ ). SD of FI is  $\sigma_{FI} = 310$ . Significance level based on the MIXED procedure (SAS Inst. Inc., Cary, NC).



### 3. Effect of gestating sow features on grow-finish pigs



**Figure 3.4.** The effect of gestation day sow entered group as class variable (■), as a deviation from the class with most observations, 3<sup>rd</sup> day of gestation, for: growth rate of grow-finish pigs ( $P=0.06$ ) – GR (g/day), growth rate of grow-finish pigs fed restricted ( $P=0.04$ ) – GR-restr (g/day), and growth rate of grow-finish pigs fed *ad libitum* ( $P=0.1$ ) – GR-adlib (g/day). ▲ – as linear variable (GR –  $P=0.04$ , GR-restr –  $P=0.04$ , GR-adlib –  $P=0.7$ ); ● – as linear and quadratic variable (GR –  $P=0.9$ , GR-restr –  $P=0.9$ , GR-adlib –  $P=0.6$ ). SD of GR is  $\sigma_{GR} = 95.4$  and SD. Class ‘18’ represents the sows that entered a gestation group between 14<sup>th</sup> and 28<sup>th</sup> day of gestation. Significance level based on the MIXED procedure (SAS Inst. Inc., Cary, NC).

#### ***Sow gestation group***

The new legislation is introducing the group-housing for gestating sows. The group-housing will lead to interactions between sows, which could affect sow environment during gestation and therefore also the offspring performance. Characteristics of group-housed sows were included in current study to investigate optimal conditions for the new housing system for gestating sows. From all the analyzed gestation features from this cluster, gestation day sow entered the group had a significant effect on all grow-finish pig traits (Figure 3.4) and number of sows in group had a significant effect on FI.

Sows that were mixed early in gestation (during the first 8 days after insemination), had better performing offspring than the sows that entered a group later (Figure 3.4). During the first 8 days of gestation most sows were moved from the individual crate, where the insemination took place, to the gestation pen, where they were housed with other sows. For only 125 gestations (out of 2,521), sows were introduced to the group later, between the 9<sup>th</sup> and the 28<sup>th</sup> day of gestation. Thus, for these 125 gestations, the sow entered a gestation group at different stage of gestation than the other sows in that group. A sow could stay longer in individual crate for several reasons, for example, potentially failed insemination or health problems. The new European Union legislation for group-housing of gestating sows, allows to create groups after 21 days from insemination. Introducing sows to a new gestation group is a stressful moment for a sow, which could affect sow's reproduction (Spooler *et al.* 2009). Literature, however, shows contradicting results. Kirkwood *et al.* (2005) showed that farrowing rate was significantly higher in sows mixed on the 2<sup>nd</sup> day (86%) of gestation in comparison with sows mixed on the 14<sup>th</sup> day (70%), indicating that mixing early in gestation is better for sows performance. But, Bokma (1990) showed 20% return to estrus in sows mixed on the first week of gestation in comparison with 10% return rate when mixing in the 4<sup>th</sup> week. Results of the current paper suggest that mixing of the sows should take place already within the first 8 days after insemination. However, if the sow had health problems before entering the group this could also affect the offspring. Therefore, the effect of day of mixing the sows might not be the only factor causing differences between offspring performance.

Number of sows in a group had significant and negative effect only for FI (-9 [g/day]/group\_member,  $P=0.04$ , results not shown). The estimated effects of gestation group size on growth rate traits were also negative, but not significant (results not shown). Size of gestation group is an important topic in a debate on group-housing system (Spooler *et al.* 2009). Negative effect of number of sows shown in current study may be due to a difference in the interactions among sows

### 3. Effect of gestating sow features on grow-finish pigs

---

in small versus large groups. The impact of gestation group size has been investigated in studies on sow behavior, stress levels, and aggression (Brouns *et al.* 1994; Boyle *et al.* 2002; Anil *et al.* 2006). However, there is no or little evidence of an optimal gestation group size (Arey *et al.* 1998; Kongsted 2004; Spoolder *et al.* 2009). Nevertheless, our results indicate that smaller gestation groups (<20 sows) are a better choice when considering performance of offspring.

Gestation group also had a significant effect on grow-finish pig traits (results not shown). The significance of gestation group is partially caused by the fact that each studied gestation group produced one of the batches in which the grow-finish pigs were born. This means that gestation group and batch effects were confounded in the model. Based on the results from this cluster of sow gestation features, no definite recommendations can be made for group-housing of gestating sows.

#### 3.4.2 Estimated effect of sow gestation features on grow-finish pig traits

The current study focused on the effect of three clusters of sow gestation features (sow body-condition, feed refusals, and gestation group) on grow-finish pigs growth and feed intake. Sow gestation features from all the clusters explained 1% to 3% of the total phenotypic variance in grow-finish pigs (based on estimates from Table 3.6 and Table 3.7). Thus effects of gestation features were significant and literature supports those findings. However, the estimated effects of gestation features were small. Similar size of the estimates for grow-finish pig traits was reported by Sell-Kubiak *et al.* (2012) for the effect of sow history features on GR and FI.

#### 3.4.3 Investigation of impact of sow features on $c^2$ and $s^2$

After the identification of significant gestation features, the second objective was to investigate whether those features can account for the variance in grow-finish pig traits due to permanent sow and common litter effects. Gestation features selected per grow-finish pig trait for 'all sow features' model are indicated by the footnote in Table 3.6 and Table 3.7.

The estimates of  $s^2$  from the base model are small, but in line with literature (Ferraz *et al.* 1993; Crump *et al.* 1997; Chen *et al.* 2002; Johnson *et al.* 2002). The estimates of  $c^2$  from the base model (Table 3.8) are in agreement with those reported in previous studies, where similar (Bergsma *et al.* 2008) or the same data were used (Sell-Kubiak *et al.* 2012). As shown in those previous studies, in the model with random group effect,  $c^2$  is lower than expected from literature (Bidanel *et al.* 1996; Johnson *et al.* 2002; Neugebauer *et al.* 2010). That is caused by partial confounding

between common litter and group, since groups in finishing stage are not composed from unrelated grow-finish pigs only, but also contain full sibs. When comparing the base model with 'all sow features' model, estimates of  $c^2$  were not affected, except for FI where it decreased considerably (Table 3.8). Thus sow gestation features were unsuccessful in explaining the variance due to common litter effect for growth related traits, whereas for FI gestation features explained half of the variance due to the common litter effect. For  $s^2$  when comparing the base model with 'all sow features' model, estimates of  $s^2$  decreased for GR-restr and FI and were not affected for GR and GR-adlib. The sow gestation features explained phenotypic variance due to permanent sow effects for GR-restr and FI, since for these grow-finish pig traits this effect decreased to (near)-zero. However,  $s^2$  effect is small and also it is not a common practice to include permanent sow effect in models for grow-finish pig traits (Ferraz *et al.* 1993; Crump *et al.* 1997). Those conclusions are in agreement with a previous study where features from sow early life (history features) were used to explain mechanisms underlying the observed common litter and permanent sow effects (Sell-Kubiak *et al.* 2012). However, the sow gestation features better explained the estimated common litter effect. Additionally, the estimates of residual variance in GR related traits almost did not change, but for FI decreased by 17% (Table 3.8).

### 3.5 Conclusions

Sow gestation features have significant effects on grow-finish pig traits. Those features, however, explained 1-3% of the total phenotypic variance in grow-finish pigs and only a small proportion of phenotypic variance due to permanent sow and common litter effects. Thus there is a small potential for improving grow-finish pigs performance by implementing sow gestation features in practice.

### 3.6 Acknowledgments

This research was financially supported by the Dutch Science Council (NWO) and part of the study was coordinated by the Dutch Technology Foundation (STW). The authors would like to thank Egbert Knol for valuable suggestions at the early stages of the analyzes. The data for this research were provided by the Topigs Norsvin (Beuningen, The Netherlands), the authors would like to especially thank Annemieke Sprangers and Yvonne Wientjes for building the dataset. Ewa Sell-Kubiak would like also to thank Susan Wijga, Katrijn Peeters, Naomi Duijvesteijn and Irene Camerlink for helpful comments and suggestions.



# 4

## **Comparison of methods to study uniformity of traits: application to birth weight in pigs**

E. Sell-Kubiak<sup>1</sup>, P. Bijma<sup>1</sup>, E.F. Knol<sup>2</sup>, H.A. Mulder<sup>1</sup>

<sup>1</sup> Animal Breeding and Genomics Centre, Wageningen University, PO Box 338, 6700 AH Wageningen, The Netherlands; <sup>2</sup> Topigs Norsvin Research Center, P.O. Box 43, 6640 AA Beuningen, The Netherlands

Journal of Animal Science (2015) doi:10.2527/jas2014-8313

## Abstract

Increasing uniformity of traits is an important objective in livestock production. This study focused on the comparison of a Double Hierarchical GLM (DHGLM) with the conventional analysis of uniformity, using within-litter variation in birth weight in pigs as a case. In pigs, within-litter variation of birth weight (BW) is a trait where uniformity is important in breeding practice. Traditionally, uniformity has been studied by analysis of standard deviations (SD) or variances. In DHGLM differences between animals are studied by analyzing the residual variance of the trait and estimating its variance components. Here we used data on birth weight, recorded in two sow lines (Large White and Landrace), to compare the estimation of genetic parameters and breeding values for uniformity from DHGLM and traditional analysis of the variance. Comparison of DHGLM with the conventional analysis using the log-transformed variance of BW was possible, because both methods were on the same scale and the models contained the same random effects. In addition, the genetic coefficient of variation at residual standard deviation level ( $GCV_{SDe}$ ) was proposed as a measure expressing the potential response to selection. Three-fold cross-validation was performed to study predictive ability of both methods. The estimated  $GCV_{SDe}$  was highly similar using both methods. Results indicate that the SD of BW can be decreased by up to ~10% after one generation of selection, indicating good prospects for response to selection. The correlation between EBVs (0.88 in both sow lines) obtained from both methods indicated high resemblance of conventional analysis and DHGLM. Comparison of accuracies of EBVs showed that both methods were comparable; with moderate accuracies achieved with ~100 piglets per maternal grandsire. Cross-validation also indicated very similar predictive ability in estimating EBV for BW variation for both methods. Thus, it was concluded that conventional analysis and DHGLM produced highly comparable results. Still, the DHGLM has potentially a broader application than conventional analysis to study uniformity of traits, because it can be used also for traits with single observations per animal.

Key words: birth weight, Double Hierarchical GLM, pigs, residual variance, uniformity

### 4.1 Introduction

Uniformity is an essential goal in various stages of livestock production. Within-litter variation of birth weight (BW) in pigs is a trait where uniformity has a high importance in breeding practice for animal survival (*e.g.* English and Smith, 1975) and from an economic perspective (Roberts and Deen, 1995). Traditionally, variation of BW is studied on the litter level, by analyzing within-litter SD or variance of BW treated as a trait of the sow (Damgaard *et al.*, 2003; Canario *et al.*, 2010). BW is also collected on each individual piglet in the litter. Recently developed Double Hierarchical Generalized Linear Model (DHGLM; Rönnegård *et al.*, 2010) may be an alternative to study uniformity of individual BW within a litter. There is empirical evidence for a genetic variance in uniformity. This is caused by heterogeneity of residual (environmental) variance, which differs among individuals and has a genetic component (Hill and Mulder, 2010). Differences in residual variance between animals can be studied using DHGLM, which analyze the residual variance of the trait and estimate its variance components. Previously, DHGLM have been used to study variation in litter size of pigs (Felleki *et al.*, 2012), in body weight in Atlantic salmon (Sonesson *et al.*, 2013), and in milk production traits in dairy cows (*e.g.* Vandenplas *et al.*, 2013). However, estimates of DHGLM have not been compared with estimates of conventional analysis that uses the SD or variance of the trait as a dependent variable.

Because DHGLM is complex, validation would be desirable. Thus, the main objective of this study was to compare two tools to study uniformity of traits: DHGLM and conventional analysis. The evaluation was performed by comparing genetic parameters, EBV and the accuracy of EBV for uniformity from both methods, and by using cross-validation to investigate the predictive ability of both methods. Observations on BW of piglets recorded in two sow lines (Large White and Landrace) were used.

### 4.2 Materials and Methods

Animal Care and Use Committee approval was not required for this study because the data were obtained from an existing database.



## 4. Comparison of methods to study uniformity of traits

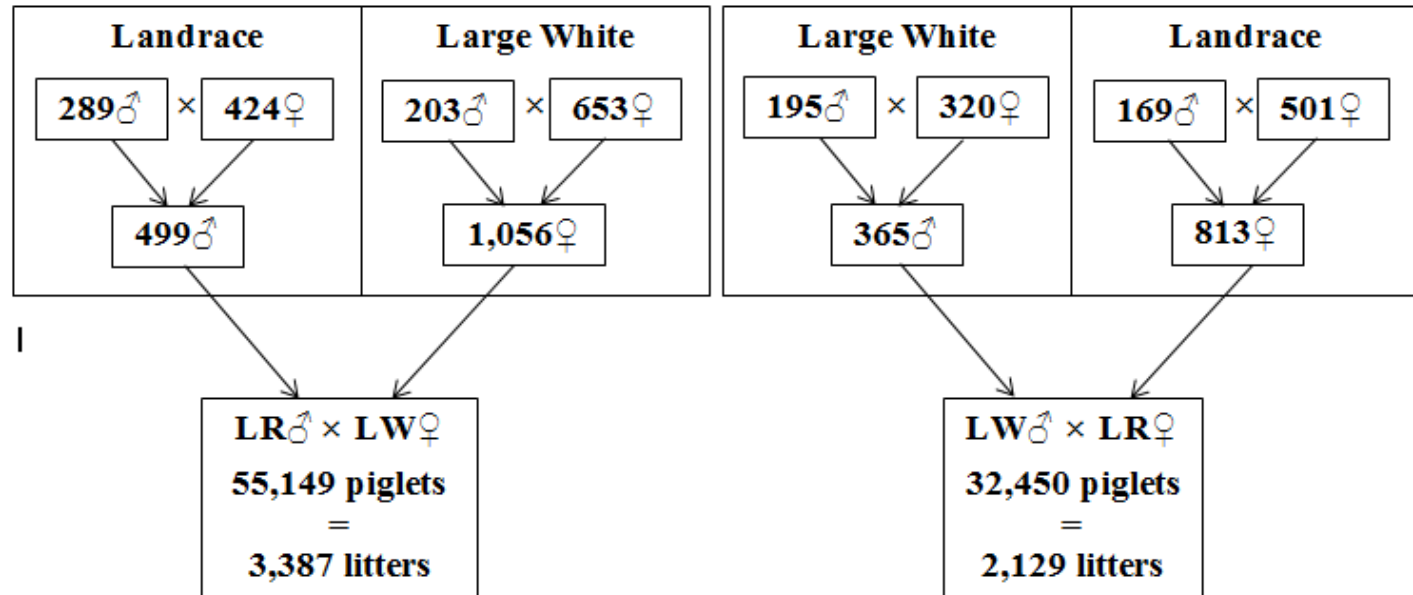
### 4.2.1 Observations on birth weight

Data were collected at nucleus farms of Topigs Norsvin (Beuningen, The Netherlands) between April 2007 and June 2013. Records of birth weight (BW) were collected on crossbred litters. Litters were obtained by mating Landrace boars to Large White sows (499 LR♂ x 1,056 LW♀; Figure 4.1) and Large White boars to Landrace sows (365 LW♂ x 813 LR♀; Figure 4.1). Since piglet's BW is considered a trait of the sow, only the sow line will be mentioned when describing the data.

The LW and LR sows produced 3,387 and 2,129 litters, respectively. Birth weight observations were available for 55,149 and 32,450 piglets in litters from LW and LR sows, respectively, and these included 5,473 (LW) and 2,376 (LR) records from stillborn piglets that were kept for the analysis. During data editing, the entire litter was excluded if it had: less than 6 piglets in total number born (TNB), piglets without information about survival at birth, piglets without a BW record, or piglets lighter than 0.3 kg (N=23) and/or heavier than 2.6 kg (N=6). Table 4.1 shows the descriptive statistics of the edited data. The complete pedigree for both breeds contained 7,415 animals over 5 generations. The two parental populations are not closely related.

**Table 4.1.** Descriptive statistics of piglet traits: birth weight (BW), standard deviation of BW (SD of BW), total number born (TNB), and number born alive (NBA); in two sow lines: Large White (LW) or Landrace (LR).

Sow line	Trait	n	Mean	SD
LW	BW_TNB, kg	55,149	1.19	0.31
	BW_NBA, kg	49,676	1.21	0.31
	BW_Stillborn, kg	5,473	1.01	0.29
	TNB per litter, n	3,387	16.3	3.1
	NBA per litter, n	3,387	14.7	2.9
	SD of BW, kg	3,387	0.25	0.01
	Stillborn per litter, n	3,387	1.6	1.9
LR	BW_TNB, kg	32,450	1.29	0.33
	BW_NBA, kg	30,074	1.31	0.33
	BW_Stillborn, kg	2,376	1.10	0.28
	TNB per litter, n	2,129	15.2	2.9
	NBA per litter, n	2,129	14.1	2.8
	SD of BW, kg	2,129	0.26	0.01
	Stillborn per litter, n	2,129	1.1	1.5



**Figure 4.1.** Overview of the family structure of piglets being crosses of two pure lines: Landrace x Large White (LR♂xLW♀) or Large White x Landrace (LW♂xLR♀).

### 4.2.2 Statistical models

In this study, three models will be described: two models representing the conventional analysis to study individual BW of offspring and within-litter variance of BW, and a Double Hierarchical GLM representing a new approach to simultaneously study individual BW of offspring and its residual variance. The DHGLM (Lee and Nelder, 2006) distinguishes two parts in the model: the trait level, *i.e.* BW itself, and the trait's variance, *i.e.* residual variance of BW. In the variance part of the model, the response variable is based on the residuals from the level part of the model (see section "*DHGLM analysis of birth weight*"). In this way, DHGLM can use individual observations of BW of offspring to study the genetic variance in residual variance of BW. A DHGLM is an example of structural modeling of residual variance (Foulley *et al.*, 1990; SanCristobal-Gaudy *et al.*, 1998).

To compare the methods, models need to be on the same scale. The DHGLM uses the residual variance of the trait and assumes an exponential model for the variance level, also referred to as a multiplicative model (SanCristobal-Gaudy *et al.*, 1998). Felleki *et al.* (2012) proposed taking a logarithm of the exponential model for the residual variance, which transforms the model into a linear model (see section "*DHGLM analysis of birth weight*"). To enable comparison of both methods, therefore, we used the log-transformed variance of within-litter BW as a response variable in the conventional analysis. Consequently, both the conventional analysis and DHGLM yield estimates on the same scale, being the log of the residual variance.

To enable comparison of the variance estimates between the methods, models also need to have the same random effects. BW is considered to be a strictly maternal trait, so most previous studies have applied a maternal genetic model (Damgaard *et al.*, 2003). However, there is also evidence for a direct genetic effect on BW (Roehe, 1999). Including a direct genetic effect in a DHGLM with single observation per individual, however, gives severe biases in the estimated variance components (Mulder *et al.*, 2013a; Sonesson *et al.*, 2013). As an alternative, the sire and dam genetic effects can be added to the model as random effects to partly account for the direct genetic effect. The dam genetic effect then becomes the sum of the pure maternal genetic effects and direct genetic effects transmitted by the dam to the offspring.

Based on Likelihood Ratio Test (LRT) and variance components estimates the best fitting models were chosen for both methods. The statistical package ASReml 2.0 (Gilmour *et al.*, 2006) was used for all analyses. The model testing is presented in the *Appendix*. The random effects are the same in both methods, except in the

analysis of the log-transformed within-litter variance of BW where the litter effect was excluded, because observations are already at litter level. In the subsequent part of this section the full models are presented for: individual BW of offspring (model 5, *Appendix A*), log-transformed within-litter variance of BW (model 3, *Appendix B*) and DHGLM (model 4, *Appendix C*).

### 4.2.3 Conventional analyses of birth weight

#### *Analysis of individual birth weight of offspring*

The conventional analysis of individual BW of piglets included in the model the fixed effects: total number of piglets born in the litter (TNB), parity of the sow (parity), the birth farm, year and season of the piglet (farm\_year\_season), and gender of the piglet (sex); as well as the random effects: dam genetic, sire genetic, permanent sow and litter. The model was:

$$\mathbf{y} = \mathbf{X}\mathbf{b} + \mathbf{Z}\mathbf{a}_d + \mathbf{Z}\mathbf{a}_s + \mathbf{U}\mathbf{pe} + \mathbf{V}\mathbf{c} + \mathbf{e},$$

where  $\mathbf{y}$  is a vector of observations on BW of piglet;  $\mathbf{X}$ ,  $\mathbf{Z}$ ,  $\mathbf{U}$ , and  $\mathbf{V}$  are known incidence matrices relating observations to fixed or random effects;  $\mathbf{b}$  is a vector of fixed effects;  $\mathbf{a}_d$  is a vector of random dam genetic effects (dam effect), with  $\mathbf{a}_d \sim N(\mathbf{0}, \mathbf{A}\sigma_{a_d}^2)$ ;  $\mathbf{a}_s$  is a vector of random sire genetic effects (sire effect), with  $\mathbf{a}_s \sim N(\mathbf{0}, \mathbf{A}\sigma_{a_s}^2)$ ;  $\mathbf{pe}$  is a vector of random non-genetic effect of the sow (permanent sow effect), with  $\mathbf{pe} \sim N(\mathbf{0}, \mathbf{I}_{pe}\sigma_{pe}^2)$ ;  $\mathbf{c}$  is a vector of random non-genetic common litter effects (litter effect), with  $\mathbf{c} \sim N(\mathbf{0}, \mathbf{I}_c\sigma_c^2)$ ;  $\mathbf{e}$  is a vector of residuals, with  $\mathbf{e} \sim N(\mathbf{0}, \mathbf{I}_e\sigma_e^2)$ . In this model the residual variance was assumed homogeneous.  $\mathbf{I}_{pe}$ ,  $\mathbf{I}_c$  and  $\mathbf{I}_e$  are identity matrices of the appropriate dimensions, and  $\mathbf{A}$  is the numerator relationship matrix based on pedigree. Dam and sire genetic effects were assumed to be independent from each other, since they originate from two genetically separate lines.

#### *Analysis of within-litter variance of birth weight*

The conventional analysis of within-litter log-transformed variance of BW was performed with the following model:

$$\mathbf{y}_v = \mathbf{X}\mathbf{b}_v + \mathbf{Z}\mathbf{a}_{dv} + \mathbf{Z}\mathbf{a}_{sv} + \mathbf{U}\mathbf{pe}_v + \mathbf{e}_v,$$

where  $\mathbf{y}_v$  is a vector of log-transformed variance of BW;  $\mathbf{b}_v$  is a vector of fixed effects;  $\mathbf{a}_{dv}$  is a vector of random dam genetic effects, with  $\mathbf{a}_{dv} \sim N(\mathbf{0}, \mathbf{A}\sigma_{a_{dv}}^2)$ ;  $\mathbf{a}_{sv}$  is

#### 4. Comparison of methods to study uniformity of traits

---

a vector of random sire genetic effects, with  $\mathbf{a}_{sv} \sim N(\mathbf{0}, \mathbf{A}\sigma_{a_{sv}}^2)$ ;  $\mathbf{pe}_v$  is a vector of random non-genetic effect of the sow (permanent sow effect), with  $\mathbf{pe}_v \sim N(\mathbf{0}, \mathbf{I}_{pe_v}\sigma_{pe_v}^2)$ ;  $\mathbf{e}_v$  is a vector of residuals, with  $\mathbf{e}_v \sim N(\mathbf{0}, \mathbf{I}_{e_v}\sigma_{e_v}^2)$ . To account for differences in residual variance due to litter size, the analyses were performed by estimating the residual variance for one of the groups of TNB piglets. In the sow line LW four groups were defined (group 1: 905 litters, TNB 6-14 piglets; group 2: 851 litters, TNB 15-16 piglets; group 3: 841 litters, TNB 17-18 piglets; group 4: 790 litters, TNB 19-24 piglets) whereas in the sow line LR three groups (group 1: 786 litters, TNB 6-14 piglets; group 2: 641 litters, TNB 15-16 piglets; group 3: 702 litters, TNB 17-24 piglets). Fixed effects in the model were: parity of the sow (parity), the birth farm, year and season of the piglet (farm\_year\_season) and frequency of male piglets multiplied by frequency of female piglets in the litter (freq $\delta$ \*freq $\phi$ ). Using freq $\delta$ \*freq $\phi$  accounts for the effect of a difference in BW between male and female piglets on the within-litter variance of BW. Potentially, also the within-family variance of male and female piglets could be different, but estimating the log-transformed within-litter variance for males and females separately as done by Wittenburg *et al.* (2008) and Wittenburg *et al.* (2010) did not meaningfully change the estimates of variance components.

##### 4.2.4 DHGLM analysis of birth weight and its variation

The recently developed method by Rönnegård *et al.* (2010) allows studying the residual variance of traits by fitting a Double Hierarchical GLM in ASReml 2.0 (Gilmour *et al.*, 2006). In Rönnegård *et al.* (2010) the response variable in the

variance model was  $\log(\phi_i) = \log\left(\frac{e_i^2}{1-h_i}\right)$ , where  $e_i^2$  is the squared residual

from the level part of the model for observation  $i$  and  $h_i$  is the leverage, the diagonal element of the hat matrix of  $\mathbf{y}$  corresponding to observation  $i$ . A log link

function was used, because  $\frac{e_i^2}{1-h_i}$  is  $\chi^2$ -distributed with one degree of freedom.

Felleki *et al.* (2012) showed that instead of using a log link function,  $\log\left(\frac{e_i^2}{1-h_i}\right)$

can be linearized using the Taylor expansion of the first order by calculating the

response variable  $\psi_i = \log(\hat{\sigma}_{e_i}^2) + \frac{\frac{e_i^2}{1-h_i} - \hat{\sigma}_{e_i}^2}{\hat{\sigma}_{e_i}^2}$ . This would enable using a

bivariate linear mixed model, where  $\hat{\sigma}_{e_i}^2$  is the predicted residual variance for observation  $i$  and  $\psi$  is a vector with the response variable in the variance part of the model. Note that  $\psi_i$  is a linearized working variable for  $\log(\phi_i)$ . The DHGLM is then as follows:

$$\begin{bmatrix} \mathbf{y} \\ \boldsymbol{\psi} \end{bmatrix} = \begin{bmatrix} \mathbf{X} & \mathbf{0} \\ \mathbf{0} & \mathbf{X}_v \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{b}_v \end{bmatrix} + \begin{bmatrix} \mathbf{Z} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_v \end{bmatrix} \begin{bmatrix} \mathbf{a}_d \\ \mathbf{a}_{dv} \end{bmatrix} + \begin{bmatrix} \mathbf{Z} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_v \end{bmatrix} \begin{bmatrix} \mathbf{a}_s \\ \mathbf{a}_{sv} \end{bmatrix} \\ + \begin{bmatrix} \mathbf{U} & \mathbf{0} \\ \mathbf{0} & \mathbf{U}_v \end{bmatrix} \begin{bmatrix} \mathbf{pe} \\ \mathbf{pe}_v \end{bmatrix} + \begin{bmatrix} \mathbf{V} & \mathbf{0} \\ \mathbf{0} & \mathbf{V}_v \end{bmatrix} \begin{bmatrix} \mathbf{c} \\ \mathbf{c}_v \end{bmatrix} + \begin{bmatrix} \mathbf{e} \\ \mathbf{e}_v \end{bmatrix}$$

where  $\mathbf{y}$  is a vector of observations on BW of piglets and  $\boldsymbol{\psi}$  is a vector of response variables in the variance part of the DHGLM; the residuals  $\mathbf{e}$  are assumed to be independent and normally distributed, but with heterogeneous variances across the observations;  $\mathbf{b}_v$  is a vector of fixed effects on  $\boldsymbol{\psi}$ ;  $\mathbf{a}_{dv}$  is a vector of random dam genetic effect on  $\boldsymbol{\psi}$  common to individuals with the same mother (dam

effect), with  $\begin{bmatrix} \mathbf{a}_d \\ \mathbf{a}_{dv} \end{bmatrix} \sim N\left(\mathbf{0}, \begin{bmatrix} \sigma_{a_d}^2 & \sigma_{a_d, a_{dv}} \\ \sigma_{a_d, a_{dv}} & \sigma_{a_{dv}}^2 \end{bmatrix} \otimes \mathbf{A}\right)$ ;  $\mathbf{a}_{sv}$  is a vector of random

sire genetic effect on  $\boldsymbol{\psi}$  common to individuals with the same father, with

$\begin{bmatrix} \mathbf{a}_s \\ \mathbf{a}_{sv} \end{bmatrix} \sim N\left(\mathbf{0}, \begin{bmatrix} \sigma_{a_s}^2 & \sigma_{a_s, a_{sv}} \\ \sigma_{a_s, a_{sv}} & \sigma_{a_{sv}}^2 \end{bmatrix} \otimes \mathbf{A}\right)$ ;  $\mathbf{pe}_v$  is a vector of random non-genetic

permanent sow effects on  $\boldsymbol{\psi}$ , with  $\begin{bmatrix} \mathbf{pe} \\ \mathbf{pe}_v \end{bmatrix} \sim N\left(\mathbf{0}, \begin{bmatrix} \sigma_{pe}^2 & \sigma_{pe, pe_v} \\ \sigma_{pe, pe_v} & \sigma_{pe_v}^2 \end{bmatrix} \otimes \mathbf{I}\right)$ ;  $\mathbf{c}_v$  is

a vector of random non-genetic common litter effects (litter effect) on  $\boldsymbol{\psi}$ , with

$\begin{bmatrix} \mathbf{c} \\ \mathbf{c}_v \end{bmatrix} \sim N\left(\mathbf{0}, \begin{bmatrix} \sigma_c^2 & \sigma_{c, c_v} \\ \sigma_{c, c_v} & \sigma_{c_v}^2 \end{bmatrix} \otimes \mathbf{I}\right)$ ; and  $\mathbf{e}_v$  is a vector of residuals, with

$\begin{bmatrix} \mathbf{e} \\ \mathbf{e}_v \end{bmatrix} \sim N\left(\mathbf{0}, \begin{bmatrix} \mathbf{W}^{-1}\sigma_e^2 & 0 \\ 0 & \mathbf{W}_v^{-1}\sigma_{e_v}^2 \end{bmatrix}\right)$ .  $\mathbf{W} = \text{diag}\left(\exp\left(\hat{\boldsymbol{\psi}}\right)^{-1}\right)$  and

#### 4. Comparison of methods to study uniformity of traits

---

$\mathbf{W}_v = \text{diag}\left(\frac{1-h}{2}\right)$  are reciprocals of the predicted residual variance from the previous iteration,  $\sigma_e^2$  and  $\sigma_{e_v}^2$  are scaling variances, which are expected to be equal to 1, since  $\mathbf{W}$  and  $\mathbf{W}_v$  already contain the reciprocals of the predicted residual variances per observation (Mulder *et al.*, 2013b). The predicted residual variances per observation  $\exp\left(\hat{\Psi}\right)$  are based on the estimated fixed and random effects for  $\Psi$  in the previous iteration of the algorithm. The method requires a number of ASReml runs to estimate all the parameters, because the residual variance in the level part of the model depends on the variance part of the model and vice versa. The initial values of residual variance for DHGLM analyses were taken from the conventional model for individual BW of offspring.

The algorithm for the iterations is as follows (Felleki *et al.* 2012):

1. Run linear mixed model for  $\mathbf{y}$  with homogeneous residual variance.
2. Calculate  $\Psi$ ,  $\mathbf{W}$  and  $\mathbf{W}_v$ , where  $\mathbf{W} = \text{diag}\left(\frac{1}{\sigma_e^2}\right)$  in the first iteration.
3. Run bivariate linear mixed model on  $\mathbf{y}$  and  $\Psi$ .
4. Update  $\Psi$ ,  $\mathbf{W}$  and  $\mathbf{W}_v$ .
5. Iterate steps 3 till 4 until convergence.

The convergence of the analysis was achieved after 20 rounds of iterations, where the sum of the relative squared differences in estimated values of all variance components (dam genetic (co)variances, sire genetic (co)variances, permanent sow (co)variances and the residual scaling variances) of DHGLM between the current and the previous iteration was  $3 \times 10^{-6}$  for sow line LW and  $9 \times 10^{-6}$  for sow line LR.

##### 4.2.5 Comparison of the DHGLM with the conventional analysis

The DHGLM and the conventional analysis used to estimate variation of individual BW of offspring were evaluated by:

1. comparison of variance components, EBVs and accuracies of EBVs estimated with DHGLM and the conventional analysis,
2. three-fold cross-validation used to predict EBVs. First, paternal families were selected with at least three half-sisters from a family with litter observations. Second, phenotypic observations for one of the paternal half-

sisters were set to missing, which resulted in removing ~10% of observations from each sow line. This was done three times to perform three-fold cross-validation. This cross-validation mimicked the situation where we want to predict the phenotype of a new-born sow, which already has some paternal sibs with farrowing records. Since both methods are on the same scale, the predicted EBVs in each of the three validation sets were correlated with either the raw log-transformed variance of BW or with the log-transformed variance of BW corrected for fixed effects, obtained from the analysis of the full dataset. These correlations give an indication of the ability of the EBV for residual variance to predict the log-transformed within-litter variance of BW. It is expected that the correlations are higher with the log-transformed within-litter variance corrected for fixed effects, and that the correlations do not differ between the conventional analysis and the DHGLM. For the conventional analysis in the cross-validation, EBVs were estimated by running BLUP in ASReml, where variance components were fixed at the values estimated from the whole data set (Gilmour *et al.*, 2006).

### 4.2.6 Interpretation of genetic variance in residual variance of birth weight

Studies using the conventional model for within-litter variability of BW have used SD of BW, whereas this study is performed on the individual level and uses the log-transformed variance of the trait to have both DHGLM and the conventional model on the same scale. Thus, comparison of estimates from this study to the literature requires converting the estimates into measures that can be compared to other studies. The literature on genetic analyses of residual variance defines the genetic coefficient of variation at the level of the residual variance, and the heritability for residual variance at the level of the squared phenotype ( $h_v^2$ ) (Hill and Mulder, 2010). Here two additional measures are introduced. First, the genetic coefficient of variation at the level of the residual standard deviation ( $GCV_{SDe}$ ), *i.e.* the genetic standard deviation in residual standard deviation divided by the mean residual standard deviation of the trait. Second, the heritability of residual variance at litter level,  $h_{v,litter}^2$ .

The measure of the genetic coefficient of variation  $GCV_{SDe}$  can be approximated as

$$GCV_{SDe} = \frac{\sigma_{a_v}(\sigma_e)}{\sigma_e} \approx \frac{1}{2} \sigma_{a_v} \quad (\text{Hill and Mulder, 2010}), \text{ where } \sigma_{a_v} \text{ is the genetic SD}$$



#### 4. Comparison of methods to study uniformity of traits

---

in residual variance. The  $GCV_{SDe}$  shows the proportional change in residual SD, when the residual variance would be changed by one unit  $\sigma_{a_v}$ . The  $GCV_{SDe}$  is, therefore, relevant describing the potential response to selection in the SD of a trait.

Two measures of heritability  $h_v^2$  and  $h_{v,litter}^2$ , are used to show the heritability of residual variance at individual and litter level. Mulder *et al.* (2007) showed that  $h_v^2$  is a useful parameter to estimate the accuracy of selection using the classical selection index theory, *e.g.* when EBVs are based on sibs or progeny. Analogous to ordinary heritability, the  $h_v^2$  is defined as the regression coefficient of the additive genetic effect for residual variance ( $\sigma_{a_v,add}^2$ ) on the squared phenotype ( $P^2$ ; Mulder *et al.*, 2007):

$$h_v^2 = \frac{\sigma_{a_v,add}^2}{2\sigma_p^4 + 3\sigma_{a_v,add}^2},$$

where  $\sigma_{a_v,add}^2$  is estimated based on the equation (Mulder *et al.*, 2007):

$$\sigma_{a_v,add}^2 = \sigma_{e,exp}^4 \exp(2\sigma_{a_v}^2) - \sigma_{e,add}^4,$$

where  $\sigma_{e,exp}^2 = \frac{\frac{1}{\bar{W}}\sigma_e^2}{\exp(0.5\sigma_{a_v}^2)}$  and  $\sigma_{e,add}^2 = \frac{1}{\bar{W}}\sigma_e^2$ , and  $\sigma_e^2$  is the residual variance

estimated in the level part of the DHGLM and  $\bar{W}$  is the average of the weights used in the level part of the model. Heritability at the litter level ( $h_{v,litter}^2$ ) can be obtained by assuming that the litter is the only information used for breeding value estimation. Thus  $h_{v,litter}^2$  can be defined as the reliability of EBVs based on a single litter. Since each piglet can be considered as a repeated observation of the dam genetic effect, then  $h_{v,litter}^2$  can be approximated using the standard equation for reliability with repeated observations (Falconer and Mackay, 1996; ignoring common litter effects on variance):

$$h_{v,litter}^2 = \frac{nh_v^2}{1 + h_v^2(n-1)},$$

where  $n$  is the average total number born (TNB) in the litter.

The measure of genetic coefficient of variation ( $GCV_{SDe}$ ) is useful to draw conclusions on potential response to selection, whereas the two measures of heritability ( $h_v^2$  and  $h_{v,litter}^2$ ) are useful to predict the accuracy of selection and show how many records/litters are needed to get a certain level of accuracy. Since both the conventional method and the DHGLM are on the same scales, the same symbols will be used to describe variance components estimates and heritability in the following sections. For the estimates of  $GCV_{SDe}$ ,  $h_v^2$  and  $h_{v,litter}^2$  obtained in DHGLM, standard errors could not be obtained, because approximations are not available (Mulder *et al.*, 2009).

### 4.3 Results and Discussion

#### 4.3.1 Variance components of individual BW of offspring

The variance components and heritability of individual BW of offspring estimated with the conventional analysis and with the level part of the DHGLM are presented in Table 4.2 for the LW sow line and in Table 4.3 for the LR sow line. The estimated variance components obtained in two methods were very similar. The dam genetic variance was 0.013 in LW and 0.014 in LR with both methods. The residual variance of individual BW of offspring was larger in the conventional analysis (0.068 in LW and 0.075 in LR) than in the DHGLM (0.049 in LW and 0.060 in LR). Observed differences might be caused by better adjusted estimates in DHGLM, since it allows for heterogeneity of residual variances across the observations. Differences in residual variance with the same dam genetic variance in both methods lead to a small difference in heritability between the methods, although not significant ( $P>0.05$ ). In the conventional analysis, the heritability was 0.143 in LW and 0.145 in LR, whereas in DHGLM, the heritability was 0.18 in LW and 0.16 in LR. Those heritability estimates are similar to values in the literature, which reports maternal heritabilities for individual BW of offspring between 0.14 and 0.26 (Roehe, 1999; Kaufmann *et al.*, 2000; Grandinson *et al.*, 2005; Arango *et al.*, 2006; Kapell *et al.*, 2011).

The sire genetic variance as expected had much lower contribution to the total variance of individual BW of offspring (0.0004 in both sow lines) than the dam

#### 4. Comparison of methods to study uniformity of traits

**Table 4.2.** Variance components (with SD) for individual birth weight of offspring (Level), log-transformed within-litter variance of birth weight and residual variance of individual birth weight of offspring (Variance), estimated in Large White using the conventional analysis and Double Hierarchical GLM (DHGLM).

Estimates		Level		Variance	
Level	Variance	Conventional	DHGLM	Conventional	DHGLM
$\sigma_{a_d}^2$	$\sigma_{a_{dv}}^2$	0.013 (0.002)	0.013 (0.002)	0.030 (0.009)	0.036 (0.010)
-	$GCV_{SDe}^1$	-	-	0.087	0.095
$\sigma_{a_s}^2$	$\sigma_{a_{sv}}^2$	0.0004 (0.0002)	0.0004 (0.0002)	0.002 (0.002)	0.002 (0.002)
$\sigma_c^2$	$\sigma_{c_v}^2$	0.007 (0.0004)	0.008 (0.0004)	-	0.097 (0.006)
$\sigma_{pe}^2$	$\sigma_{pe_v}^2$	0.0001 (0.001)	0.0002 (0.001)	0.011 (0.009)	0.009 (0.009)
$\sigma_e^2$	$\sigma_{e_v}^2$	0.068 (0.0004)	0.049	0.26 <sup>2</sup>	1.77
$h^2$	$h_v^2$	0.143 (0.04)	0.18	-	0.008 <sup>3</sup>
	$h_{v,litter}^2$	-	-	0.099	0.114 <sup>4</sup>

<sup>1</sup>Genetic coefficient of variation at residual standard deviation level, *i.e.* the genetic standard deviation in residual standard deviation divided by the mean residual standard deviation of

the trait:  $GCV_{SDe} = \frac{\sigma_{a_{dv}}(\sigma_e)}{\sigma_e} \approx \frac{1}{2} \sigma_{a_{dv}}$  (Hill and Mulder, 2010).

<sup>2</sup>An average residual variance from four groups of total number born piglets in sow line Large White.

<sup>3</sup>Heritability estimated at the level of squared phenotypic variance:  $h_v^2 = \frac{\sigma_{a_{dv},add}^2}{2\sigma_p^4 + 3\sigma_{a_{dv},add}^2}$

(Mulder *et al.*, 2007).

<sup>4</sup>Heritability of residual variance expressed on the litter level was calculated as

$h_{v,litter}^2 = \frac{nh_v^2}{1 + h_v^2(n-1)}$  where n is the average number of total number born piglets in

Large White.

#### 4. Comparison of methods to study uniformity of traits

**Table 4.3.** Variance components (with SE) for individual birth weight of offspring (Level), log-transformed within-litter variance of birth weight and residual variance of individual birth weight of offspring (Variance), estimated in Landrace using the conventional analysis and Double Hierarchical GLM (DHGLM).

Estimates		Level		Variance	
Level	Variance	Conventional	DHGLM	Conventional	DHGLM
$\sigma_{a_d}^2$	$\sigma_{a_{dv}}^2$	0.014 (0.003)	0.014 (0.003)	0.035 (0.014)	0.044 (0.013)
-	$GCV_{SDe}^1$	-	-	0.094	0.105
$\sigma_{a_s}^2$	$\sigma_{a_{sv}}^2$	0.0003 (0.0002)	0.0004 (0.0002)	0.009 (0.004)	0.006 (0.003)
$\sigma_c^2$	$\sigma_{c_v}^2$	0.007 (0.0006)	0.008 (0.0005)	-	0.082 (0.009)
$\sigma_{pe}^2$	$\sigma_{pe_v}^2$	0.001 (0.002)	0.001 (0.002)	0.040 (0.009)	0.012 (0.012)
$\sigma_e^2$	$\sigma_{e_v}^2$	0.075 (0.001)	0.060	0.20 <sup>2</sup>	1.80
$h^2$	$h_v^2$	0.145 (0.05)	0.16	-	0.011 <sup>3</sup>
	$h_{v,litter}^2$	-	-	0.123	0.143 <sup>4</sup>

<sup>1</sup>Genetic coefficient of variation at residual standard deviation level, *i.e.* the genetic standard deviation in residual standard deviation divided by the mean residual standard deviation of

the trait:  $GCV_{SDe} = \frac{\sigma_{a_{dv}}(\sigma_e)}{\sigma_e} \approx \frac{1}{2} \sigma_{a_{dv}}$  (Hill and Mulder, 2010).

<sup>2</sup>An average residual variance from four groups of total number born piglets in sow line Landrace.

<sup>3</sup>Heritability estimated at the level of squared phenotypic variance:

$$h_v^2 = \frac{\sigma_{a_{dv},add}^2}{2\sigma_P^4 + 3\sigma_{a_{dv},add}^2} \text{ (Mulder et al., 2007).}$$

<sup>4</sup>Heritability of residual variance expressed on the litter level was calculated as

$$h_{v,litter}^2 = \frac{nh_v^2}{1 + h_v^2(n-1)} \text{ where n is the average number of total number born piglets in}$$

Landrace.

#### 4. Comparison of methods to study uniformity of traits

---

genetic variance. Those estimates suggest a very small impact of the sire genetic effect on the BW of a piglet. Previous studies indicated a direct genetic effect on BW, caused by the genetic potential of the embryo itself to grow and to support the elongation process (Kaufmann *et al.*, 2000; Grandinson *et al.*, 2005; Arango *et al.*, 2006; Kapell *et al.*, 2011). However, the estimates of the direct heritability are much lower than the ones reported for maternal heritability of BW and vary from 0.02 to 0.09 (Roehe, 1999; Kaufmann *et al.*, 2000; Grandinson *et al.*, 2005; Arango *et al.*, 2006; Kapell *et al.*, 2011).

##### 4.3.2 Variance components of birth weight variation

Although the conventional analysis uses variation of BW on the litter level, whereas DHGLM uses variation of BW on the individual level, the estimates from the two methods can be fully compared, because the scales of the analyses are the same. Variance components and heritability of BW variation estimated with conventional analysis and with the variance part of the DHGLM are presented in Table 4.2 for sow line LW and in Table 4.3 for sow line LR.

The dam genetic variance estimated with both methods was slightly lower with the conventional analysis than with the DHGLM, however, not significantly different ( $P>0.05$ ). In sow line LW the estimates were 0.030 in conventional analysis and 0.036 in DHGLM, whereas in sow line LR the estimates were 0.035 and 0.044.

Heritability of BW variation estimated on the litter level in both sow lines was lower in the conventional analysis (0.099 in LW and 0.123 in LR) than in DHGLM (0.114 in LW and 0.143 in LR). The estimates from two methods were, however, not significantly different from each other ( $P>0.05$ ). Two studies using log-transformed variance of birth weight in pigs reported the maternal heritability in a LR line (0.084) and in a LW line (0.088) for NBA (Wittenburg *et al.*, 2008) and 0.106 (TNB) and 0.123 (NBA) in a LR line (Wittenburg *et al.*, 2010). The literature reports also maternal heritability of BW variation on SD level between 0.08 and 0.11 (Högberg and Rydhmer, 2000; Hermes *et al.*, 2001; Damgaard *et al.*, 2003; Canario *et al.*, 2010; Kapell *et al.*, 2011). Thus values found here are in the range reported in literature.

Estimated  $GCV_{SDe}$  were around 0.10 (Table 4.2 and Table 4.3). Assuming that an efficient breeding program can generate a response of  $\sim 1$  genetic standard deviation per generation, the  $GCV_{SDe}$  of 0.10 indicates that the SD of BW can be reduced by  $\sim 10\%$  per generation. Thus in sow line LW the SD of BW ( $=0.264$ ) could be decreased to 0.241, whereas in sow line LR the SD of BW ( $=0.288$ ) could be

decreased to 0.263. Our estimates of  $GCV_{SDe}$  are comparable to the value estimated for birth weight in rabbits (Garreau *et al.*, 2008).

The paternal genetic effect had a small contribution to the BW variation for both methods (conventional analysis: 0.002 in LW and 0.009 in LR; DHGLM: 0.002 in LW and 0.006 in LR). High estimates were observed in this study for the common litter variance (Table 4.2 and Table 4.3) in the variance level of DHGLM (0.097 in LW and 0.082 in LR). Previous studies using DHGLM also found high estimates of common (permanent) environment for litter size in pigs (Rönnegård *et al.*, 2010; Felleki *et al.*, 2012) and for somatic cell score in dairy cows (Mulder *et al.*, 2013a).

In the conventional analysis the differences in number of piglets per sex and their BW was accounted by including the frequency of males multiplied by frequency of females in the litter ( $freq_{\text{♂}} \times freq_{\text{♀}}$ ). Including this fixed effect in the model gave very similar results as separately analyzing the log-transformed variance per sex within the litter (results not shown), as proposed by Wittenburg *et al.* (2008). In the DHGLM it was possible to include the sex of the individual piglets in the model. The estimated effects of sex showed that male piglets were on average heavier (3% in LW and 4% in LR) and had more variation in BW (8% in LW and 9% in LR) than female piglets (results not shown).

#### 4.3.3 Correlations between the level and variance of BW

Since the DHGLM is effectively a bivariate model, it was possible to estimate correlations between random effects on the level and the variance of BW (Table 4.4). The estimated correlations between the additive dam genetic effects on the level and the variance were moderate and positive (0.62 in LW and 0.55 in LR). This could also be expected from the biological point of view, since often the increase in the mean is associated with the increase in variation of the trait. Similar values of the correlation between maternal genetic effects for SD of BW and mean BW (about 0.6) were found by Damgaard *et al.* (2003). Canario *et al.* (2010) showed lower estimate of 0.36 for the same traits in pigs, whereas a much higher correlation of 0.97 was reported by Gutiérrez *et al.* (2006) for the mean individual birth weight and its log-transformed variance in litters of mice. The positive correlations reported in this study are an unfavorable result, since they indicate that with an increase in individual BW of offspring, the variation of BW will also increase. This is partly a scaling effect, but not completely since the genetic correlation deviated significantly from a value of one. Therefore, to maintain the optimum BW, it is necessary to select for both BW and its variation simultaneously, *i.e.* using index selection (Mulder *et al.*, 2008).

#### 4. Comparison of methods to study uniformity of traits

**Table 4.4.** Correlation estimates between the random effects on the level and the variance of BW, estimated from the Double Hierarchical GLM in two sow lines: Large White (LW) and Landrace (LR).

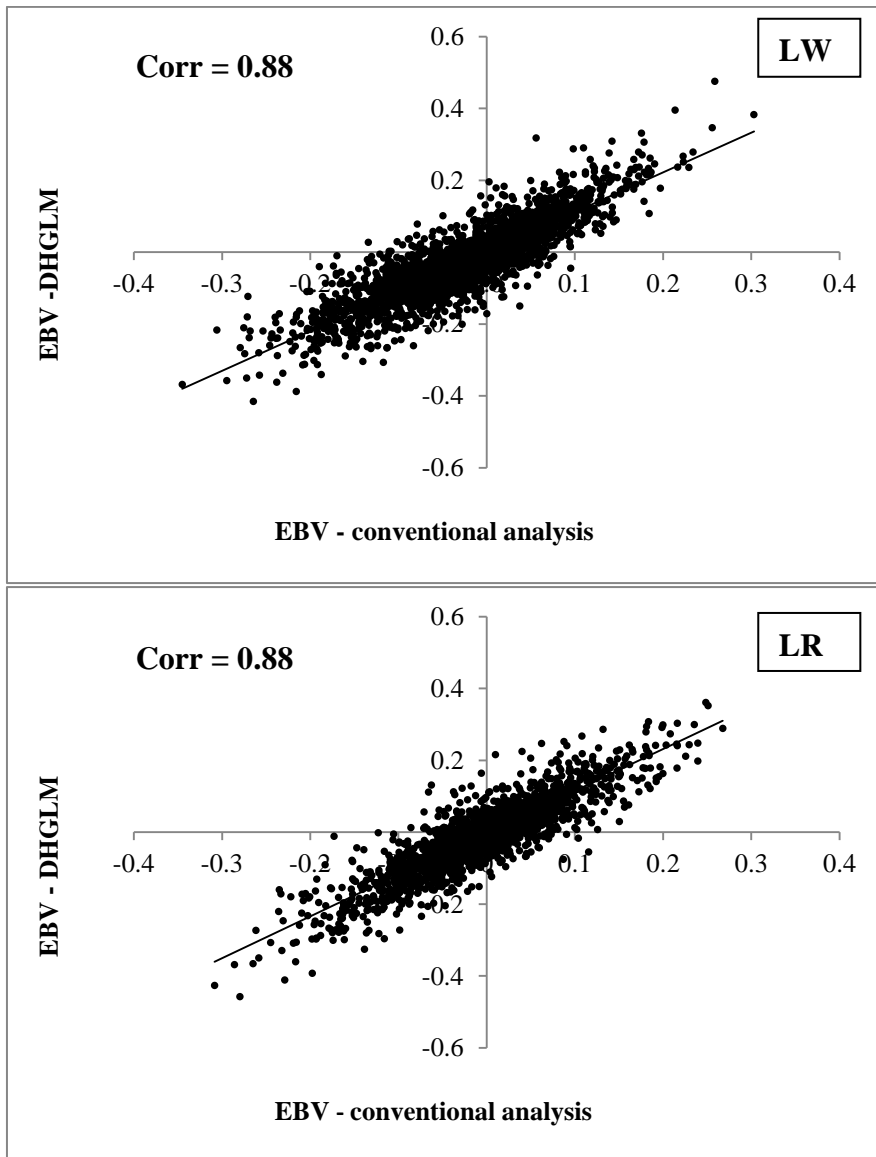
Effects	LW	LR
Dam genetic	0.62 (0.12)	0.55 (0.14)
Sire genetic	0.55 (0.44)	0.23 (0.41)
Common litter	-0.10 (0.04)	-0.07 (0.06)
Permanent sow	0.84 (2.42)	0.52 (0.70)

**Table 4.5.** Correlation between EBVs (obtained from three-fold cross-validation of conventional analysis and Double Hierarchical GLM, with ~10% of observations set to missing) and:1) raw log-transformed within-litter variance of birth weight –  $\log(\text{var}(\text{BW}))$ , or 2) log-transformed within-litter variance of BW corrected for fixed effects in Large White.

Validation run	EBVs from validation vs. $\log(\text{var}(\text{BW}))$		EBV from validation vs. $\log(\text{var}(\text{BW}))$ corrected for fixed effects	
	Conventional	DHGLM	Conventional	DHGLM
1	0.11	0.14	0.55	0.57
2	0.17	0.16	0.41	0.46
3	0.13	0.13	0.51	0.51
Average	0.14	0.14	0.49	0.51

**Table 4.6.** Correlation between EBVs (obtained from three-fold cross-validation of conventional analysis and Double Hierarchical GLM, with ~10% of observations set to missing) and:1) raw log-transformed within-litter variance of birth weight –  $\log(\text{var}(\text{BW}))$ , or 2) log-transformed within-litter variance of BW corrected for fixed effects in Landrace.

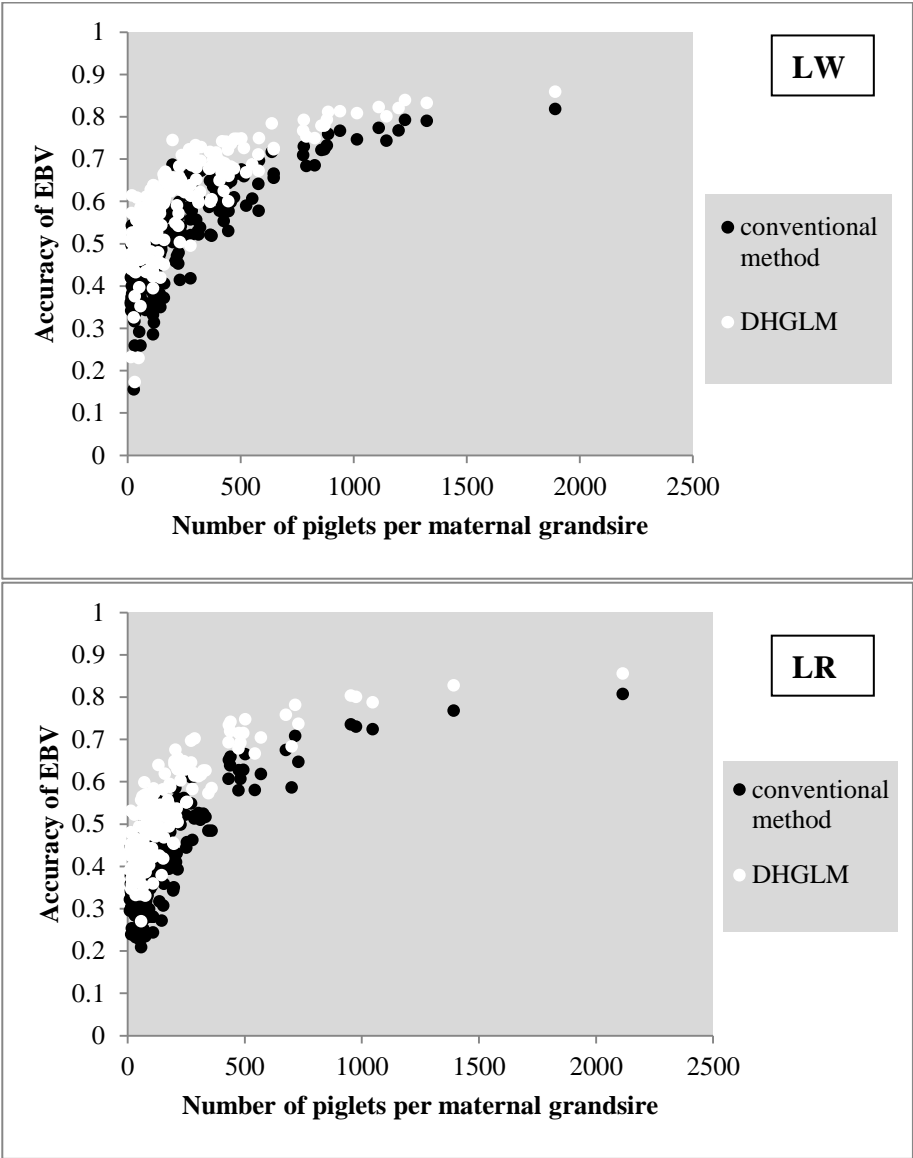
Validation run	EBVs from validation vs. $\log(\text{var}(\text{BW}))$		EBV from validation vs. $\log(\text{var}(\text{BW}))$ corrected for fixed effects	
	Conventional	DHGLM	Conventional	DHGLM
1	0.16	0.12	0.40	0.32
2	0.13	0.10	0.34	0.36
3	0.10	0.09	0.26	0.33
Average	0.13	0.10	0.33	0.34



**Figure 4.2.** Comparison of the EBVs estimated based on the complete pedigree (7,415 animals over 5 generations) with the conventional analysis (log-transformed variance of within-litter birth weight) and the Double Hierarchical GLM (residual variance of individual birth weight of offspring) in two sow lines Large White (LW) and Landrace (LR).



4. Comparison of methods to study uniformity of traits



**Figure 4.3.** Comparison of the accuracies of EBVs of maternal grandsires estimated with the conventional analysis (log-transformed variance of within-litter birth weight) and the Double Hierarchical GLM (residual variance of individual birth weight of offspring) in two sow lines: Large White (LW) and Landrace (LR).

The estimated correlations between the common litter effects on the level and the variance of BW were -0.10 in sow line LW and -0.07 in LR, but the latter was not significantly different from zero. These correlations suggest that heavier litters have lower variability of BW due to the common litter effect. Based on studies focused on phenotypic level of birth weight variation, this would be the expected direction of correlation. Milligan *et al.* (2001) reported a negative correlation between mean birth weight and birth weight coefficient of variation (-0.491). Thus, higher within-litter variation of BW is associated with more piglets with low BW, rather than heavier piglets. This negative correlation is also connected to litter size, since larger litters tend to have higher variation in birth weight and higher number of piglets with low BW (Van der Lende and de Jager, 1991; Milligan *et al.*, 2002; Foxcroft *et al.*, 2006; Foxcroft 2012). Here a linear relationship was observed between litter size and birth weight, with increase in litter size the BW of piglets decreased (results not shown). However, no clear pattern was present for the variance of BW (results not shown). Results in this study suggested that the genetic and litter correlations have opposite signs.

The correlations for the sire genetic effects and the permanent sow effects on the level and the variance of BW were not significantly different from zero and could not be estimated precisely (Table 4.4).

### 4.3.4 DHGLM vs. conventional analysis

Figure 4.2 shows the correlation between EBVs of maternal grandsires for variation of BW from the conventional analysis and from the DHGLM. The correlation estimates were 0.88 in both sow lines. Those estimates indicate high resemblance of DHGLM and the conventional analysis. Furthermore, comparison of accuracies of the EBVs, as reported by ASReml 2.0 (Gilmour *et al.*, 2006), shows that both methods give comparable estimates, with slightly lower values for the conventional analysis (Figure 4.3). Moderate accuracies can be achieved with ~100 piglets per maternal grandsire.

The correlations of predicted EBV with log-transformed variance of BW, or corrected phenotypes, *i.e.* log-transformed variance of BW corrected for fixed effects are presented in Table 4.5 for sow line LW and Table 4.6 for sow line LR. The correlations obtained in the cross-validation for conventional analysis and DHGLM indicate very similar predictive ability of both methods in estimating EBVs for BW variation, with a small advantage for the DHGLM.

The findings presented above show high resemblance of two methods for studying variation of a trait. However, the conventional method can be used only for traits recorded on a group of animals (*e.g.* within-litter BW variation) or when repeated

observations per animal are available (e.g. litter size in pigs). Many of the production traits would benefit economically from low variability, but have only a single observation per animal, e.g. body weight, daily gain, backfat. The DHGLM, as presented here, shows also high potential to be used in traits with a single observation. One could argue that the conventional analysis works faster and, at this stage, gives less computing/re-scaling issues than the DHGLM. Indeed there are some challenges of fitting a DHGLM, but for all of them the solutions are already available. First, when direct genetic effects are to be included, a DHGLM requires repeated observations per animal, to avoid bias in estimates. In the case of single observations per animal, it is recommended to use a sire-dam model as presented by Sonesson *et al.* (2013) in birth weight of Atlantic salmon or a sire model as presented by Mulder *et al.* (2013b) in milk yield in dairy cows. To have sufficient precision of estimates of variance components with single observations per animal, the dataset needs to contain at least a 100 sires each with 100 offspring (Mulder *et al.*, 2013b). Second, the estimates from a DHGLM require re-scaling to allow comparison to other studies. As shown in this study, the  $GCV_{SDe}$  can facilitate straightforward comparison of methods/studies and provides an indicator of potential response to selection in breeding programs.

#### 4.4 Acknowledgments

This research was financially supported by the Dutch Science Council (NWO) and part of the study was coordinated by the Dutch Technology Foundation (STW). This research was also supported by Breed4Food, a public-private partnership in the domain of animal breeding and genomics and Topigs Norsvin (Vught, The Netherlands). Data for this study were provided by Topigs Norsvin (Beuningen, The Netherlands) with special thanks to Marcos Lopes. The authors would like to thank Johan van Arendonk and Egiel Hanenberg for valuable comments at earlier stages of writing this manuscript and the anonymous reviewers for significant help with improving it further. Ewa Sell-Kubiak also thanks Susan Wijga, Katrijn Peeters and Naomi Duijvesteijn for helpful discussions and comments.

## Appendix

### *Model testing*

This *Appendix* contains model testing for: individual birth weight of offspring (A), log-transformed variance of birth weight (B) and Double Hierarchical GLM (C) used to simultaneously study individual birth weight of offspring and the residual variance of birth weight. Explanation of abbreviations used in the models:

**X, Z, U, V** – known incidence matrices;

**b** – vector of fixed effects;

**a<sub>d</sub>** – vector of dam genetic effect;

**a<sub>s</sub>** – vector of sire genetic effect;

**pe** – vector of permanent sow effect;

**c** – vector of common litter effect;

**a<sub>dv</sub>** – vector of dam genetic effect in residual variance;

**a<sub>sv</sub>** – vector of sire genetic effect in residual variance;

**pe<sub>v</sub>** – vector of permanent sow effect in residual variance;

**c<sub>v</sub>** – vector of common litter effect in residual variance.

### **A. Selecting the model for conventional analysis of the individual birth weight of offspring**

$$1. BW = Xb + Za_d + Vc + e$$

$$2. BW = Xb + Za_s + Upe + Vc + e$$

$$3. BW = Xb + Za_d + Za_s + Vc + e$$

$$4. BW = Xb + Za_d + Upe + Vc + e$$

$$5. BW = Xb + Za_d + Za_s + Upe + Vc + e$$

The fixed effects were: the total number of piglets born in the litter (TNB), parity of the sow (parity), the birth farm, year and season of the piglet (farm\_year\_season) and gender of the piglet (sex).

#### 4. Comparison of methods to study uniformity of traits

**Table 4.7.** Results of likelihood ratio test (LRT) assuming  $\chi^2$ -distribution with one degree of freedom, performed to select best fitting model for birth weight analysis.

Model	LW			LR		
	logL	LRT	p-value	logL	LRT	p-value
1	104			101		
2	54			69		
3	112			102		
4	104			101		
5	112			102		
1 vs 2		100	<.0001		64	<.001
1 vs 3		16	<.001		2	n.s.
1 vs 4		0	n.s.		0	n.s.
1 vs 5		16	<.001		2	n.s.
2 vs 5		116	<.0001		66	<.001
3 vs 5		0	n.s.		0	n.s.
4 vs 5		16	<.001		2	n.s.

Based on LRT and variance components estimates, model 5 was selected to be used in analysis of individual BW of offspring of piglets.

#### B. Selecting the model for conventional analysis of log-transformed within-litter variance of BW

$$1. \text{Log}(\text{var}(\text{BW})) = \mathbf{Xb} + \mathbf{Za_d} + \mathbf{e}$$

$$2. \text{Log}(\text{var}(\text{BW})) = \mathbf{Xb} + \mathbf{Za_d} + \mathbf{Upe} + \mathbf{e}$$

$$3. \text{Log}(\text{var}(\text{BW})) = \mathbf{Xb} + \mathbf{Za_d} + \mathbf{Za_s} + \mathbf{Upe} + \mathbf{e}$$

The fixed effects were: the total number of piglets born in the litter (TNB), parity of the sow (parity), the birth farm, year and season of the piglet (farm\_year\_season) and frequency of males multiplied by frequency of females in the litter ( $\text{freq}_{\text{♂}} \times \text{freq}_{\text{♀}}$ ). Using  $\text{freq}_{\text{♂}} \times \text{freq}_{\text{♀}}$  accounts for the proportion of the sexes in the litter, the potential differences in piglets BW in males and females and the effect the two could have on within-litter variance of BW.

#### 4. Comparison of methods to study uniformity of traits

**Table 4.8.** Results of likelihood ratio test (LRT) assuming  $\chi^2$ -distribution with one degree of freedom, performed to select best fitting model for  $\log(\text{var}(\text{BW}))$  analysis.

Model	LW			LR		
	logL	LRT	p-value	logL	LRT	p-value
1	40.2			26		
2	40.5			27.4		
3	41.4			29		
1 vs 2		0.6	n.s.		2.8	n.s.
1 vs 3		2.4	n.s.		6	0.049
2 vs 3		1.8	n.s.		3.2	n.s.

Based on LRT and variance components estimates, model 3 was selected to be used in analysis of  $\log(\text{var}(\text{BW}))$ .

#### C. Selecting the model for DHGLM to analyze the individual BW of offspring and the variation in residual variance of individual BW of offspring

1.

$$\begin{bmatrix} \mathbf{y} \\ \boldsymbol{\psi} \end{bmatrix} = \begin{bmatrix} \mathbf{X} & \mathbf{0} \\ \mathbf{0} & \mathbf{X}_v \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{b}_v \end{bmatrix} + \begin{bmatrix} \mathbf{Z} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_v \end{bmatrix} \begin{bmatrix} \mathbf{a}_d \\ \mathbf{a}_{dv} \end{bmatrix} + \begin{bmatrix} \mathbf{V} & \mathbf{0} \\ \mathbf{0} & \mathbf{V}_v \end{bmatrix} \begin{bmatrix} \mathbf{c} \\ \mathbf{c}_v \end{bmatrix} + \begin{bmatrix} \mathbf{e} \\ \mathbf{e}_v \end{bmatrix}$$

2.

$$\begin{bmatrix} \mathbf{y} \\ \boldsymbol{\psi} \end{bmatrix} = \begin{bmatrix} \mathbf{X} & \mathbf{0} \\ \mathbf{0} & \mathbf{X}_v \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{b}_v \end{bmatrix} + \begin{bmatrix} \mathbf{Z} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_v \end{bmatrix} \begin{bmatrix} \mathbf{a}_d \\ \mathbf{a}_{dv} \end{bmatrix} + \begin{bmatrix} \mathbf{U} & \mathbf{0} \\ \mathbf{0} & \mathbf{U}_v \end{bmatrix} \begin{bmatrix} \mathbf{pe} \\ \mathbf{pe}_v \end{bmatrix} + \begin{bmatrix} \mathbf{V} & \mathbf{0} \\ \mathbf{0} & \mathbf{V}_v \end{bmatrix} \begin{bmatrix} \mathbf{c} \\ \mathbf{c}_v \end{bmatrix} + \begin{bmatrix} \mathbf{e} \\ \mathbf{e}_v \end{bmatrix}$$

3.

$$\begin{bmatrix} \mathbf{y} \\ \boldsymbol{\psi} \end{bmatrix} = \begin{bmatrix} \mathbf{X} & \mathbf{0} \\ \mathbf{0} & \mathbf{X}_v \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{b}_v \end{bmatrix} + \begin{bmatrix} \mathbf{Z} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_v \end{bmatrix} \begin{bmatrix} \mathbf{a}_d \\ \mathbf{a}_{dv} \end{bmatrix} + \begin{bmatrix} \mathbf{Z} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_v \end{bmatrix} \begin{bmatrix} \mathbf{a}_s \\ \mathbf{a}_{sv} \end{bmatrix} + \begin{bmatrix} \mathbf{V} & \mathbf{0} \\ \mathbf{0} & \mathbf{V}_v \end{bmatrix} \begin{bmatrix} \mathbf{c} \\ \mathbf{c}_v \end{bmatrix} + \begin{bmatrix} \mathbf{e} \\ \mathbf{e}_v \end{bmatrix}$$

4.

$$\begin{bmatrix} \mathbf{y} \\ \boldsymbol{\psi} \end{bmatrix} = \begin{bmatrix} \mathbf{X} & \mathbf{0} \\ \mathbf{0} & \mathbf{X}_v \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{b}_v \end{bmatrix} + \begin{bmatrix} \mathbf{Z} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_v \end{bmatrix} \begin{bmatrix} \mathbf{a}_d \\ \mathbf{a}_{dv} \end{bmatrix} + \begin{bmatrix} \mathbf{Z} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_v \end{bmatrix} \begin{bmatrix} \mathbf{a}_s \\ \mathbf{a}_{sv} \end{bmatrix} + \begin{bmatrix} \mathbf{U} & \mathbf{0} \\ \mathbf{0} & \mathbf{U}_v \end{bmatrix} \begin{bmatrix} \mathbf{pe} \\ \mathbf{pe}_v \end{bmatrix} + \begin{bmatrix} \mathbf{V} & \mathbf{0} \\ \mathbf{0} & \mathbf{V}_v \end{bmatrix} \begin{bmatrix} \mathbf{c} \\ \mathbf{c}_v \end{bmatrix} + \begin{bmatrix} \mathbf{e} \\ \mathbf{e}_v \end{bmatrix}$$

#### 4. Comparison of methods to study uniformity of traits

The fixed effects were: the total number of piglets born in the litter (TNB), parity of the sow (parity), the birth farm, year and season of the piglet (farm\_year\_season) and gender of the piglet (sex).

**Table 4.9.** Results of likelihood ratio test (LRT) assuming  $\chi^2$ -distribution with one degree of freedom, performed to select best fitting DHGLM

Model	LW			LR		
	APHL <sup>1</sup>	LRT	p-value	APHL <sup>1</sup>	LRT	p-value
1	88			85		
2	95			90		
3	102			284		
4	112			291		
1 vs 2		7	0.046		5	0.049
1 vs 3		14	<.001		149	<.001
1 vs 4		24	<.001		206	<.001
2 vs 4		17	<.001		201	<.001
3 vs 4		10	<.001		7	0.046

<sup>1</sup>The adjusted profile h-likelihood (APHL) was multiplied by -1, so that higher APHL means a better fit. In addition, the LRT uses the difference in APHL from two models directly without multiplying by two, because APHL is already based on twice the log-likelihood from the DHGLM (see Mulder *et al.* (2013b) for details).

Based on LRT and variance components estimates, model 4 was selected to be used in DHGLM analysis of individual BW of offspring.







# 5

## **Genome-wide association study reveals novel loci for litter size and its variability in pigs**

E. Sell-Kubiak<sup>1</sup>, N. Duijvesteijn<sup>2</sup>, M. S. Lopes<sup>2</sup>, E.F. Knol<sup>2</sup>, P. Bijma<sup>1</sup>, H. A. Mulder<sup>1</sup>

<sup>1</sup> Animal Breeding and Genomics Centre, Wageningen University, PO Box 338, 6700 AH Wageningen, The Netherlands; <sup>2</sup> Topigs Norsvin Research Center, P.O. Box 43, 6640 AA Beuningen, The Netherlands

To be submitted

## Abstract

Productivity of a sow is measured by the number of piglets weaned per year. Thus one of the main breeding goals in pig breeding is increasing total number born in a litter (TNB). The variation in this trait is large and increasing TNB in a population could exceed the physiological capacity of a sows' to provide for the large litter during gestation. Thus there is a desire to breed for increased mean TNB while at the same time reducing variability of TNB. Here we study the variation of TNB in a Large White pig population by applying Double Hierarchical Generalized Linear model (DHGLM) and a genome-wide association study (GWAS). The residual variance of TNB (varTNB) and its variance components were estimated with DHGLM in ASReml. For this step, 263,088 observations on TNB were available. Estimated breeding values (EBV) obtained with DHGLM were used to calculate the deregressed EBV for 2,351 sows and boars genotyped with 64k chip. The GWAS was performed with a Bayesian Variable Selection method in Bayz. The SNPs were considered significant if their Bayes Factor was above 30. Genetic coefficient of variation of the standard deviation for varTNB was estimated as 0.09, indicating good opportunities for improvement of uniformity by selection. Genetic correlation between additive genetic effects on TNB and on its variation was 0.5. This indicates that an increase in TNB increases the variation of TNB. In total, ten SNPs were detected for TNB and nine SNPs for varTNB. The significant SNPs explained 0.83% of genetic variance in TNB and 1.44% in varTNB. The most significant SNP (on chromosome 11) explained 0.4% of genetic variance in TNB and 0.5% in varTNB (on chromosome 7). Possible candidate genes for varTNB on SSC7 are: heat shock protein (*HSPCB*), vascular endothelial growth factor (*VEGFA*), and protein regulating p53 function (*CUL9*). This is the first study reporting SNPs and candidate genes associated with varTNB in pigs.

Key words: Double Hierarchical GLM, GWAS, pigs, residual variance, total number born

### 5.1 Introduction

Productivity of a sow is measured by the number of piglets weaned per year. This is derived from the goal to obtain a high number of slaughter pigs per sow per year (Spötter *et al.*, 2006; Dekkers *et al.*, 2011; Rutherford *et al.*, 2013). Thus in pig breeding, genetic selection continues to increase litter size. Genetic trend for litter size in effective breeding programs was shown to be +0.16 (Tomiyaama *et al.*, 2011; Merks *et al.*, 2012), +0.25 (Vidović *et al.*, 2012), and even up to +0.5 (Taylor *et al.*, 2005) piglets per year.

Besides selection for the mean litter size, there is considerable variation in this trait between sows and between parities within a sow. Low reproductive performance, mostly failure to come into heat or to return into heat, remains one of the most common factors leading to culling (30%) of the sows (Stalder *et al.*, 2005; Hoving *et al.*, 2010; de Jong *et al.*, 2014). Simultaneously, litters of 25 piglets (or more) are above the physiological capacity of the single sow to provide for the litter, for example because of the limitations of the uterine capacity and its blood supplies (Foxcroft *et al.*, 2006; Pardo *et al.*, 2013; de Jong *et al.*, 2014). Sows with large litters can experience welfare issues such as high energy demand during gestation (Rutherford *et al.*, 2013). Increasing litter size has also its consequences for the piglets' welfare, since it decreases individual piglet's chance for survival in prenatal life and until weaning (Foxcroft, 2007; Foxcroft *et al.*, 2009; Knol *et al.*, 2010; Baxter *et al.*, 2013; Rutherford *et al.*, 2013). Despite that, large litters will still produce higher numbers of weaned piglets and later slaughter pigs than small litters (Beaulieu *et al.*, 2010). Different management strategies can be used to manage the largest litters until weaning, *e.g.*, cross-fostering, use of nurse sow systems and early weaning (Baxter *et al.*, 2013). Such management techniques are, however, labor intensive and disturb natural behavior of pigs.

Currently in pig breeding, the goal is towards more sustainable production that will increase piglet survival regardless of increasing litter size (Beaulieu *et al.*, 2010; Kapell *et al.*, 2011; Merks *et al.*, 2012; Nielsen *et al.*, 2013). Decreasing variation in litter size between sows could lead to more sustainable breeding in terms of lower mortality of piglets and easier to manage sows. The variation of the trait can be studied by analyzing its residual variance, which can be heterogeneous across the observations and can have a genetic component (Hill and Mulder, 2010). The Double Hierarchical Generalized Linear model (DHGLM; Rönnegård *et al.*, 2010; Felleki *et al.*, 2012) can be used to study the genetic variance in residual variance of the trait. Sorensen and Waagepetersen (2003), Rönnegård *et al.* (2010) and Felleki *et al.* (2012) showed on the same dataset that variability in litter size (total number

born) in pigs is heritable. Genome-wide association studies (GWAS) for variability in litter size, however, were not yet performed. A GWAS for variability of litter size could give more insight in the genetic and biological control of variability in litter size.

Therefore, the objectives were to estimate the genetic components of the residual variance of litter size (total number born) using DHGLM, and to identify SNPs associated with litter size and its variation through a multi-SNP GWAS applying a Bayesian Variable Selection method.

## 5.2 Materials and Methods

### 5.2.1 Phenotypes

Data for this study were collected between February 1998 and July 2014. In total 264,419 litter size (total number born, TNB) observations were available from 69,549 Large White sows. Litters were kept in the data if they contained at least 4 piglets in TNB (1,331 litters removed), whereas litters of 27 piglets or larger were all considered “27” (43 litters). Most sows had repeated observations; number of parities recorded varied between 1 and 16 per sow. The parities 10 and higher were all considered “10” (2,682 litters). After data editing 263,088 litters from 69,238 Large White sows remained for the analysis. The descriptive statistics of edited data are presented in Table 5.1. The pedigree was on average 5 generations deep and consisted of 83,571 animals.

### 5.2.2 Estimation of residual variance of litter size

Estimation of residual variance was performed on the full data set. A Double Hierarchical Generalized Linear model (DHGLM) as presented by Rönnegård *et al.* (2010) allows estimations of variance components of residual variance in ASReml 2.0 (Gilmour *et al.*, 2006). The further extended method by Felleki *et al.* (2012), enables to use bivariate linear mixed model for the level (TNB) and variance (TNB variation, varTNB) part of the model. In Rönnegård *et al.* (2010) the response

variable in the variance model was  $\log(\phi_i) = \log\left(\frac{e_i^2}{1-h_i}\right)$ , where  $e_i^2$  is the

squared residual from the level part of the model for observation  $i$  and  $h_i$  is the leverage, the diagonal element of the hat matrix of  $\mathbf{y}$  corresponding to observation

$i$ . A log link function was used, because  $\frac{e_i^2}{1-h_i}$  is  $\chi^2$ -distributed with one degree

of freedom. Felleki *et al.* (2012) showed that instead of using a log link function,

$\log\left(\frac{e_i^2}{1-h_i}\right)$  can be linearized using the Taylor expansion of the first order by

calculating the response variable  $\psi_i = \log(\hat{\sigma}_{e_i}^2) + \frac{\frac{e_i^2}{1-h_i} - \hat{\sigma}_{e_i}^2}{\hat{\sigma}_{e_i}^2}$ . This would

enable using a bivariate linear mixed model, where  $\hat{\sigma}_{e_i}^2$  is the predicted residual variance for observation  $i$  and  $\boldsymbol{\psi}$  is a vector with the response variable in the variance part of the model. Note that  $\psi_i$  is a linearized working variable for  $\log(\phi_i)$ . The DHGLM is then as follows:

$$\begin{bmatrix} \mathbf{y} \\ \boldsymbol{\psi} \end{bmatrix} = \begin{bmatrix} \mathbf{X} & \mathbf{0} \\ \mathbf{0} & \mathbf{X}_v \end{bmatrix} \begin{bmatrix} \mathbf{b} \\ \mathbf{b}_v \end{bmatrix} + \begin{bmatrix} \mathbf{Z} & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_v \end{bmatrix} \begin{bmatrix} \mathbf{a} \\ \mathbf{a}_v \end{bmatrix} + \begin{bmatrix} \mathbf{U} & \mathbf{0} \\ \mathbf{0} & \mathbf{U}_v \end{bmatrix} \begin{bmatrix} \mathbf{pe} \\ \mathbf{pe}_v \end{bmatrix} + \begin{bmatrix} \mathbf{e} \\ \mathbf{e}_v \end{bmatrix},$$

where  $\mathbf{y}$  is a vector of observations on TNB in the litter and  $\boldsymbol{\psi}$  is a vector of response variables on the variance part of DHGLM; the residuals  $\mathbf{e}$  are assumed to be independent and normally distributed, but with heterogeneous variances across the observations;  $\mathbf{b}$  and  $\mathbf{b}_v$  are vectors of fixed effects (parity of the sow and farm\_year\_season of the farrowing) on  $\mathbf{y}$  and  $\boldsymbol{\psi}$ ;  $\mathbf{a}_d$  and  $\mathbf{a}_{dv}$  are vectors of random

additive genetic effects on  $\mathbf{y}$  and  $\boldsymbol{\psi}$ , with  $\begin{bmatrix} \mathbf{a} \\ \mathbf{a}_v \end{bmatrix} \sim N\left(\mathbf{0}, \begin{bmatrix} \sigma_a^2 & \sigma_{a,av} \\ \sigma_{a,av} & \sigma_{av}^2 \end{bmatrix} \otimes \mathbf{A}\right)$ ;  $\mathbf{pe}$

and  $\mathbf{pe}_v$  are vectors of random non-genetic permanent sow effects on  $\mathbf{y}$  and  $\boldsymbol{\psi}$ ,

with  $\begin{bmatrix} \mathbf{pe} \\ \mathbf{pe}_v \end{bmatrix} \sim N\left(\mathbf{0}, \begin{bmatrix} \sigma_{pe}^2 & \sigma_{pe,pe_v} \\ \sigma_{pe,pe_v} & \sigma_{pe_v}^2 \end{bmatrix} \otimes \mathbf{I}\right)$ ; and  $\mathbf{e}$  and  $\mathbf{e}_v$  vectors of residuals,

with  $\begin{bmatrix} \mathbf{e} \\ \mathbf{e}_v \end{bmatrix} \sim N\left(\mathbf{0}, \begin{bmatrix} \mathbf{W}^{-1}\sigma_e^2 & 0 \\ 0 & \mathbf{W}_v^{-1}\sigma_{e_v}^2 \end{bmatrix}\right)$ , where  $\mathbf{W} = \text{diag}\left(\exp\left(\hat{\boldsymbol{\psi}}\right)^{-1}\right)$

and  $\mathbf{W}_v = \text{diag}\left(\frac{1-h}{2}\right)$  are expected reciprocals of the residual variance from

the previous iteration, and  $\sigma_e^2$  and  $\sigma_{e_v}^2$  are scaling variances, which are expected to be equal to 1 (Mulder *et al.*, 2013). The predicted residual variances per

observation,  $\exp\left(\hat{\Psi}\right)$ , are based on the estimated fixed and random effects for

$\Psi$  in the previous iteration of the algorithm. The method iterates the bivariate model a number of times, since the residual variance part (varTNB) depends on the level part (TNB) of the model and the other way around. The starting values of residual variance for DHGLM were taken from univariate analysis of TNB.

Comparison of estimates from this study to the literature requires converting the estimates into measures that can be compared to other studies. Here two measures will be used to allow the comparison with the literature using standard deviation (SD) of traits: Genetic Coefficient of Variation and the heritability for residual variance. Genetic Coefficient of Variation on standard deviation level (GCV<sub>SDe</sub>; Hill and Mulder, 2010) was applied to transform the estimates from the

variance to SD level. The GCV<sub>SDe</sub> can be estimated as 
$$GCV_{SDe} = \frac{\sigma_{av}(\sigma_e)}{\sigma_{e,add}} \approx \frac{1}{2} \sigma_{av}$$

where  $\sigma_{av}$  is the genetic SD in residual variance. The GCV<sub>SDe</sub> shows the proportional change in residual SD, when the residual variance would be changed by one unit  $\sigma_{av}$ . This allows seeing the true magnitude of potential response to selection of the varTNB. The literature on genetic analyses of residual variance defines also the heritability for residual variance at the level of the squared phenotype ( $h_v^2$ ), which is equal to the genetic variance in residual variance as a proportion of the variance of  $P^2$  (Hill and Mulder, 2010) and equals: 
$$h_v^2 = \sigma_{av}^2 / (2\sigma_P^4 + 3\sigma_{av}^2).$$

### 5.2.3 Using deregressed estimated breeding values for litter size and litter size variation

Recently, deregressed estimated breeding values (EBV) have been used in GWAS on sperm motility in pigs (Diniz *et al.*, 2014). The deregression is performed to avoid double counting because of various information sources and complex family structure (Garrick *et al.*, 2009). This is achieved by subtracting the parent average from individual's EBV. Thus the sow's (or boar's) deregressed EBV contained only the information on own and progeny performance.

In this study, the available data provided a large number of phenotypic observations for TNB, but with a lower number of the sows and boars being genotyped (see *Genotypes* below). Also the boars had only observations through their daughters', sisters' and mothers' performance. Therefore, for the optimal use

of the entire data in the GWAS, the EBV obtained with DHGLM were deregressed following Garrick *et al.* (2009).

For calculation of deregressed EBV, the reliability of EBV was required. It was calculated following the equation (Gilmour *et al.*, 2006):

$$r^2 = \sqrt{1 - \frac{s_i^2}{(1+f)\sigma_a^2}},$$

where  $s_i$  is the standard error reported for the EBV of the  $i^{\text{th}}$  individual;  $f$  is the inbreeding coefficient;  $1 + f$  is the diagonal element of relationship matrix and  $\sigma_a^2$  is the additive genetic variance. Garrick *et al.* (2009) showed also that deregressed EBV have heterogeneous variances, which should be corrected by weighing the residuals. The weights for deregressed EBV were estimated following Garrick *et al.* (2009) methodology.

Deregressed EBV were obtained based on EBV from the univariate analysis of the traits based on the results from the final iteration of DHGLM (see *Estimation of residual variance*). The EBV from univariate analysis were used to avoid EBV for one trait to be affected by the other trait in the bivariate analysis. The deregressed EBV for litter size variation have overall low reliabilities (mainly due to low heritability of that trait). To maintain a sufficient number of genotyped animals for the GWAS, a threshold of 0.05 was used as an acceptable reliability of the deregressed EBV of the animal (Table 5.2).

### 5.2.4 Genotypes

Genotypes were available for 2,679 Large White sows and 426 boars (Table 5.2). All animals were genotyped with the Illumina PorcineSNP60 Beadchip. Samples of blood, hair and ear punches used to extract DNA were collected in the process of routine procedure within the breeding program. Quality control removed SNPs with GenCall score <0.15, minor allele frequency <0.01, and call rate <95%, as well as SNPs from the sex chromosome or with unknown position on build 10.2. As a result, from 64,232 genotyped SNPs, 40,969 SNPs remained in the data set. Also the animals were removed from the data set if their call rate was <95% and if pedigree or genotype could not be linked to the animal. Subsequently, 2,351 animals remained in the set with litter size observations and 2,067 in the set for residual variance of litter size.



## 5. GWAS for litter size and its variability in pigs

**Table 5.1.** Descriptive statistics of the litter size (TNB) observation.

Observation	All sows
#sows with TNB recorded	69,238
#litters records	263,088
Litter size (TNB), n	13.5±3.5
Number born alive (NBA), n	12.5±3.2

**Table 5.2.** Total number of genotyped animals (sows and boars) with deregressed EBV with reliability ( $r^2$ ) >0.05 or >0.2.

Number of observations		$r^2 > 0.05$		$r^2 > 0.2$	
		TNB	varTNB	TNB	varTNB
Total	3,105	3,105	2,651	2,997	326
Boars/Sows	426/2,679	426/2,679	391/2,260	408/2,589	244/82

**Table 5.3.** Variance components (with standard error) for traditional univariate analysis of litter size (TNB).

Estimate	TNB
Additive genetic variance	1.31 (0.04)
Permanent sow variance	0.87 (0.03)
Residual variance	7.14 (0.02)
Heritability	0.14 (0.004)

### 5.2.5 Statistical analyses used for GWAS – Bayesian Variable Selection method

Multi-SNP genome-wide association was performed using a Bayesian Variable Selection method (George and McCulloch, 1993), which estimates the effect of the marker simultaneously using all available SNPs. The methodology was previously applied by Duijvesteijn *et al.* (2014). The fitted model was:

$$y = \mu + X\beta + e,$$

where  $y$  is an  $n$ -vector of deregressed EBV for the litter size or its variation on  $n$  animals;  $\mu$  is an  $n$ -vector equal to the mean;  $X$  is a matrix with dimensions  $n$  by  $p$ , where  $p$  SNPs are coded as 0, 1, 2 copies of specific allele vector; and  $\beta$  is a  $p$ -vector with the markers effects;  $e$  is an  $n$ -vector of weighted random residual effects assumed to be normally distributed  $N(0, \sigma_e^2 W_t)$ , where  $W_t$  is the diagonal matrix with  $w_{t1}, \dots, w_{tn}$  elements. On the marker effect the Bernoulli distribution was applied:

$$\beta \sim \begin{cases} N(0, \sigma_{g_0}^2) & \text{with probability : } \pi_0 \\ N(0, \sigma_{g_1}^2) & \text{with probability : } \pi_1 \end{cases}$$

where the first distribution refers to the null distribution and it is assumed that the SNPs have small effect ( $\sigma_{g_0}^2$ ); the second distribution refers to the SNPs that are assumed to have a large effect, which explains a large part of variance ( $\sigma_{g_1}^2$ ) of the analyzed traits. In this study a relatively restrict prior was selected of  $\pi_1 = 0.001$ , meaning that only 1 in 1,000 SNPs will be in the second distribution in each cycle. In total 500,000 MCMC chains with a burn-in of 5,000 cycles were run. The analysis was performed in Bayz (Heuven and Janss, 2010).

A Metropolis-Hastings sampler was applied to get good convergence which was assessed by visual inspection of the trace and with Gelman and Rubin's convergence diagnostic based on deviance (Gelman and Rubin, 1992) using the R package CODA (Plummer *et al.*, 2006).

### 5.2.6 Identification of significant SNPs

The Bayes Factor (BF) was calculated for each SNP to determine the significant associations:

$$BF = \frac{\hat{p}_i / (1 - \hat{p}_i)}{\pi_1 / \pi_0},$$

## 5. GWAS for litter size and its variability in pigs

where  $\pi_1$  and  $\pi_0$  are the prior probabilities and  $\hat{p}_i$  is the posterior probability of fraction of times SNP was in the distribution with large effect. Following the definitions of Kass and Raftery (1995), the SNPs with  $BF > 30$  are described as “very strong” association and with  $BF > 150$  as “decisive”. The variance explained by significant SNP was estimated as a fraction of the total genetic variance explained by SNPs. All previously reported quantitative trait loci (QTL) for TNB were available via PigQTLdb (<http://www.animalgenome.org/QTLdb/pig.html>). The candidate gene search was performed with software BIOMART available in Ensembl Sscrofa 10.2 (<http://www.ensembl.org>) by entering position of a SNP.

**Table 5.4.** Variance components (with standard error) for litter size (TNB) and residual variance of litter size (varTNB) estimated in Large White sows using Double Hierarchical GLM.

Estimates	TNB	varTNB
Additive genetic variance	1.18 (0.04)	0.03 (0.003)
Permanent sow variance	0.69 (0.02)	0.15 (0.004)
Residual variance	4.4	1.88
Heritability	0.19	0.006 <sup>1</sup>
$GCV_{SDe}^2$		0.087

<sup>1</sup>Heritability estimated at the level of squared phenotypic variance:

$$h_{av}^2 = \sigma_{av}^2 / (2\sigma_p^4 + 3\sigma_{av}^2) \text{ (Mulder et al., 2007).}$$

<sup>2</sup>Genetic coefficient of variation at residual standard deviation level, *i.e.* the genetic standard deviation in residual standard deviation divided by the mean residual standard deviation of the trait:

$$GCV_{SDe} = \sigma_{a_d} (\sigma_{e,add}) / \overline{\sigma_{e,add}} \approx \frac{1}{2} \sigma_{a_d} \text{ (Hill and Mulder, 2010).}$$

**Table 5.5.** Correlation estimates between the random effects on the level and the variance of litter size, estimated in Large White sows using the Double Hierarchical GLM.

Effect	Correlation
Additive genetic	0.49 (0.04)
Permanent	-0.83 (0.02)

### 5.3 Results and discussion

#### 5.3.1 Results of the DHGLM analysis of litter size and its variation

In Table 5.3 are shown estimates of variance components and heritability obtained from the univariate analysis of TNB. The heritability estimate is within the range known from the literature, where heritability estimates for TNB vary from 0.10 to 0.16 (Roehe and Kennedy, 1995; Crump *et al.*, 1997; Hanenberg *et al.*, 2001; Nielsen *et al.*, 2013; Kapell *et al.*, 2011).

The variance components for TNB and varTNB from the DHGLM are presented in Table 5.4. The heritability for TNB (0.19) is above the upper range found in the literature. The estimate was also higher than the heritability from the univariate analysis (Table 5.3), although not significantly different ( $P>0.05$ ). The high estimate of the heritability of TNB from the DHGLM is caused by a lower residual variance, which inflates the heritability. When using the residual variance from the univariate analysis of TNB ( $=7.14$ ), the heritability estimate drops to a value of 0.13, which is in the range of literature values. A lower residual variance in the level part of the DHGLM compared to a conventional analysis was also observed for birth weight in pigs (Sell-Kubiak *et al.*, 2015a;b). The additive and permanent environment variances are in the expected range (Roehe and Kennedy, 1995; Hanenberg *et al.*, 2001; Nielsen *et al.*, 2013; Crump *et al.*, 1997; Kapell *et al.*, 2011).

The estimate of additive genetic variance in the varTNB is 0.03, which is lower than previously reported for this trait (Rönnegård *et al.*, 2010; Felleki *et al.*, 2012). The heritability of the varTNB (0.006) is also lower than previously reported in the literature (Rönnegård *et al.*, 2010; Felleki *et al.*, 2012). Note that this heritability is a measure of the reliability of EBV for varTNB based on single observations; it does not reflect the magnitude of the genetic variance in varTNB (Mulder *et al.*, 2007). The estimated  $GCV_{SDe}$  is 0.09, indicating sufficient potential for selection to reduce variation in TNB. By assuming that in an efficient breeding program a response of  $\sim 1$  genetic standard deviation per generation can be achieved, the  $GCV_{SDe}$  of 0.09 indicates that the SD of TNB can be reduced by 9% per generation.

In Table 5.5 are shown the genetic correlations between random effects in the level and variance part of the model. The additive genetic correlation between TNB and the varTNB is positive and moderate 0.49. This correlation is unfavorable, and indicates that sows with genetically large litters tend to have more variation in litter size. The correlation between the permanent sow effects on TNB and varTNB has the opposite direction: -0.83. This indicates that sows with large litters have a strong phenotypic tendency to have lower variation between their litters.

To further investigate the large difference between the permanent and genetic correlations obtained with the DHGLM, we also performed a conventional bivariate analysis of mean TNB and the log-transformed varTNB ( $\log(\text{varTNB})$ ) per sow (results not shown). The estimated additive genetic variance was 1.23 for mean TNB and 0.04 for  $\log(\text{varTNB})$ , which is similar to values obtained from the DHGLM. The conventional bivariate analysis yields correlations between additive genetic effects and residuals of TNB and  $\log(\text{varTNB})$ . (The conventional analysis has no correlation for the permanent sow effect, since there is only a single observation per sow.) The estimated additive genetic correlation was 0.68, whereas the residual correlation was -0.12. Those correlations have the same sign as those from the DHGLM, but their size is different. When considering the covariances rather than the correlations, the residual covariance from the conventional analysis (-0.82) exceeds the permanent covariance from the DHGLM (-0.27). In the DHGLM we assumed that the residuals are independent from each other. Hence, in the DHGLM, the permanent covariance has to account for fully non-genetic covariance between TNB and varTNB, which probably causes the extremely negative correlation between permanent effects.

Felleki *et al.* (2012) reported an additive genetic correlation of -0.6 between TNB and varTNB, which has the opposite sign to the value reported here. The model used by Felleki *et al.* (2012), however, did not include a covariance for permanent sow effect. When this covariance is not included, the model does not separate the effects properly. When the permanent covariance was omitted in our study, the additive genetic correlation had a negative value of -0.57. To fully account for all existing effects it is necessary to include the covariance structure between both permanent and additive genetic effects in the two parts of the model.

### 5.3.2 Reliability and strength of the GWAS

In this study, a rather stringent prior of 0.001 was used in the Bayesian Variable Selection method. This allowed only ~41 SNPs per cycle to have an effect on the traits. To secure that all the SNPs were used, a total of 500,000 cycles was performed. Selecting a stringent prior provides a more precise distinction between SNPs with large and small effects on the trait (Van Den Berg *et al.*, 2013; Duijvesteijn *et al.*, 2014). The use of deregressed EBV of animals instead of their phenotype is also expected to give more reliable results, since accounting for offspring and parents information increases the power of the GWAS (Ostersen *et al.*, 2011).

During the genomic data exploration, the stratification in the Large White population was detected (see *Appendix*, Figure 5.5). This caused inflation of the P-

values in a preliminary GWAS analysis performed with single-SNP regression and a polygenic effect with a pedigree relationship matrix (see *Appendix*, Figure 5.6). The use of a genomic relationship matrix instead of a pedigree relationship matrix removed the inflation of the P-values (see *Appendix*, Figure 5.7). For the results presented in this study, we used the multi-SNP approach, which also accounts for the population stratification by fitting all SNPs simultaneously.

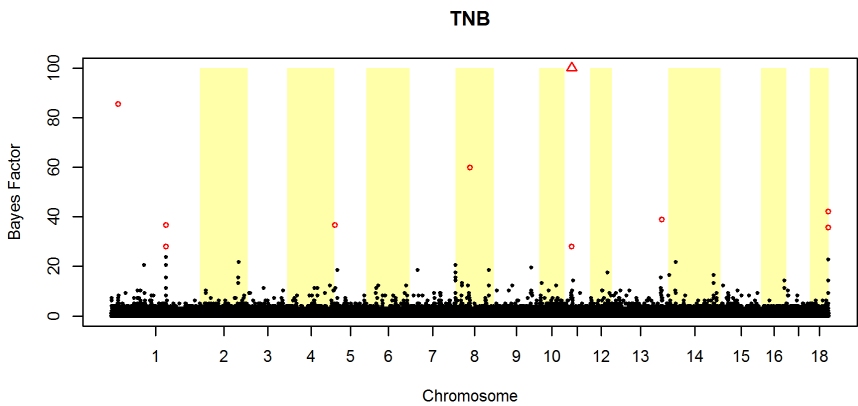
### 5.3.3 Significant associations for TNB and varTNB

In total, ten SNPs were detected for TNB (Figure 5.1) and nine SNPs for varTNB (Figure 5.2). The significant associations found for TNB were located mostly on the same swine chromosomes (SSC) as reported in previous genome-wide associations for this trait (PigQTLdb). Since this is the first GWAS to report SNPs for variance of litter size in pigs, there are no studies available for comparison.

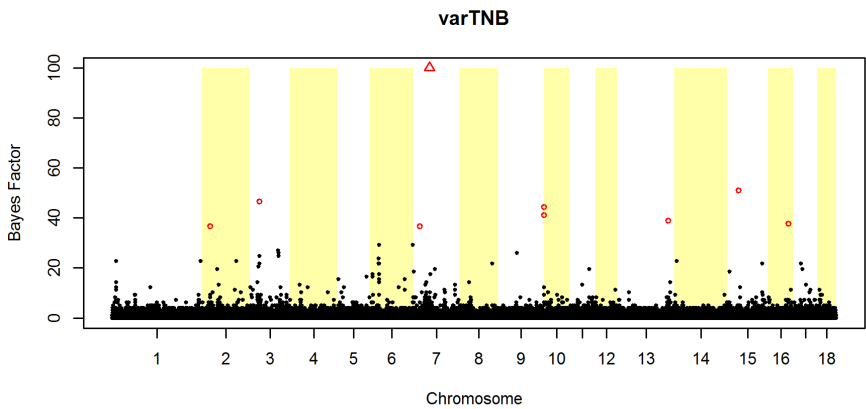
Overall the significant SNPs explained 0.83% of the total genetic variance in TNB, and 1.44% of the variation in varTNB (Table 5.6 and 5.7). In both traits, the most significant SNPs explained the most genetic variance. Therefore, the chromosomes with the most variance explained were SSC11 for TNB and SSC7 for varTNB (Figure 5.3 and 5.4). On SSC11, ASGA0050328 associated with TNB explained 0.36% of the total genetic variance. The estimated allele substitution effect at this locus was 0.1 piglet (Table 5.6). The SNP with the second largest effect on TNB was located on SSC1; it explained 0.10% of genetic variance and its allele substitution effect was 0.05 piglet (Table 5.6). On SSC7, INRA0025193 explained 0.5% of the genetic variance for varTNB. The allele substitution effect at this locus was 2.3% of the mean value of varTNB (Table 5.7; note that values are given on log-variance scale). The SNP with the second largest effect for varTNB was located on SSC3; it explained 0.2% of the genetic variance, and had an allele substitution effect of 1.6% (Table 5.7). The small genetic variance explained by the significant associations indicates that both litter size and its variation are highly polygenic traits.

The genetic variance explained by detected SNPs was low. Thus the deregressed EBV obtained with the DHGLM for TNB, were compared with those from the traditional method (results not shown). The correlation between deregressed EBV for TNB from both methods was 0.988.

5. GWAS for litter size and its variability in pigs



**Figure 5.1.** Genome-wide association for litter size (TNB) in 2,351 purebred boars and sows from a Large White population. Red circles indicate SNPs with BF of >30, red triangles indicate SNP with BF >100.



**Figure 5.2.** Genome-wide association for variation in litter size (varTNB) in 2,067 purebred boars and sows from a Large White population. Red circles indicate SNPs with BF of >30, red triangles indicate SNP with BF >100.

## 5. GWAS for litter size and its variability in pigs

**Table 5.6.** Significant SNPs per swine chromosome (SSC) associated with litter size in boars and sows from a Large White population, with minor allele frequency (MAF), allele substitution effect and significance level in Bayes Factor (BF).

SSC	Significant SNP	Position (Mbp)	MAF	Allele subs. effect <sup>1</sup>	BF	Gen. var. expl. by region(%)
1	ALGA0001244	17.28	0.30	0.052	85.4	0.10
1	ASGA0005117	182.38	0.48	0.039	36.6	0.07
1	ALGA0006771	182.42	0.48	0.034	30.1	0.05
5	ASGA0023713	1.38	0.35	0.034	36.6	0.04
8	ASGA0097249	42.52	0.42	0.021	59.9	0.02
11	ASGA0050328	23.81	0.26	0.105	295.5	0.36
11	MARC0020561	23.87	0.45	0.030	30.1	0.04
13	ASGA0059543	192.72	0.25	0.042	38.8	0.06
18	ALGA0098906	58.86	0.29	0.038	35.5	0.05
18	INRA0056201	58.88	0.29	0.036	42.1	0.04

<sup>1</sup>Allele substitution effects were estimated as  $\alpha = \sqrt{\sigma_a^2 (2pq)^{-1}}$ , where  $\sigma_a^2$  is the genetic variance explained by the SNP, and p and q are the frequencies of the two alleles (Weller, 2009).

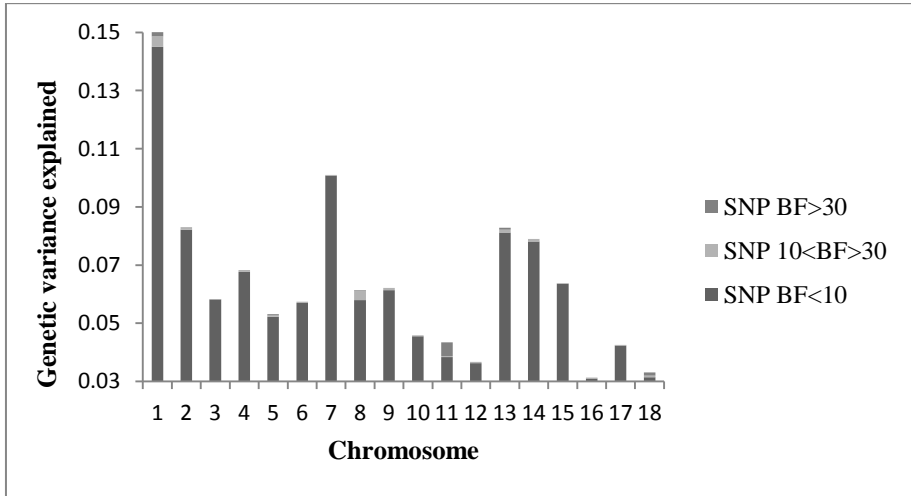


## 5. GWAS for litter size and its variability in pigs

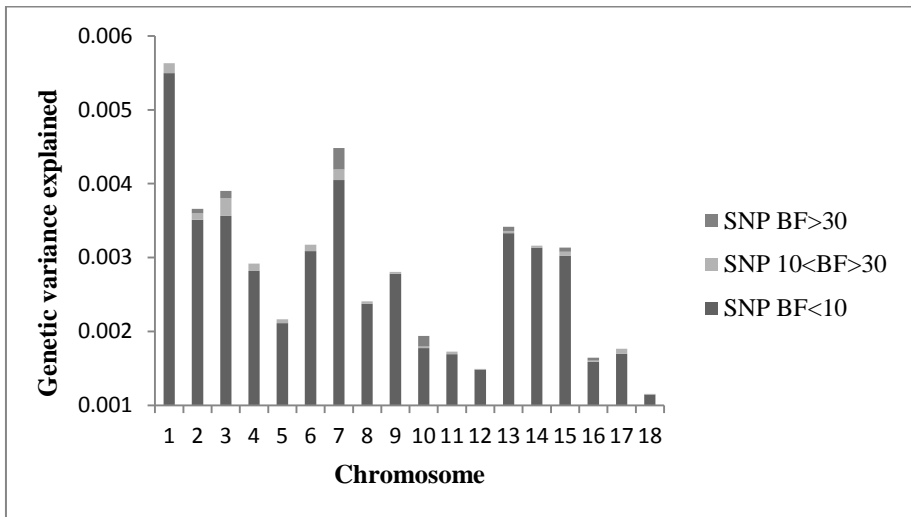
**Table 5.7.** Significant SNPs per swine chromosome (SSC) associated with variation in litter size in boars and sows from a Large White population, with minor allele frequency (MAF), allele substitution effect and significance level in Bayes Factor (BF).

SSC	Significant SNP	Position (Mbp)	MAF	Allele subs. effect <sup>1</sup>	BF	Gen. var. expl. by region(%)
2	ALGA0106652	27.17	0.44	0.011	36.6	0.11
3	MARC0056802	28.40	0.27	0.016	46.4	0.20
7	INRA0025193	43.76	0.48	0.023	167.2	0.50
7	ASGA0031511	17.47	0.20	0.010	36.6	0.06
10	H3GA0055101	0.05	0.47	0.011	44.2	0.12
10	MARC0015344	0.06	0.47	0.012	41.0	0.15
13	DRGA0013310	194.39	0.32	0.011	38.8	0.10
15	MARC0077161	35.59	0.39	0.010	50.9	0.10
16	DRGA0016314	73.39	0.31	0.009	37.7	0.07

<sup>1</sup>Allele substitution effects were estimated as  $\alpha = \sqrt{\sigma_a^2(2pq)^{-1}}$ , where  $\sigma_a^2$  is the genetic variance explained by the SNP, and p and q are the frequencies of the two alleles (Weller, 2009). The estimated allele substitution effects are refer to the log-variance.



**Figure 5.3.** Genetic variance of litter size (TNB) explained per chromosome by significant SNPs with Bayes Factor (BF)>30 (SNP BF>30), SNPs with BF between 10-30 (SNP BF<30), and non-significant SNPs with BF<10 (SNP BF<10).



**Figure 5.4.** Genetic variance of litter size variation (varTNB) explained per chromosome by significant SNPs with Bayes Factor (BF)>30 (SNP BF>30), SNPs with BF between 10-30 (SNP BF<30), and non-significant SNPs with BF<10 (SNP BF<10).

### 5.3.4. Candidate genes and QTL associated with TNB

The two SNPs detected on SSC11 are the first for TNB found on this chromosome. No other study available in PigQTLdb (based on February 2015 search) reported significant associations for TNB on SSC11. The most significant SNP (ASGA0050328) for TNB was located at 23.81 Mbp on SSC11. Only one study reported QTL for reproduction trait in this region of SSC11, which was a QTL for number of teats (Guo *et al.*, 2008).

Within the region of  $\pm 50$  kbp around ASGA0050328, no possible candidate genes were located (Ensembl Sscrofa 10.2; February 2015). The closest gene located at 24.16-24.48 Mbp is *ENOX1*. One SNP associated with TNB (with BF=10.2) was located in this region. The *ENOX1* is a protein coding gene from the ecto-CNOX family being part of electron transport pathways associated with mitochondrial membranes (Scarlett *et al.*, 2005). To its functions belong cellular defense and growth as well as cell survival. The functions of *ENOX1* indicate that this gene might be a new region relevant for TNB in pigs.

Also the region detected on SSC18 (58.86-58.88 Mbp) shows relevance for TNB in pigs. Three QTL related to reproduction traits were previously described within this region (PigQTLdb; February 2015). Those QTL were for: TNB (Onteru *et al.*, 2012), corpus luteum number (Schneider *et al.*, 2014), and gestation length (Onteru *et al.*, 2012).

### 5.3.5 Candidate genes and QTL for variability of TNB

Quantitative trait loci associated with phenotypic variability are defined in the literature as vQTL (Rönnegård and Valdar, 2011). In this study, the SNPs associated with varTNB are the first vQTL reported in pigs. Detected SNPs for varTNB were located within regions of different QTL related to reproduction traits in pigs. In Table 5.8 those QTL are summarized.

Within the region of the most significant SNP (INRA0025193) for varTNB at 43.76 Mbp on SSC7, one candidate gene was located called *CUL9* (SSC7:43,72-43,76 Mbp). *CUL9* is a cytoplasmic anchor protein in complex associated with p53 (Nikolaev *et al.*, 2003). The p53 is a protein, which regulates the cycle of the cell and acts as a tumor suppressor. *CUL9* is controlling the localization and the function of p53 in the cell. Even though *CUL9* was not yet described in swine, its functions can be important in affecting litter size variation in pigs, especially since *CUL9* was expressed in embryonic, placental, and uterus tissues in the human.

Two more SNPs on SSC7 associated with varTNB (with BF 10.2 and 17.5) were located within the regions of two other possible candidate genes already described in swine: *HSPCB* (SSC7: 45.11-45.12 Mbp) and *VEGFA* (SSC7: 44.46-44.47 Mbp). The first gene belongs to the *Sus scrofa* heat shock protein family. This protein family is referred to as molecular chaperones since they are activated under various stress condition, such as heat (Van Wijk *et al.*, 1994), hyperthermia (Huang *et al.*, 1999), and inflammation (Zhang and Mosser, 2008). Their function is to maintain proper folding of the proteins within a cell as well as re-folding denatured proteins post-stress (Fujisawa *et al.*, 1996; Lund *et al.*, 2001). The second gene, *VEGFA*, is a vascular endothelial growth factor, which is a protein mediator growth factor activated in angiogenesis and vasculogenesis in the fetus (and adult) (Cimpean *et al.*, 2008) as well as in endothelial cell growth (Woolard *et al.*, 2004). These two candidate genes are relevant for varTNB, since they affect the response of the pig to environmental (stress) factors (*HSPCB*) and provide the vascular network to the placenta (*VEGFA*).

**Table 5.8.** Overview of QTL reported for reproduction traits in pigs (based on PigQTLdb; February, 2015) within the regions of SNPs associated with variation in litter size.

SSC	SNP	Position	Trait
3	MARC0056802	28.40	corpus luteum number (Cassady <i>et al.</i> , 2001) plasma concentration of FSH (Cassady <i>et al.</i> , 2001)
7	ASGA0031511	17.47	corpus luteum number (Hernandez <i>et al.</i> , 2014) female age at puberty (Cassady <i>et al.</i> , 2001)
7	INRA0025193	43.76	corpus luteum number (Hernandez <i>et al.</i> , 2014) birth weight (Bidanel <i>et al.</i> , 2001; Sanchez <i>et al.</i> , 2006; Guo <i>et al.</i> , 2008; Ai <i>et al.</i> , 2012)
10	H3GA0055101	0.05	number of stillborn (Onteru <i>et al.</i> , 2011)
10	MARC0015344	0.06	
13	DRGA0013310	194.39	corpus luteum number (Hernandez <i>et al.</i> , 2014)
15	MARC0077161	35.59	corpus luteum number (Hernandez <i>et al.</i> , 2014)
16	DRGA0016314	73.39	birth weight (Guo <i>et al.</i> , 2008)

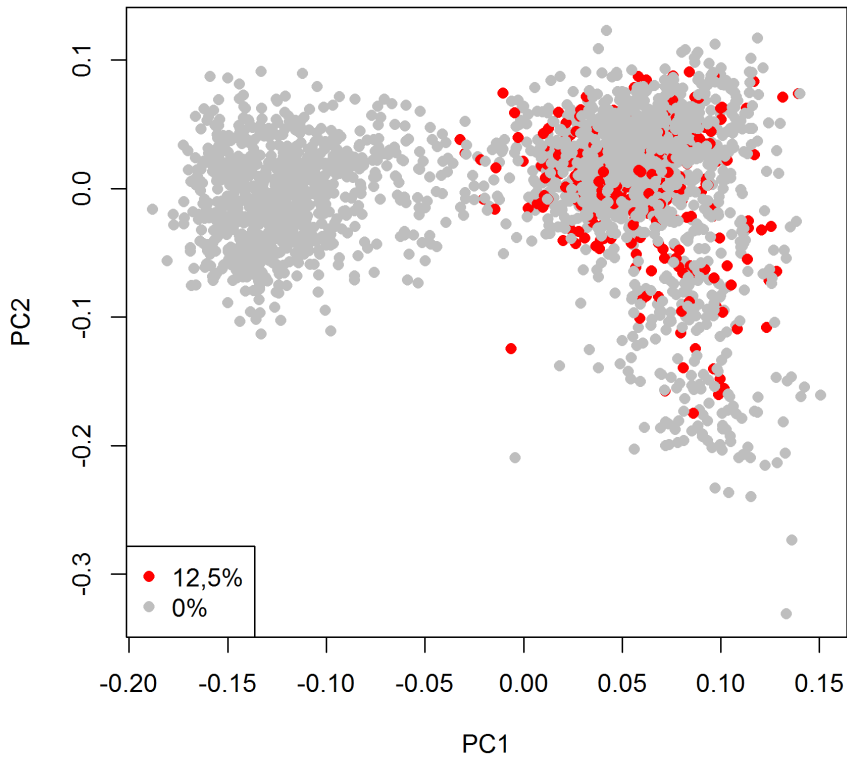
### 5.4 Implications for pig breeding

In this study we have detected several loci, which are possibly controlling the variability of litter size in pigs. One of the main breeding goals in pigs is to increase the litter size. We found a positive genetic correlation between TNB and its variance, indicating that selection for TNB will increase the varTNB. In consequence, the detection of genes that buffer environmental factors, and thus decrease the variance in TNB, is highly desirable. Such gene(s) can buffer changes in environment, which are hard to predict (*e.g.*, diseases) or avoid (*e.g.*, changes of seasons). From the detected regions, *HSPCB* (by the name *HSP90*) was already described in *Drosophila* and *Arabidopsis* as a gene buffering the environmental factors (environmental canalization) (Queitsch *et al.*, 2002; Rutherford *et al.*, 2007; Sangster *et al.*, 2007). Even though *HSPCB* is one of many genes involved in buffering (Debat *et al.*, 2006; Takahashi *et al.*, 2010), it is the most promising candidate gene detected for varTNB in this study.

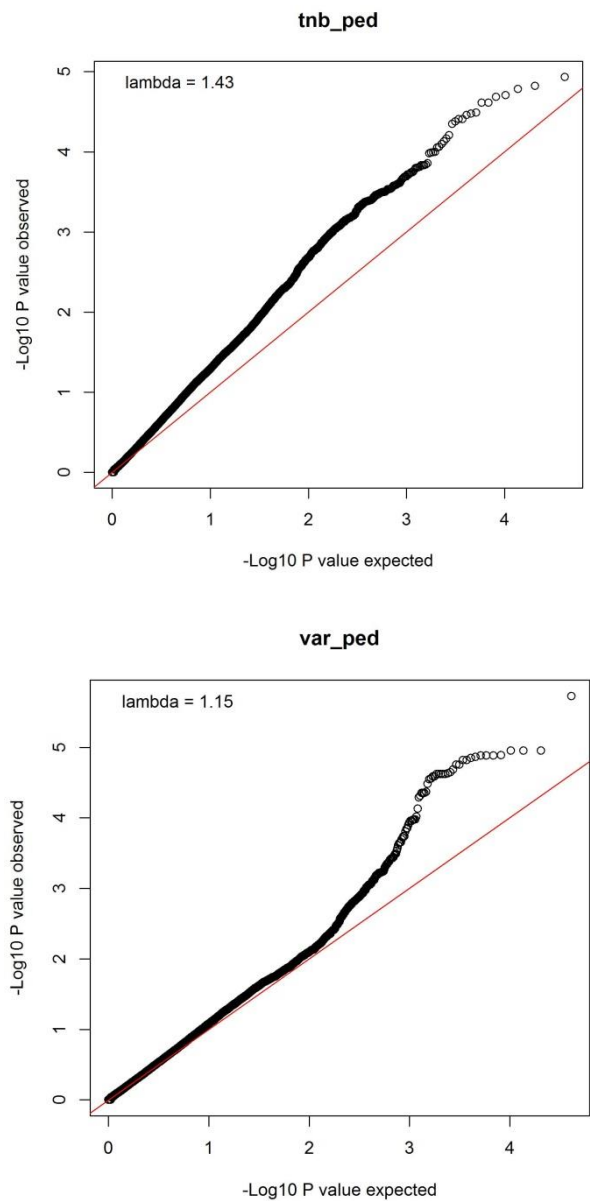
### 5.5 Acknowledgments

This research was financially supported by the Dutch Science Council (NWO) and part of the study was coordinated by the Dutch Technology Foundation (STW). This research was also supported by Breed4Food, a public-private partnership in the domain of animal breeding and genomics and Topigs Norsvin (Vught, The Netherlands). Data for this study were provided by Topigs Norsvin (Beuningen, The Netherlands). The authors would like to thank Luc Janss and Johan van Arendonk for the valuable comments during writing of this manuscript. Ewa Sell-Kubiak also thanks Susan Wijga for helpful discussions and comments.

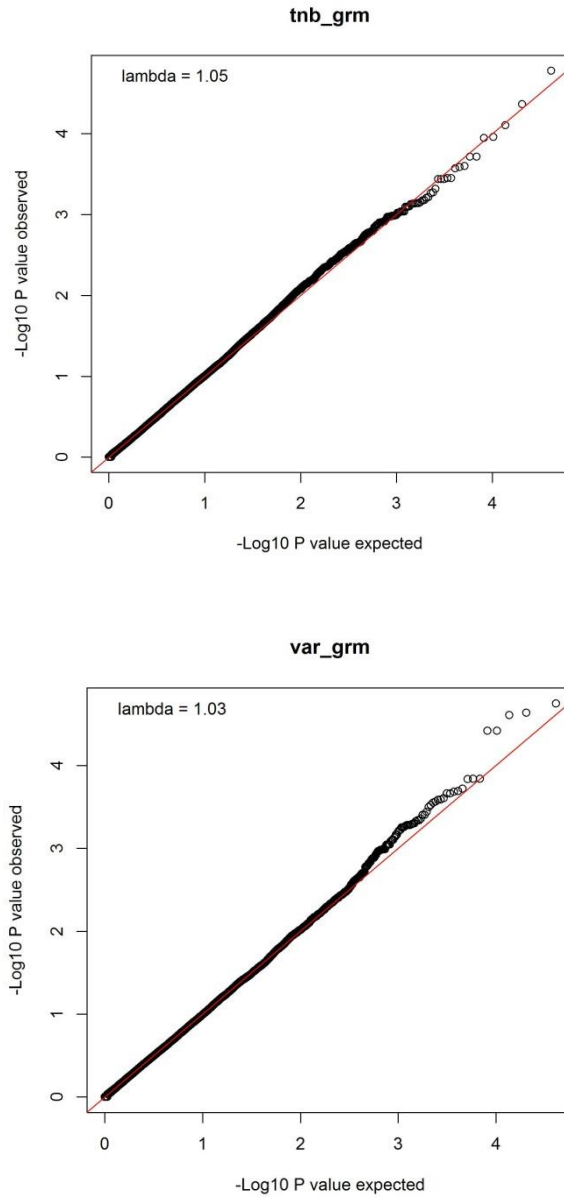
## Appendix



**Figure 5.5.** Genotyped animals mapped to the space of the first two principal components (PC1 and PC2) of kinship matrix with indication of the contribution of the second Large White line (0% or 12.5%) within an animal. Kinship matrix was built with R package GenABEL (Aulchenko *et al.*, 2007).



**Figure 5.6.** Expected and observed  $-\text{Log}_{10}$  P-values of SNPs from the single-SNP GWAS with pedigree for deregressed EBV of litter size (tnb\_ped) or variation of litter size (var\_ped) in Large White population.



**Figure 5.7.** Expected and observed  $-\log_{10}$  P-values of SNPs from the single-SNP GWAS with G-matrix for deregressed EBV of litter size (tnb\_grm) or variation of litter size (var\_grm) in Large White population.





# 6

## **General discussion**



## 6.1 Introduction

### 6.1.1 Thesis objectives

The main objective of this thesis was to study the origin of random variance in production traits of grow-finish pigs and reproduction traits of sows. In pig production for many traits it is important not only to improve the mean of the trait, but also to lower its variation. Uniformity of reproduction and production traits in pigs has several advantages for pig producers. A better understanding of the origin of variance can be used to improve pig productivity and potentially also to improve uniformity of traits.

In this thesis different approaches were used to study the random variance found in reproduction traits of sows and production traits in grow-finish pigs. The first approach focused on finding the origin of the non-genetic variance of common litter. As the common litter effect is closely related to the sow, the origin of common litter variance was studied by exploring the effect of the sow characteristics described by various sow features before the first insemination and during each gestation. The sow features were selected as potentially explaining the background of the common litter effects present in production traits. The second approach focused on studying the residual variance in sow reproduction traits by application of Double Hierarchical Generalized Linear model (DHGLM), which allowed estimating the variance components of the residual variance. The residual variance describes the variation of the trait within the population. Residual variance has a genetic component and as such it has potential to be used to obtain more uniform pigs or uniform litter size in sows. Finally, the genetic architecture of residual variance was explored with application of genome-wide association study (GWAS).

### 6.1.2 Main results

In this thesis, the variance found in reproduction traits of sows and production traits in grow-finish pigs was studied to improve pigs productivity and uniformity of pig traits. The section *“Importance of uniformity for pig breeding”* of this Chapter describes the challenges caused by high variation in reproduction and production traits and the reasons to breed for more uniform pigs.

Results presented in Chapters 2 and 3 showed that the approach to use sow features to explore the origin of common litter variance was not successful. The impact of various sow features on mean growth rate and feed intake of grow-finish pigs was very small. More importantly, sow features did not explain the phenotypic variance due to common litter effects found in production traits of pigs. Still, reducing the variance due to common litter effects could be beneficial for pig

breeding. In the section *“Studying the origin of common litter effects”* of this Chapter, discussion focuses on the opportunities and needs to further study the origin of common litter effects.

In Chapters 4 and 5 the residual variance of birth weight and litter size – studied as traits of sows – were found to have a genetic component. The genetic coefficient of variation at residual standard deviation level ( $GCV_{SDe}$ ) was proposed as a measure to express the potential response to selection (Chapter 4). For both birth weight and litter size the estimated  $GCV_{SDe}$  was about 10%, indicating sufficient potential for response to selection, to increase the uniformity. In Chapter 4 it was shown that analyzing variation in traits applying Double Hierarchical Generalized Linear model (DHGLM) were highly comparable with the conventional analysis of standard deviation (SD) of a trait. Application of DHGLM allows for simultaneous analysis of the mean and the variance of a trait and provides information on the genetic correlations between the random effects for the mean and the variance. The correlation between the additive genetic effects for birth weight and for its residual variance was 0.6 (Chapter 4), whereas for litter size and its residual variance the correlation was 0.5 (Chapter 5). Those moderate correlations are an important indication for the direction of correlated selection response in the variance of traits if selection is on the mean. Increasing the mean birth weight or litter size will lead to increase in variation of those traits. The DHGLM provides good opportunities to study and to select for uniformity of traits. In addition, in Chapter 5 a genome-wide association study (GWAS) for litter size variation, revealed nine significant SNP located on 7 chromosomes. The most significant SNP was found on chromosome 7, near gene coding heat shock protein *HSPCB*, which buffers the effect of stress factors (e.g. heat, inflammation) on growth of cell. Also, the first SNP associated with litter size was found on chromosome 11. The section *“Heterogeneity of residual variance in traits of pigs”* focuses on possibilities of applying results of Chapters 4 and 5 in pig breeding.

The section *“Breeding for uniform and robust pigs”* discusses macro-environmental sensitivity and joint analyses of macro- and micro-environmental sensitivity as well as application of genomic selection, which are topics highly relevant for breeding uniform pigs.

### 6.2 Importance of uniformity for pig breeding

In pig breeding the uniformity has a high importance for both reproduction (maternal) traits of sows and production traits. Uniformity in maternal traits is favorable for welfare and management of the sows and piglets (Baxter *et al.*, 2013;

Rutherford *et al.*, 2013) and it can lead to lower variation at weaning, which decreases the labor required in later stages of production (Merks *et al.*, 2012). Uniformity in production traits is desired since at slaughter penalties are given for carcasses outside a specified weight range (Kanis *et al.*, 2006), but also extending the period to obtain the desired slaughter weight for the lighter pigs creates additional costs (Merks *et al.*, 2012). A more uniform pig production, reflected in reduced variation in the reproduction and production traits is, therefore, related to a higher farm profit.

### 6.2.1 Uniformity of sow reproduction traits

Efficient pig production aims to obtain high number of slaughter pigs per sow per year (Spötter and Distl, 2006; Dekkers *et al.*, 2011; Rutherford *et al.*, 2013). Therefore, in pig breeding genetic selection continues to increase the litter size. The annual genetic trend for litter size in different pig breeding programs was shown to be +0.16 (Merks *et al.*, 2012; Tomiyama *et al.*, 2011), +0.25 (Vidović *et al.*, 2012), and even up to +0.5 (Taylor, *et al.*, 2005) piglets per year per sow. Still, the variation in this trait is large. Poor reproductive performance remains one of the most common reasons for culling (30%) of the sows (Stalder *et al.*, 2005; Hoving *et al.*, 2010; de Jong *et al.*, 2014). At the same time, in the extreme cases litter size goes above 25 piglets, which exceeds the physiological capacity of the sow to provide for the litter during gestation and post-farrowing. Sows with the large litters can also experience welfare issues such as high energy demands during gestation (Rutherford *et al.*, 2013) and shoulder sores during lactation (Zurbrigg, 2006; Herskin *et al.*, 2011). Moreover, an increasing litter size affects also welfare and survival of the piglets.

Selection for larger litters increased the ovulation rate in sows. During gestation, uterine capacity and its blood supplies are the physiological factors limiting possibility for all the fetuses to fully develop (Foxcroft *et al.*, 2006; Pardo *et al.*, 2013; Jang *et al.*, 2014). The ovulation rate is genetically correlated (0.34) with number of stillborn (Johnson *et al.*, 1999). This correlation is a consequence of intra-uterine competition between embryos, which affects piglets' survival pre-farrowing.

Litter size is also closely related to the piglets' birth weight, which is considered a sow reproduction trait (Roehe, 1999; Damgaard *et al.*, 2003; Canario *et al.*, 2010). From a welfare and management perspective high birth weight is a very important trait for piglets' survival till weaning (Foxcroft *et al.*, 2007; Foxcroft *et al.*, 2009; Knol *et al.*, 2010; Rutherford *et al.*, 2013; Baxter *et al.*, 2013). Larger litters, however, phenotypically tend to have higher variation in birth weight (Van der

Lende and de Jager, 1991; Milligan *et al.*, 2002; Foxcroft 2006). Thus the pre-weaning survival is decreased by increased competition between the piglets resulting from higher variation of within-litter birth weight observed in the large litters (Foxcroft *et al.*, 2006; Kapell *et al.*, 2011; Rutherford *et al.*, 2013). To manage the largest litters it is often necessary to apply nursing techniques such as: cross-fostering (moving a piglet to a different sow with more milk), the use of nurse sow systems, which are either life sows or artificial rearing boxes, and early weaning (Baxter *et al.*, 2013). These management techniques are, however, labor intensive and disturb nursing behavior of the sows and piglets.

Despite affecting the survival of the piglets, larger litters will still result in higher number of weaned piglets and slaughter pigs than small litters (Beaulieu *et al.*, 2010). Thus currently in pig breeding, the goal is towards more sustainable production that will increase the piglet's survival regardless of increasing litter size (Beaulieu *et al.*, 2010; Kapell *et al.*, 2011; Merks *et al.*, 2012; Nielsen *et al.*, 2013). To facilitate sustainable pig production a good balance needs to be found between sows' and piglets' welfare and the economic result. Improved uniformity of litter size (and ovulation rate) can reduce the number of extremely large litters with accounting for the physiological capacity of the sow. This will also improve piglets' welfare and survival with maintaining high litter size.

### 6.2.2 Uniformity of production traits

Breeding for uniformity in production traits in pigs starts with birth weight of the piglets. Birth weight is one of the most important traits for the entire productive life of the pig (Bee, 2004; Gondret *et al.*, 2005; Foxcroft *et al.*, 2006; Rehfeldt *et al.*, 2008; Fix *et al.*, 2010; Schinckel *et al.*, 2010). Besides its effect on piglet's survival, it can also affect muscle development (Bee, 2004; Fix *et al.*, 2010; Schinckel *et al.*, 2010) and postnatal growth performance (Gondret *et al.*, 2005, Foxcroft *et al.*, 2006; Rehfeldt *et al.*, 2008, Schinckel *et al.*, 2010).

The piglets with low birth weight have slower pre- and post-weaning growth than heavier piglets. Merks *et al.* (2012) showed that the piglets smaller by about 30% than the average at birth are on average 5% lighter at slaughter and spend 10 days more than average in grow-finish pens. In contrast, piglets 30% heavier than average at birth reach a higher slaughter weight (by 3%) 4 days earlier than average. The difference in growth rate between the heaviest and the lightest grow-finish pigs creates additional costs and labor for farmers. These additional costs and labor are needed to deliver batches of equal-weight pigs to avoid penalties for carcasses outside the range (Kanis *et al.*, 2006).

Variation in production traits and in time to achieve desired weight between animals contributes to price per kg of the carcass, which is highly relevant from the economic and management perspective of the farm (“all in, all out”). Lowering the variation in production traits is possible with the selection for improved uniformity of birth weight. It is necessary, however, to simultaneously maintain desired direction of selection for the mean birth weight since this trait affects the post-weaning growth of the pigs.

### **6.3 Studying the origin of common litter effects**

Common litter effects describe similarities within a group of piglets sharing the same prenatal and postnatal environment provided by the sow (mother). Finding the origin of the common litter effects could lead to reducing the phenotypic variance due to these effects. This can be beneficial for pig breeding, since reducing the variance in production traits can lead to a decrease in the variation between animals. For this, however, the origin of the common litter effects should be identified. In Chapters 2 and 3, I tested the hypothesis that sow features can explain the common litter variance present in production traits. To test this hypothesis, the sow features were used as additional fixed effects in the animal model in analysis of production traits. This approach revealed that some of the sow features had significant effect on the traits of grow-finish pigs, but they did not significantly contribute to the phenotypic variance due to the common litter effect. The failure to explain common litter effects could be due to the selected sow history or gestation features included in the analyses in Chapters 2 and 3. The list of already tested features can be extended by other factors that could be improved by management, for instance environmental enrichment (*e.g.*, Oostindjer *et al.*, 2011). The common litter effect, however, is likely a combination of many factors which are hard to quantify or estimate. Thus the expected decrease in variation in production traits might not be achieved, since many factors can be beyond management control. Some of such factors can be: the milk production of the sow (*e.g.*, Kruse *et al.*, 2011) or behavioral characteristics, for instance the behavior of the sow towards piglets and the degree of interaction with them (Oostindjer *et al.*, 2011), within-litter behavior of piglets (*e.g.*, Oostindjer *et al.*, 2011) and piglet’s “personality” (*e.g.*, Bolhuis *et al.*, 2006). In addition, part of the common litter variance can be linked to the maternal genetic variance, as some sows provide better environment to their offspring than others. Thus aiming for a precise identification of the origin of common litter effects is difficult.



The literature provides evidences of a large contribution of common litter effects to the total environmental variance in production traits of the grow-finish pigs. Yet, in Chapters 2 and 3 the common litter variance was much lower than expected from literature: 5 – 7% in growth rate traits and 3 – 6% in feed intake traits. Bergsma *et al.* (2008) showed that the significant drop in the common litter effects can be expected when a random group effect is included in the model. Previous studies accounted for the group, however, as a fixed effect (Chen *et al.*, 2002; Johnson *et al.*, 2002; Kuhlers *et al.*, 2003; Van Wijk *et al.*, 2005). The random effect of the group accounts for the similarities of the grow-finish pigs kept in one pen during the grow-finish phase of production. In Bergsma *et al.* (2008), in the model without the group effect, the common litter effect was 12% for growth rate and 16% for feed intake. Whereas in the model with group effects those estimates were 4% for growth rate and 3% for feed intake, which is similar to the estimates presented in Chapters 2 and 3. Duijvesteijn *et al.* (2012), on partially similar data as in Chapters 2 and 3, estimated slightly higher common litter for growth rate (9%) with models including the group effect. As argued in the discussion of Chapter 2, large common litter effects in models without group effects are caused by the composition of grow-finish groups, which often contain full-sibs. This leads to a partial confounding with the common litter effect and to overestimation of common litter effects if the group effect is not accounted for (Bergsma *et al.*, 2008; Chapter 2). Animal models fitted for production traits should, therefore, include both common litter and group random effects.

To conclude, reducing the variation in production traits is very difficult to be achieved by reducing the common litter variance. Firstly, only part of many possible factors affecting common litter effects is measurable and could be controlled by management. Secondly, actual estimate of common litter effects in production traits depends greatly on a proper fit of the genetic model. Finally, even accurately estimated common litter effect appears to have very small contribution to the variation of the production traits. An alternative approach can be studying the residual variance of traits, as discussed in the next section.

### **6.4 Heterogeneity of residual variance in traits of pigs**

#### **6.4.1 Decreasing variation of reproduction traits with DHGLM**

There are certain challenges related to unbalanced selection for increased litter size in pigs. A possible solution can be simultaneous selection for uniformity of within-litter birth weight and litter size. Result of Chapters 4 and 5 can be used to predict an outcome of single trait selection. An effective breeding program can change one unit of genetic SD in one generation of selection. Based on this

assumption it is predicted that SD of birth weight can be decreased by 10% (Chapter 4), and the SD of litter size by 9% in one generation of selection (Chapter 5). It needs to be noted that moderate genetic correlations were found between birth weight and its variation (0.6; Chapter 4) and litter size and its variation (0.49; Chapter 5). Therefore, simultaneous selection of those traits and their variation is needed to achieve a desired direction of improvement in the mean and the variance of traits. This is very important for pig production, since decreasing the mean of litter size and birth weight is not desirable from the economic perspective of the farm. In addition, there is a negative genetic correlation between survival of the piglets and the litter size (Knol, 2001), as well as survival and birth weight variation (Mulder *et al.*, 2015). Merks *et al.* (2012) showed that in commercial setting, selection not only for increased litter size, but also increased survival of the piglets is possible. Simultaneous selection for improved uniformity of litter size and piglets' survival will facilitate more sustainable breeding in terms of lower mortality of piglets and decreased need for management interventions during the nursing period. Still, decreasing the variation in birth weight is needed to lower the variation in production traits of pigs.

Selection index calculations can be used to obtain clear overview for the utility of simultaneous selection of those traits in a practical breeding program. An extended DHGLM analysis can provide the required genetic parameters for such selection index calculations. Mulder *et al.* (2015) applied a trivariate DHGLM including a genetic covariance between residual variance of birth weight and survival of the piglets. In addition, by applying DHGLM breeding values can be obtained for the mean and variation of a trait.

#### **6.4.2 Potential to decrease variation of production traits**

Conventional methods for studying the variation of traits are based on standard deviation (SD). Many production traits have, however, only a single observation per animal and the methods using SD cannot be applied to them. Studying the origin of the common litter effect was not successful to improve the uniformity in growth rate and feed intake of grow-finish pigs (Chapters 2 and 3). DHGLM presented in Chapters 4 and 5 shows potential to be used as an alternative method to reduce the variation in production traits.

In Chapters 4 and 5, I demonstrated that DHGLM can successfully be applied to study variation of traits. Also the DHGLM has potential to replace the traditional method of genetic evaluation based on SD to decrease the variation of traits (Chapter 4). In case of single observations per animal, however, DHGLM gives biased estimates of variance components when the animal model is used. It is,

therefore, recommended to use a sire-dam (Sonesson *et al.*, 2013) or a sire (Mulder *et al.*, 2013b) model to estimate variance components. For sufficient precision of estimates the dataset has to consist of at least 100 sires, each with 100 offspring (Mulder *et al.*, 2013b). In addition, it is expected that unbiased breeding values for mean and variance can be estimated with an animal model version of DHGLM when variance components are known, *i.e.* normal procedure for best linear unbiased prediction (BLUP) (Mulder *et al.*, 2013b). The results from a DHGLM require some re-scaling to allow comparison to other studies focusing on variation. In Chapter 4, I have shown that the  $GCV_{SDe}$  can facilitate straightforward comparison of methods/studies. In addition, it provides an indicator of potential response to selection in breeding programs.

Assuming that in the production traits with application of DHGLM a similar improvement of uniformity as in reproduction traits can be achieved, a decrease in variation of about 10% can be obtained, for example in growth rate (assuming single trait selection). One of the paying systems used in the Netherlands, can be used to calculate the change in financial loss due to reduction in traits variation (E. Hanenberg, personal communication). With a fixed age at slaughter and based on SD of growth rate=80, the financial loss due to carcasses outside the desired range was estimated to be -0.33 euro/pig. By reducing the SD of the growth rate by 10% (SD=72), the financial loss decreased to -0.21 euro/pig. Based on average Dutch farm size of 600 sows producing 28 slaughter pigs/year and average price for slaughter pig being 1.41 euro/kg (Jan-Dec 2014, LEI-Wageningen UR), the difference of 0.12 euro/pig rounds up to additional 2,016 euro of the farm profit/year.

Presented calculations were simplified. They did not take into account extra feeding and housing costs of growing smaller animals for a longer period or delivering fast growing pigs in earlier batch to the slaughter house. Still, it is clear that improved uniformity of production traits such as growth rate has high economic benefits. Achieving the improvement in uniformity of production traits requires first and foremost breeding for low birth weight variation within litters. Reducing variation in birth weight – and with this in growth rate in pigs – will lead to reduced variation in slaughter weight. Since the positive correlation is present between birth weight and its variance, the biggest, *i.e.* also the fastest growing pigs, will be lost when selecting for lower variation. Thus selection for birth weight and its variation should be performed simultaneously to maintain high mean of the birth weight as it is important for the post-weaning performance of the pigs.

**Table 6.1.** Examples of detected vQTL affecting the variability of quantitative traits

Authors	Species	Trait	Additional
Mackay and Lyman (2005)	<i>Drosophila melanogaster</i>	Bristle number	Coefficient of variation of a trait, varies between chromosomal substitution lines
Ordas <i>et al.</i> (2008)	Maize	Days to flowering, ear height and tassel length	Several significant vQTL
Paré <i>et al.</i> (2010)	Human	Levels of inflammatory biomarkers	1) interaction of SNP for the prediction of C-reactive protein with body mass index, 2) interaction of SNP for biomarker ICAM-1 with smoking behavior
Perry <i>et al.</i> (2012)	F2 cross of the genetically hypercalciuric <i>Rattus norvegicus</i> with normocalciuric Wistar-Kyoto	Urinary calcium levels	Several significant vQTL.
Shen <i>et al.</i> (2012)	<i>Arabidopsis thaliana</i>	Cellular control of molybdenum concentration	vQTL on the exon of <i>MOT1</i>
Yang <i>et al.</i> (2012)	Human	Body mass index (BMI)	SNP located within <i>FTO</i> (gene related to obesity) associated with variability of BMI
Mulder <i>et al.</i> (2013a)	Dairy cows	Somatic cell score (SCS)	Three highly significant SNPs for variance of SCS in the location associated with: 1) marker BR4502 on BTA3 associated with chronic mastitis, 2) two associated with SCS
Nelson <i>et al.</i> (2013)	<i>S. cerevisiae</i> strains	Expression-traits in different treatments	Several vQTL, most important close to <i>DIA2</i> . Evidence for the epistasis.
Chapter 5	Pigs	Litter size	9 significant SNPs. Most significant SNP on <i>SSC7</i> with candidate genes: heat shock protein ( <i>HSPCB</i> ), vascular endothelial growth factor ( <i>VEGFA</i> ), and protein regulating p53 function ( <i>CUL9</i> )

### 6.4.3 Genetic architecture of environmental variability

Quantitative trait loci (QTL) from traditional analysis can be defined as the mean-controlling genes, as they affect the observed average of the phenotype. The literature demonstrates that there are also QTL associated with the phenotypic variability – vQTL (Rönnegård and Valdar, 2011). The development of new statistical methods facilitates the study of genetic architecture of complex traits such as phenotypic variability (Rönnegård and Valdar, 2012, Cao *et al.*, 2014). A number of studies have reported vQTL in plant and animal species and in humans as presented in overview in Table 6.1. In Chapter 5 of this thesis, significant SNP for residual variance in litter size were detected (see Table 6.1 for details). Those are the first SNP associated with variation of a trait reported in pigs.

A vQTL in a population indicates the existence of unmodeled interaction associated with the locus (Rönnegård and Valdar, 2012; Shen *et al.*, 2012; Nelson *et al.*, 2013). Three types of interactions can be distinguished, in which vQTL could be involved: interaction between the genes, interaction between the gene and known/unknown environmental factor (Paré *et al.*, 2010; Struchalin *et al.*, 2010) or parallel presence of both of those interactions (Rönnegård and Valdar, 2011).

The gene-by-gene interaction implies the presence of epistasis. In the presence of epistatic interaction the individuals with a certain genotype show more phenotypic variation than individuals with a different genotype at the same locus (Rönnegård and Valdar, 2012). This can be explained by the presence of vQTL buffering effects of other genes (genetic canalization). Evidence for epistasis were found, for instance in *S. cerevisiae* (Nelson *et al.*, 2013; see Table 6.1 for details).

In the presence of the gene-by-environment interaction, the variability of a trait is strongly affected by unmodeled environmental factors, which can be buffered (environmental canalization) by the presence of vQTL (Paré *et al.*, 2010; Nelson *et al.*, 2013). This type of interaction was described in humans (Paré *et al.*, 2010; see Table 6.1 for details). Also in Chapter 5 the most promising candidate gene for variability of litter size was *HSPCB*, which is one of the genes from the heat shock family involved in buffering various stress factors (Queitsch *et al.*, 2002; Debat *et al.*, 2006; Rutherford *et al.*, 2007; Sangster *et al.*, 2007; Takahashi *et al.*, 2010).

The third type of possible interaction combines the gene-by-gene and gene-by-environment interactions (Hill and Mulder, 2010; Fraser and Schadt, 2010; Rönnegård and Valdar, 2011).

In breeding practice, an interaction of vQTL with hard to predict (*e.g.*, diseases) or avoid (*e.g.*, changes in temperature) environmental factors is highly relevant as it can affect the expected performance of an animal. Moreover, detection of genes that can buffer environmental factors, and thus decrease the variance of traits, is

highly desirable. This is especially important since pig breeding needs to fulfil requirements of different production systems in different parts of the world.

### **6.5 Breeding for uniform and robust pigs**

Globalization of the livestock breeding requires selection for genotypes that have the capacity to buffer various environmental factors. To do that, the opportunities to select for animals performing in different production systems, parities or climates need to be quantified. Chapters 4 and 5 analyzed overall variation of a trait with DHGLM. In this section of discussion, I will focus on a few other methods that can be used to study and improve the uniformity of reproduction and production traits in pigs.

#### **6.5.1 Macro- and micro-environmental sensitivity**

The residual variance studied in Chapters 4 and 5 gathers the environmental variance that cannot be measured by known factors. In the literature these unknown factors are also referred to as micro-environment (Jinks and Pooni, 1988). The environment in which the animal performs can be characterized by a number of known factors, *e.g.*, farming system, management, temperature, or feed quality. Those known factors can be defined as macro-environment. To breed for robust and uniform animals across production systems it is important to gain knowledge on both macro- and micro-environmental sensitivity of the animals. In the following part, an application of reaction norm and macro-micro models will be discussed.

#### ***Applying Reaction Norm models***

In the livestock breeding the improvement is achieved by selection of genotypes, whereas the success of selection depends on the interaction between the genotype and environment (GxE, Falconer and Mackay, 1996). Presence of GxE indicates a macro-environmental sensitivity of the genotype. The genetic variation in macro-environmental sensitivity can be expressed by the variation in the response to macro-environmental factors (Jinks and Pooni, 1988).

To explain the genetic background of the response in performance of the animals to different macro-environmental factors, the reaction norm models can be applied (Van Tienderen and Koelewijn, 1994; Lynch and Walsh, 1998; Calus and Veerkamp, 2003; Knap and Su, 2008). Reaction norms are functions that allow relating the phenotypic response to the change of environment and quantifying this relationship (Lynch and Walsh, 1998). A number of studies used this methodology to study the effect of herd\*year\*season interaction in dairy cattle and pigs (Calus

and Veerkamp, 2003; Knap and Su, 2008; Rashidi *et al.*, 2014). In practice, an environmental factor can be defined by any known factor causing genotypes to respond differently, for instance parity of the sow, farming system or temperature. Reaction norms, thus, allow quantifying the animal's macro-environmental sensitivity to a certain change in environment. This can help to breed animals with phenotypic plasticity to perform on the same level throughout the productive or reproductive live despite changes in environmental factors.

### ***Combined analysis for macro- and micro-environmental sensitivity***

To fully grasp the potential of animals to perform in a uniform manner in every environment a combined analysis of the macro- and micro-environmental sensitivity is needed. Such analysis allows studying simultaneously the change in the mean of a trait in different environments and overall variation of a trait in the population. Mulder *et al.* (2013b) described the quantitative model underlying the genetic variance in macro- and micro-environment. The DHGLM proposed by Rönnegård *et al.* (2010) was extended with the reaction norm model by Mulder *et al.* (2013b), which provided a method for a simultaneous analysis of macro- and micro-environmental sensitivity.

The extended DHGLM with the sire model was successfully applied to milk yield in dairy cows (Mulder *et al.*, 2013b) and somatic cell count in dairy cows (Wijga, 2013). In both cases the presence of macro- and micro- environmental sensitivity was shown. This indicates that macro-micro models give more precise indication for the predicted performance of the animals in different environments. The genetic correlation estimated between the macro- and micro-sensitivity was estimated on the level of about 0.8 (Mulder *et al.*, 2013b; Wijga, 2013). The high similarity of the two types of sensitivity suggests that there are good opportunities to improve overall robustness of the animals with selection.

Macro-micro model needs to be applied to pig traits to investigate whether the same level of correlated response can be achieved as in dairy cattle. If detected, high similarity of macro- and micro-environmental sensitivity can be very useful to reduce the variability of traits in pigs. There are, however, certain challenges involved with applying this methodology. Breeding more uniform and robust animals across different production systems worldwide is desired for reproduction and production traits. It can, however, be harmful for traits related to health of the animal. For example, breeding for robust reaction to the selected pathogen(s), could limit the immunological response of the animal to known pathogens only.

This could be very challenging for the entire population in case of a contact with a new pathogen.

### **6.5.2 Genomic information in breeding for improved uniformity**

Currently, pig breeding programs benefit from the genotyping of the pigs with single nucleotide-polymorphism (SNP) markers (Merks *et al.*, 2012). The accessibility of Porcine Illumina SNP60 BeadChip (Ramos *et al.*, 2009) is increasing with decreasing costs of genotyping. One way to utilize SNPs is to perform a genome-wide association studies (GWAS) to detect regions in genome which are associated with particular traits. Numerous GWAS were performed in pigs, which detected a high number of QTL with small effects on quantitative traits (PigQTLdb, <http://www.animalgenome.org/QTLdb/pig.html>). Yet, using many QTL with small effects in breeding programs might be difficult or even not feasible in practice. Another way to utilize SNPs is genomic selection, which is described in the following section.

#### **Genomic selection**

In genomic selection many SNPs are used at the same time to improve the accuracy of estimated breeding values of selection candidates. Such genomic evaluation is also used to describe the relationships of the animals by constructing relationships matrices: **G**-matrix for all genotyped animals (VanRaden, 2008, Yang *et al.*, 2010) or **H**-matrix for both genotyped and ungenotyped animals in the population (Forni *et al.*, 2011). The difference in genomic evaluation with **G** or **H** is that the **H** combines both pedigree and genomic relationship matrix, whereas **G** is based only on the marker information. Thus, breeding values estimated with **H**, combine the pedigree- and genomic-based breeding values (GEBV), whereas **G** gives direct genomic breeding values (DGV).

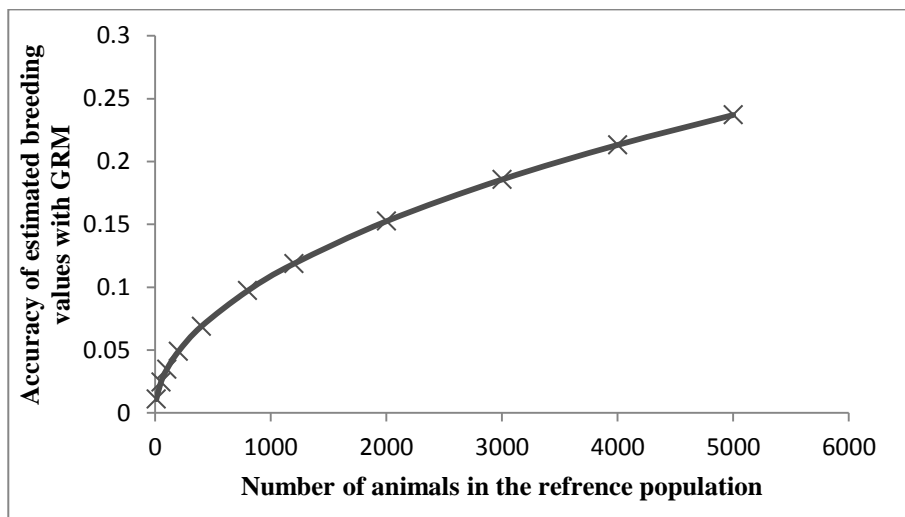
So far two studies used **G** in DHGLM to analyze the variation of a trait. Mulder *et al.* (2013a) analyzed variation of somatic cell score in dairy cattle, whereas Sell-Kubiak *et al.* (2015b) analyzed birth weight variation in pigs. Only in dairy cattle data the accuracies of EBV were higher with **G** compared to pedigree relationship A-matrix. For pigs, a larger reference population of at least 2,000 animals is required to obtain significantly higher estimates with **G** (Sell-Kubiak *et al.*, 2015b).

#### **Benefits of genomic selection in breeding for uniformity**

As shown in earlier studies, application of **G** in DHGLM to study the variability of traits is possible. It also has potential to contribute to the select animals with high



uniformity in a trait of interest. Especially, since many aspects of genomic selection could be very beneficial when selecting animals for improved uniformity of traits. Firstly, the genomic evaluation of an animal gives more precise indication of the genetics underlying the observed phenotype, leading to an increased accuracy of the estimated breeding values (EBV). This is, especially, important for traits with a low heritability, *e.g.*, residual variance. In general, the heritability of residual variance was reported as being below 0.05 (*e.g.*, Ibáñez-Escriche *et al.*, 2008; Felleki *et al.*, 2012; Mulder *et al.*, 2013a). In this thesis heritability of the residual variance was estimated on the level of about 0.01 in birth weight in two sow lines ( $h_v^2$ ; Chapter 4) and 0.006 in litter size ( $h_v^2$ ; Chapter 5). Secondly, the genomic selection improves the accuracy of non-phenotyped selection candidates. This is important for many reproduction and production traits, since they are recorded later in life, *e.g.*, reproduction performance, or have only single observation per animal, *e.g.*, slaughter weight and backfat.



**Figure 6.1.** Prediction of genomic accuracy for the litter size variation in Large White using different sizes of reference population.

The benefits of applying genomic selection to traits with low heritability and single observation can be illustrated by taking the litter size variation as an example. Assuming the selection of the sows based on own performance and one observation only, the accuracy of EBV for litter size variation can be estimated as  $r_{IH} = \sqrt{h_v^2} = 0.08$ . Using the equation of Goddard (2009) the number of independent chromosome segments can be estimated as  $Me = 2N_e L(\ln(4N_e L))^{-1} = 504$ , where  $N_e=100$  is the effective population size and  $L=23$  is the length of the genome (~23 Morgans; Rohrer *et al.*, 1996). Subsequently, accuracy of genomic selection can be estimated based on different sizes of the reference population ( $N_p$ ) as  $r_{IH} = \sqrt{N_p h^2 (N_p h^2 + Me)^{-1}}$  (Daetwyler *et al.*, 2013). Already with 2,000 genotyped and phenotyped sows the accuracy of selection, for a trait with a very low heritability, is twice the accuracy based on own performance only (Figure 6.1).

The genomic selection in combination with DHGLM gives good indications which individuals and families have smaller variation in reproduction and production traits. This will help selecting pigs that have low variation in traits of interest with maintaining the mean of those traits on desirable level.



## **Summary**



## Summary

Livestock breeding is focused on the selection of desirable genotypes. The expression of the genes, however, is strongly influenced by the environment in which the animal is born and kept throughout the reproductive and productive lifetime. The environment in which the animal performs can be characterized by a number of known factors e.g. farming system, management, temperature, or feed quality. Those known factors are defined as macro-environment. Yet, not all of environmental effects are already defined (measured) or possible to obtain. In the literature these unknown factors are referred to as micro-environment. Since the environment affects success of selection, the environmental effects are always taken into account in breeding practice. In genetic (animal) models they are included as non-genetic fixed or random effects.

The main objective of this thesis was to study the origin of random variance in reproduction and production traits of pigs. In pig breeding for many traits it is important not only to improve the reproduction and production trait itself, but also its variation. Obtaining uniform pigs on various production stages is an important goal in pig breeding. The variance can be used to improve pig productivity, and potentially also to improve uniformity of traits. In this thesis the variance was studied with several approaches. First by exploring the effect of the various sow features that could explain the background of the common litter and permanent sow effects in grow-finish pig traits (Chapters 2 and 3), second by studying the residual variance in sow reproduction traits (Chapter 4), and finally by exploring the genetics of residual variance with genome-wide association study (GWAS) (Chapter 5). Whereas Chapter 6 discusses the overall findings of this thesis.

Chapter 2 focuses on sow history features, so features that characterize early life of the sow (birth litter size, birth year and season, birth farm, weaning age, age being transferred to experimental farm, and age at 1<sup>st</sup> insemination), and their effect on grow-finish pig production traits: feed intake and growth rate. First, the sow features were tested whether they affected grow-finish pig traits. Second, significant sow features ( $P < 0.1$ ) were simultaneously included into the full animal model to study their impact on common litter and permanent sow effects. Selected sow features do affect grow-finish pigs' traits, but their estimates are small and explain only a small proportion of the differences in growth rate and feed intake of grow-finish pigs. The heritability estimates for growth rate and feed intake (only in the phase two of grow-finish stage) decreased after adding the sow features to the model. The sow features partially explained the permanent sow effect of feed intake related traits and did not explain the common litter effect.

In Chapter 3 concept of the sow characteristics affecting grow-finish pig traits is investigated further. This time sow features collected on group-housed gestating sows were used to study their effect on grow-finish pig performance. Sow features were collected during multiple gestations and divided into three clusters describing: *i.* sow body-condition, *i.e.*, weight, backfat, gestation length; *ii.* sow feed refusals, difference between offered and eaten feed during three periods of gestation: 1-28, 25-50, 45-80 days; *iii.* sow group features, *i.e.*, number of sows, average parity. Investigated sow gestation features explained 1% to 3% of the total variance in grow-finish pigs. Moreover, adding sow features to the animal model for production traits did explain phenotypic variance due to permanent sow and part of phenotypic variance due to common litter effects for feed intake, but not for growth rate.

In Chapter 4 the methods used to study variation of traits (application to birth weight in pigs) are compared: the traditional method based on traits variance and Double Hierarchical Generalized Linear model (DHGLM) based on residual variance. Traditionally, birth weight uniformity was studied by analysis of its standard deviation or variance. DHGLM allows studying differences between animals by analyzing the residual variance of the trait and estimating its variance components in ASReml. The comparison with the conventional analysis using log-transformed variance of birth weight was possible, because both methods were on the same scale and models contained the same random effects. Also DHGLM allows for simultaneous analysis of the trait and the trait variation, therefore, it was possible to obtain genetic correlations between the level and the variance part of the model. The genetic correlation between additive genetic variance in two parts of the model was estimated on the level of 0.6. This correlation indicates that with increase of birth weight the variation of this trait is also increasing. In addition, the genetic coefficient of variation at residual standard deviation level ( $GCV_{SDe}$ ) was proposed as a measure expressing the potential response to selection. Estimated  $GCV_{SDe}$  was highly similar in both methods and showed that standard deviation of birth weight could be decreased by maximum of ~10% after one generation of selection. The conventional analysis and DHGLM produced highly comparable results (estimated breeding values, reliability of estimated breeding values (EBV) and accuracy of EBV from cross-validation). DHGLM could serve as an alternative to conventional analysis to study uniformity of traits.

In Chapter 5 the genetic background of residual variance in litter size is studied by use of DHGLM and GWAS. First, the EBV are obtained for residual variance of the total number born (TNB) using DHGLM in ASReml. Second, EBV are deregressed to

provide most optimal usage of the entire data. Third, the GWAS is performed on the deregressed EBV with a Bayesian Variable Selection model in Bayz. A relatively strict prior (0.001) was applied, meaning that 1 in 1,000 single nucleotide polymorphisms (SNPs) was in a distribution with large effects in each cycle. SNPs were considered significant if their Bayes Factor was above 30. Genetic coefficient of variation on standard deviation level for residual variance of TNB (varTNB) was estimated as 0.09, showing good opportunities for improvement of uniformity with selection. Genetic correlation between additive genetic effects of TNB and its variation was 0.5. This indicates that an increase in TNB can increase the variation of TNB. Ten SNPs were detected for TNB and nine SNPs for varTNB. Overall, the significant SNP's explained 0.83% of total genetic variance in TNB and 1.44% in varTNB. The most significant SNP explained 0.4% of genetic variance in TNB (chromosome 11) and 0.5% in varTNB (chromosome 7). Possible candidate genes for varTNB on chromosome 7 are: heat shock protein (*HSPCB*), vascular endothelial growth factor (*VEGFA*), and *CUL9* protein regulating p53 function. This is the first study reporting SNPs and candidate genes associated with varTNB in pigs.

Finally, in Chapter 6 the overall findings of this thesis are discussed in a broader perspective. First, the meaning of uniformity in reproduction and production traits is described in detail. Intensive selection for increased litter size brings several challenges, as the extreme litter size is exceeding the physiological capacity of the sow to provide for her litter pre- and post-farrowing. Increasing litter size affects also the birth weight of piglets, which is highly important trait for overall performance of the pig and the economic success of pig production.

Second, the results of the thesis are discussed in detail with the focus on which method provides best opportunities for selection. Despite evidence that the common litter effects have a large contribution to total variance, its actual estimate in production traits depends greatly on the proper fit of the genetic model. Thus, reducing the variation in production traits is very difficult to be achieved by explaining the origin of common litter effects. An alternative approach can be studying the residual variance of traits. In reproduction traits of sows (litter size and birth weight) with application of DHGLM it was showed that about 10% of improvement in trait's variation can be achieved after one generation of selection. The selection for the mean and the variance of traits should be performed simultaneously as the positive genetic correlation is present between them and also it should account for the survival of the piglets. The DHGLM applied to production traits can be very useful as it is can be used to obtain the breeding values for the variation of a trait with single observation. Possible improvement of uniformity in production traits such as growth rate can lead to reducing the



penalties for delivering carcasses outside the expected range. In addition, the biological mechanisms underlying the presence of quantitative trait loci (QTL) associated with variation (vQTL) is described, since an occurrence of vQTL in the population indicates the existence of unmodeled interaction associated with the locus.

Lastly, the discussion focuses on the opportunities to select for animals performing in a uniform manner in different production systems, parities, or climates. This is important because globalization of livestock breeding requires selection for genotypes that have the capacity to buffer various environmental factors. This part of discussion focuses on the macro-environmental sensitivity and joint analyses of macro- and micro-environmental sensitivity as well as application of genomic selection, which are topics highly relevant for breeding uniform and robust pigs.

## **Samenvatting**



## Samenvatting

Veefokkerij richt zich op de selectie van gewenste genotypes. De expressie van de genen wordt echter sterk beïnvloed door de omgeving waarin het dier geboren en gehouden wordt gedurende zijn reproductieve en productieve leven. De omgeving waarin het dier functioneert kan worden gekarakteriseerd door middel van een aantal factoren, bijv. het houderijsysteem, management, temperatuur of de kwaliteit van het voer. Deze factoren vormen het macro-milieu. Niet alle omgevingsfactoren zijn echter vooraf bepaald of meetbaar. In de literatuur worden deze onbekende factoren aangeduid als het micro-milieu. Aangezien de omgeving het succes van selectie beïnvloedt, wordt er in de fokkerij altijd rekening gehouden met de omgevingseffecten. In genetische (dier)modellen worden ze meegenomen als niet-genetische vaste of random effecten.

Het doel van dit proefschrift was om de niet-genetische random variatie in de reproductie- en productie-eigenschappen van varkens te bestuderen. In de varkensfokkerij is het voor veel eigenschappen van belang om niet alleen de reproductie- en productie-eigenschap zelf te verbeteren, maar ook te streven naar een uniforme productie. Het verkrijgen van uniforme varkens in verschillende productiestadia is een belangrijk doel in de varkensfokkerij. Genetische variantie van uniformiteit kan gebruikt worden om de varkensproductiviteit te verbeteren. In dit proefschrift is de variantie bestudeerd met behulp van verschillende methodes. Ten eerste door het effect van verschillende zeugkenmerken te onderzoeken die de achtergrond van de de toom en het permanente zeugeffect in de eigenschappen van vleesvarkens kunnen verklaren (Hoofdstuk 2 en 3). Ten tweede door de residuele variantie van reproductie-eigenschappen van zeugen te bestuderen (Hoofdstuk 4) en ten slotte door de genetica van de residuele variantie te onderzoeken door middel van een genoomwijde associatiestudie (GWAS). In hoofdstuk 6 worden de algemene bevindingen van dit proefschrift bediscussieerd. Hoofdstuk 2 richt zich op historische kenmerken van zeugen, dus kenmerken die het jonge leven van de zeug karakteriseren (toomgrootte bij geboorte, geboortjaar en -seizoen, bedrijf van geboorte, speenleeftijd, leeftijd waarop de zeug wordt overgebracht naar de proefboerderij en leeftijd van eerste inseminatie) en het effect van deze kenmerken op de productie-eigenschappen van de nakomelingen van deze zeugen, de vleesvarkens: voedselopname en groei. Ten eerste is getest of de zeugkenmerken de eigenschappen van vleesvarkens beïnvloedden. Ten tweede zijn significante zeugkenmerken ( $P < 0.1$ ) gemeenschappelijk in het diermodel meegenomen om hun invloed op de toom en permanente zeugeffecten te bestuderen. Geselecteerde zeugkenmerken beïnvloeden inderdaad de eigenschappen van vleesvarkens, maar de schattingen zijn klein en verklaren slechts een klein gedeelte van de verschillen in groei en voedselopname tussen vleesvarkens. De erfelijkheidsgraden van groei en voedselopname (alleen in fase twee van de vleesvarkenfase) namen af, na toevoeging van de zeugkenmerken aan het model. De zeugkenmerken verklaarden het permanente zeugeffect op voedselopname-gerelateerde eigenschappen ten dele en ze verklaarden de toom

niet.

In hoofdstuk 3 wordt de invloed van zeugkenmerken op de eigenschappen van vleesvarkens verder onderzocht. In dit geval zijn de zeugkenmerken van zeugen verzameld die in groepen gehuisvest waren gedurende de dracht om het effect op de prestaties van vleesvarkens te bestuderen. Zeugkenmerken zijn verzameld tijdens meerdere drachten en verdeeld in drie clusters die het volgende beschrijven: *i.* conditie-score van de zeug, d.w.z. gewicht, spekdikte, duur van de dracht; *ii.* voedselweigering van de zeug, d.w.z. het verschil tussen het aangeboden en opgegeten voer tijdens drie periodes van de dracht: 1-28, 25-50, 45-80 dagen; *iii.* zeuggroepskenmerken, d.w.z. aantal zeugen, gemiddelde pariteit binnen de groep. De onderzochte drachtkenmerken van zeugen verklaarden 1% tot 3% van de totale variantie in vleesvarkens. Bovendien verklaarde de toevoeging van zeugkenmerken aan het diermodel de fenotypische variantie ten gevolge van het permanente zeugeffect en een deel van de fenotypische variantie ten gevolge van de toom voor voedselopname, maar niet voor groei.

In hoofdstuk 4 worden methodes om variatie in eigenschappen te modelleren (toegepast op geboortegewicht van varkens) met elkaar vergeleken: de traditionele methode gebaseerd op variatie van de eigenschap en het Dubbel Hiërarchisch GLM (DHGLM) gebaseerd op residuele variantie. Traditioneel wordt uniformiteit van geboortegewicht bestudeerd door een analyse van de bijbehorende standaarddeviatie (SD) of van de variatie. DHGLM maakt het mogelijk de verschillen tussen dieren te bestuderen door de residuele variantie van de eigenschap te analyseren en de variantiecomponenten ervan in ASReml te schatten. Vergelijking met de conventionele analyse door middel van log-getransformeerde variantie in het geboortegewicht was mogelijk doordat beide methodes op dezelfde schaal waren en de modellen dezelfde random effecten bevatten. Ook maakt DHGLM de gelijktijdige analyse van het niveau van de eigenschap en de variatie erin mogelijk. Daardoor was het mogelijk genetische correlaties te verkrijgen tussen het niveau en de variatie. De genetische correlatie tussen het niveau en de variatie was 0.6. Deze correlatie wijst erop dat met een toename van het geboortegewicht de variatie binnen deze eigenschap ook toeneemt. Bovendien is de genetische coëfficiënt van de variatie op het residuele-standaarddeviatie (GCV SDe) voorgesteld als maat voor de potentiële respons op selectie. De geschatte GCV SDe was in hoge mate vergelijkbaar in beide methodes en toonde dat de SD van het geboortegewicht verminderd kon worden met maximaal ~10% na één selectieronde. De conventionele analyse en DHGLM gaven sterk vergelijkbare resultaten (geschatte fokwaarden, betrouwbaarheid van de fokwaarde en nauwkeurigheid van fokwaarde in een cross-validatie). DHGLM zou kunnen dienen als alternatief voor de conventionele analyse om de uniformiteit van eigenschappen te bestuderen.

In hoofdstuk 5 is de genetische achtergrond van de residuele variatie in toomgrootte bestudeerd door middel van DHGLM en GWAS. Ten eerste zijn de geschatte fokwaarden (EBV) verkregen voor de residuele variatie van de toomgrootte (TNB) te berekenen met DHGLM in ASReml. Ten tweede is deregressie

toegepast op de EBV om optimaal gebruik te maken van de gehele dataset. Ten derde is GWAS toegepast op de deregressie-EBV met een Bayesiaans Variabele-selectie model in Bayz. Een relatief strikte a priori-kans (0.001) is toegepast, wat betekent dat 1 op de 1000 SNPs in een verdeling met grote effecten terecht komt per cyclus. SNPs werden als significant aangemerkt als hun Bayes Factor hoger was dan 30 (een maat voor significantie). De genetische variatiecoëfficiënt op de standaarddeviatie voor toomgrootte is geschat op 0.09, wat goede mogelijkheden biedt om uniformiteit te verbeteren. De genetische correlatie tussen additieve genetische effecten van het toomgrootte en de variatie daarin was 0.5. Dit geeft aan dat een toename van het toomgrootte, ook de variatie van toomgrootte kan doen toenemen. Tien SNPs zijn gedetecteerd voor toomgrootte en negen SNPs voor de variatie in toomgrootte. Over het geheel genomen verklaarden de significante SNPs 0.83% van de totale genetische variantie in toomgrootte en 1.44% in de variatie in toomgrootte. De meest significante SNP verklaarde 0.4% van de genetische variantie van toomgrootte (SSC 11) en 0.5% in variatie in toomgrootte (SSC 7). Mogelijke kandidaatgenen voor variatie in toomgrootte op SSC 7 zijn: heat shock protein (HSPCB), vascular endothelial growth factor (VEGFA) en CUL9 proteïne dat het functioneren van p53 reguleert. Dit is de eerste studie die SNPs en kandidaatgenen beschrijft die geassocieerd zijn met variatie in toomgrootte in varkens.

Ten slotte worden in hoofdstuk 6 de algehele bevindingen van dit proefschrift in een breder perspectief bediscussieerd. Ten eerste wordt de betekenis van uniformiteit in reproductie- en productie-eigenschappen gedetailleerd beschreven. De aandacht is vooral gericht op de uitdagingen van intensieve selectie wat betreft toomgrootte. De fysiologische capaciteit van de zeug om haar toom zelfstandig groot te brengen zowel voor als na het werpen, is een uitdaging. Het vergroten van de toom beïnvloedt ook het geboortegewicht van biggen, wat een zeer belangrijke eigenschap is voor het algehele presteren van de varkens en het economische succes van de varkensproductie.

Ten tweede worden de resultaten van dit proefschrift gedetailleerd bediscussieerd met betrekking tot de methode welke de beste mogelijkheden voor selectie oplevert. Ondanks aanwijzingen dat de toom een grote bijdrage levert aan de totale variantie hangt de werkelijke schatting in productie-eigenschappen in grote mate af van het juiste genetische model. Daardoor is het heel moeilijk een reductie in variatie van de productie-eigenschappen te bereiken door effecten die de toom verklaren aan het model toe te voegen. Een alternatieve benadering kan het bestuderen van de residuele variantie van eigenschappen zijn. In reproductie-eigenschappen van zeugen (toomgrootte en geboortegewicht) is met toepassing van DHGLM aangetoond dat een verbetering van ongeveer 10% in de variatie in eigenschappen bereikt kan worden na één selectieronde. De selectie voor het niveau en de variatie van eigenschappen dient gelijktijdig uitgevoerd te worden, aangezien een positieve genetische correlatie tussen hen aanwezig is en ook verantwoordelijk zou moeten zijn voor het overleven van biggen. DHGLM,

toegepast op de productie-eigenschappen, kan zeer nuttig zijn, aangezien het gebruikt kan worden om fokwaarden voor variatie van een eigenschap met één enkele observatie te verkrijgen. Een mogelijke verbetering van de uniformiteit in productie-eigenschappen zoals groei kan leiden tot lagere verliezen door het leveren van karkassen buiten de gewichtsgrenzen. Bovendien worden de biologische mechanismen beschreven die ten grondslag liggen aan QTLs die 'geassocieerd zijn met variatie (vQTLs). Het aanwezig zijn van een vQTL in de populatie wijst erop dat er een ongemodelleerde interactie bestaat die geassocieerd is met de locus.

Ten slotte richt de discussie zich op de mogelijkheden om dieren te selecteren die op een uniforme manier presteren in verschillende productiesystemen, pariteiten of klimaten. Dit is belangrijk omdat globalisatie van de veefokkerij selectie vereist op genotypes die bestand zijn tegen verschillende omgevingsfactoren. Dit deel van de discussie richt zich op de gevoeligheid voor het macro-milieu en de gezamenlijke analyse van de gevoeligheid voor het macro- en micro-milieu. Daarnaast richt dit laatste deel van de discussie zich op de toepassing van genomische selectie, welke, naast milieugevoeligheid, een onderwerp is met een grote relevantie voor het fokken van uniforme en robuuste varkens.

## **References**





**A**

- Ai, H., J. Ren, Z. Zhang, J. Ma, Y. Guo, B. Yang, and L. Huang. 2012. Detection of quantitative trait loci for growth-and fatness-related traits in a large-scale White Duroc×Erhualian intercross pig population. *Animal genetics* 43:383-391.
- Andersson, H. K., A. Hullberg, L. Malmgren, K. Lundström, L. Rydhmer, and J. Squires. 1999. Sexual maturity in entire male pigs:Environmental effects, relations to skatole level and female puberty. *Acta Agric. Scand., Sect. A* 49:103-112.
- Anil, L., S. S. Anil, J. Deen, S. K. Baidoo, and R. D. Walker. 2006. Effect of group size and structure on the welfare and performance of pregnant sows in pens with electronic sow feeders. *Can. J. Vet. Res.* 70:128–136.
- Arango, J., I. Misztal, S. Tsuruta, M. Culbertson, J. Holl, and W. Herring. 2006. Genetic study of individual preweaning mortality and birth weight in large white piglets using threshold linear models. *Livest. Prod. Sci.* 101:208–218.
- Arey, D., and S. Edwards. 1998. Factors influencing aggression between sows after mixing and the consequences for welfare and production. *Livest. Prod. Sci.* 56:61–70.
- Aulchenko, Y. S., S. Ripke, A. Isaacs, and C. M. Van Duijn. 2007. GenABEL: an R library for genome-wide association analysis. *Bioinformatics* 23(10):1294-1296.

**B**

- Baxter, E. M., K. M. D. Rutherford, R. B. D'Eath, G. Arnott, S. P. Turner, P. Sandøe, V. A. Moustsen, F. Thorup, S.A. Edwards, and A. B. Lawrence. 2013. The welfare implications of large litter size in the domestic pig II: Management factors. *Animal Welfare* 22:219-238.
- Beaulieu, A., J. Aalhus, N. Williams, and J. Patience. 2010. Impact of piglet birth weight, birth order, and litter size on subsequent growth performance, carcass quality, muscle composition, and eating quality of pork. *J. Anim. Sci.* 88(8):2767-2778.
- Bee, G. 2004. Effect of early gestation feeding, birth weight, and gender of progeny on muscle fiber characteristics of pigs at slaughter. *J. Anim. Sci.* 82:826–836.
- Bergsma, R., E. Kanis, E. Knol, and P. Bijma. 2008. The contribution of social effects to heritable variation in finishing traits of domestic pigs (*Sus scrofa*). *Genetics* 178:1559–1570.

## References

---

- Bidanel, J. P., J. Gruand, and C. Legault. 1996. Genetic variability of age and weight at puberty, ovulation rate and embryo survival in gilts and relations with production traits. *Genet. Sel. Evol.* 28:103–115.
- Bidanel, J. P., D. Milan, N. Iannuccelli, Y. Amigues, M. Y. Boscher, F. Bourgeois, J. C. Caritez, J. Gruand, P. L. Roy, and H. Lagant. 2001. Detection of quantitative trait loci for growth and fatness in pigs. *Genetics Selection Evolution* 33:289-310.
- Bokma, S. 1990. Housing and management of dry sows in groups in practice:Partly slatted systems. Electronic identification in pig production. Monograph Series. Vol. 10. Royal Agricultural Society, Kenilworth, Warwickshire, UK. p. 37–46.
- Bolhuis, J. E., W. G. Schouten, J. W. Schrama, and V. M. Wiegant. 2006. Effects of rearing and housing environment on behaviour and performance of pigs with different coping characteristics. *App. Anim. Behav. Sci.* 101(1):68-85.
- Boyle, L., F. Leonard, P. Lynch, and P. Brophy. 2002. Effect of gestation housing on behaviour and skin lesions of sows in farrowing crates. *Appl. Anim. Behav. Sci.* 76:119–134.
- Brouns, F., and S. Edwards. 1994. Social rank and feeding behaviour of group-housed sows fed competitively or ad libitum. *Appl. Anim. Behav. Sci.* 39:225–235.

## C

- Calus, M., and R. Veerkamp. 2003. Estimation of environmental sensitivity of genetic merit for milk production traits using a random regression model. *J. Dairy Sci.* 86:3756-3764.
- Canario, L., H. Lundgren, M. Haandlykken, and L. Rydhmer. 2010. Genetics of growth in piglets and the association with homogeneity of body weight within litters. *J. Anim. Sci.* 88:1240–1247.
- Cao, Y., T. J. Maxwell, and P. Wei. 2014. A Family-Based Joint Test for Mean and Variance Heterogeneity for Quantitative Traits. *Ann. Hum. Genet.* 79(1):46-56.
- Cassady, J. P., R. K. Johnson, D. Pomp, G. A. Rohrer, L.D. Van Vleck, E. K. Spiegel, and K. M. Gilson. 2001. Identification of quantitative trait loci affecting reproduction in pigs. *J. Anim. Sci.* 79:623–633
- Chen, P., T. Baas, J. Mabry, J. Dekkers, and K. Koehler. 2002. Genetic parameters and trends for lean growth rate and its components in US Yorkshire, Duroc, Hampshire, and Landrace pigs. *J. Anim. Sci.* 80:2062–2070.

- Cimpean, A. M., M. Raica, S. Encica, R. Cornea, and V. Bocan. 2008. Immunohistochemical expression of vascular endothelial growth factor A (VEGF), and its receptors (VEGFR1, 2) in normal and pathologic conditions of the human thymus. *Annals of Anatomy-Anatomischer Anzeiger* 190:238-245.
- Clay, J., W. Vinson, and J. White. 1979. Heterogeneity of daughter variances of sires for milk yield. *J. Dairy Sci.* 62(6):985-989.
- Costello, P., R. Cripps, N. Bearpark, A. Rowleron, L. Hollis, H. Patel, A. Aihie Sayer, M. Hanson, S. Ozanne and L. Green. 2008. Effect of maternal diet and body condition on glucose metabolism and skeletal muscle structure in mature adult sheep offspring. *Proc. Physiol. Soc.* 11:C32.
- Crump, R., C. Haley, R. Thompson, and J. Mercer. 1997. Individual animal model estimates of genetic parameters for performance test traits of male and female Landrace pigs tested in a commercial nucleus herd. *Anim. Sci.* 65:275-283.

## D

- Daetwyler, H. D., M. P. Calus, R. Pong-Wong, G. de los Campos, and J. M. Hickey. 2013. Genomic prediction in animals and plants:simulation of data, validation, reporting, and benchmarking. *Genetics* 193:347-365.
- Damgaard, L., L. Rydhmer, P. Lovendahl, and K. Grandinson. 2003. Genetic parameters for within-litter variation in piglet birth weight and change in within-litter variation during suckling. *J. Anim. Sci.* 81:604-610.
- de Jong, E., R. Appeltant, A. Cools, J. Beek, F. Boyen, K. Chiers, and D. Maes. 2014. Slaughterhouse examination of culled sows in commercial pig herds. *Livest. Sci.* 167:362-369.
- Debat, V., C. C. Milton, S. Rutherford, C. P. Klingenberg, and A. A. Hoffmann. 2006. Hsp90 and the quantitative variation of wing shape in *Drosophila melanogaster*. *Evolution* 60:2529-2538.
- Dekkers, J. C., P. K. Mathur, and E. F. Knol. 2011. Genetic improvement of the pig. The genetics of the pig:390-425.
- Diniz, D. B., M. S. Lopes, M. L. W. J. Broekhuijse, P. S. Lopes, B. Harlizius, S. E. F. Guimarães, N. Duijvesteijn, E. F. Knol, and F. F. Silva. 2014. A genome-wide association study reveals a novel candidate gene for sperm motility in pigs. *Anim. Reprod. Sci.* 151:201-207.

## References

---

- Duijvesteijn, N., E. Knol, and P. Bijma. 2012. Direct and associative effects for androstene and genetic correlations with backfat and growth in entire male pigs. *J. Anim. Sci.* 90:2465-2475.
- Duijvesteijn, N., J. M. Veltmaat, E. F. Knol, and B. Harlizius. 2014. High-resolution association mapping of number of teats in pigs reveals regions controlling vertebral development. *BMC genomics* 15:542.
- Dwyer, C. M., N. C. Stickland, and J. M. Fletcher. 1994. The influence of maternal nutrition on muscle fiber number development in the porcine fetus and on subsequent postnatal growth. *J. Anim. Sci.* 72:911–917.

## E

- English, P., and W. Smith. 1975. Some causes of death in neonatal piglets. *Vet. Annu.* 15:95–104.

## F

- Fahey, A., J. Brameld, T. Parr, and P. Buttery. 2005. The effect of maternal undernutrition before muscle differentiation on the muscle fiber development of the newborn lamb. *J. Anim. Sci.* 83:2564–2571.
- Falconer, D. S., and T. F. C. Mackay. 1996. *Introduction to quantitative genetics*. 4th edition Pearson Education Limited, Essex, United Kingdom.
- Felleki, M., and H. Chalkias. 2010. A Double Hierarchical Generalized Linear Model For Teat Number In Pigs. *Proceedings of the 9th World Congress on Genetics Applied to Livestock Production, Leipzig, Germany, August 1-6, 2010. Communication:0178 PP3-56.*
- Felleki, M., D. Lee, Y. Lee, A. R. Gilmour, and L. Rönnegård. 2012. Estimation of breeding values for mean and dispersion, their variance and correlation using double hierarchical generalized linear models. *Genet. Res.* 94:307–317.
- Ferraz, J. B., and R. K. Johnson. 1993. Animal model estimation of genetic parameters and response to selection for litter size and weight, growth, and backfat in closed seedstock populations of Large White and Landrace swine. *J. Anim. Sci.* 71:850–858.
- Fix, J., J. Cassady, W. Herring, J. Holl, M. Culbertson, and M. See. 2010. Effect of piglet birth weight on body weight, growth, backfat, and longissimus muscle area of commercial market swine. *Livest. Sci.* 127:51–59.

- Forni, S., I. Aguilar, and I. Misztal. 2011. Different genomic relationship matrices for single-step analysis using phenotypic, pedigree and genomic information. *Genet. Sel. Evol.* 43:1.
- Foulley, J. L., D. Gianola, M. San Cristobal, and S. Im. 1990. A method for assessing extent and sources of heterogeneity of residual variances in mixed linear models. *J. Dairy Sci.* 73:1612–1624.
- Foxcroft, G. R. 2007. Pre-natal programming of variation in post-natal performance—how and when. *Adv. Pork Prod* 18:167-189.
- Foxcroft, G. R. 2012. Reproduction in farm animals in an era of rapid genetic change: Will genetic change outpace our knowledge of physiology? *Reprod. Domest. Anim.* 47(Suppl. 4):313–319.
- Foxcroft, G. R., W. T. Dixon, S. Novak, C. T. Putman, S. C. Town, and M. D. A. Vinsky. 2006. The biological basis for prenatal programming of postnatal performance in pigs. *J. Anim. Sci.* 84:105–112.
- Foxcroft, G., W. T. Dixon, M. K. Dyck, S. Novak, J. C. S. Harding, and F. C. R. L. Almeida. 2009. Prenatal programming of postnatal development in the pig. In: *Control of Reproduction VIII: Proceedings of the Eighth International Conference on Pig Reproduction*. p 213-231.
- Fraser, H. B., and E. E. Schadt. 2010. The quantitative genetics of phenotypic robustness. *PloS one* 5(1):e8635.
- Fujisawa, K., H. Asahara, K. Okamoto, H. Aono, T. Hasunuma, T. Kobata, Y. Iwakura, S. Yonehara, T. Sumida, and K. Nishioka. 1996. Therapeutic effect of the anti-Fas antibody on arthritis in HTLV-1 tax transgenic mice. *Journal of Clinical Investigation* 98:271.

## G

- Garreau, H., G. Bolet, C. Larzul, C. Robert-Granie, G. Saleil, M. SanCristobal, and L. Bodin. 2008. Results of four generations of a canalising selection for rabbit birth weight. *Livest. Sci.* 119:55–62.
- Garrick, D. J., J. F. Taylor, and R. L. Fernando. 2009. Deregressing estimated breeding values and weighting information for genomic regression analyses. *Genet Sel Evol* 41(55):44.
- Gelman, A., and D. B. Rubin. 1992. Inference from iterative simulation using multiple sequences. *Statistical science*:457-472.
- George, E. I., and R. E. McCulloch. 1993. Variable selection via Gibbs sampling. *Journal of the American Statistical Association* 88:881-889.

## References

---

- Gilmour, A., B. Gogel, B. Cullis, and R. Thompson. 2006. ASReml user guide release 2.0. VSN Int. Ltd., Hemel Hempstead, UK.
- Goddard, M. 2009. Genomic selection: prediction of accuracy and maximisation of long term response. *Genetica* 136:245-257.
- Gondret, F., L. Lefaucheur, I. Louveau, B. Lebret, X. Pichodo, and Y. Le Cozler. 2005. Influence of piglet birth weight on postnatal growth performance, tissue lipogenic capacity and muscle histological traits at market weight. *Livest. Prod. Sci.* 93:137–146.
- Grandinson, K., L. Rydhmer, E. Strandberg, and F. Solanes. 2005. Genetic analysis of body condition in the sow during lactation, and its relation to piglet survival and growth. *Anim. Sci.* 80:33–40.
- Guo, Y. M., G. Lee, A. Archibald, and C. Haley. 2008. Quantitative trait loci for production traits in pigs: a combined analysis of two Meishan× Large White populations. *Animal genetics* 39:486-495.
- Gutiérrez, J. P., B. Nieto, P. Piqueras, N. Ibáñez, and C. Salgado. 2006. Genetic parameters for canalisation analysis of litter size and litter weight traits at birth in mice. *Genet. Sel. Evol.* 38:445–462.

## H

- Hanenberg, E., E. Knol, and J. Merks. 2001. Estimates of genetic parameters for reproduction traits at different parities in Dutch Landrace pigs. *Livest. Prod. Sci.* 69:179-186.
- Hermesch, S., B. Luxford, and H. Graser. 2001. Genetic parameters for piglet mortality, within litter variation of birth weight, litter size and litter birth weight. In: *Proc. Assoc. Adv. Anim. Breed. Genet.*, Queenstown, NZ. p. 211–214.
- Hernandez, S., H. Finlayson, C. Ashworth, C. Haley, and A. Archibald. 2014. A genome-wide linkage analysis for reproductive traits in F2 Large White× Meishan cross gilts. *Animal genetics* 45:191-197.
- Heuven, H. C., and L. L. Janss. 2010. Bayesian multi-QTL mapping for growth curve parameters. In: *BMC proceedings*. p S12.
- Heyer, A., H. Andersson, J. Lindberg, and K. Lundström. 2004. Effect of extra maternal feed supply in early gestation on sow and piglet performance and production and meat quality of growing/finishing pigs. *Acta Agric. Scand., Sect. A* 54:44–55.
- Hill, W. G., and H. A. Mulder. 2010. Genetic analysis of environmental variation. *Genet. Res. (Camb.)* 92:381–395.

- Högberg, A., and L. Rydhmer. 2000. A genetic study of piglet growth and survival. *Acta Agric. Scand., Sect. A* 50:300–303.
- Hoving, L., N. Soede, E. Graat, H. Feitsma, and B. Kemp. 2010. Effect of live weight development and reproduction in first parity on reproductive performance of second parity sows. *Anim. Reprod. Sci.* 122:82–89.
- Huang, H.-C., W-C Lee, J-H Lin, H-W Huang, S-C Jian, S. J. T. Mao, P-C Yang, T-Y Huang, and Y-C Liu. 1999. Molecular cloning and characterization of porcine cDNA encoding a 90-kDa heat shock protein and its expression following hyperthermia. *Gene* 226:307–315.

## I

- Ibáñez-Escriche, N., L. Varona, D. Sorensen, and J. L. Noguera. 2008. Genetic parameters related to environmental variability of weight traits in a selection experiment for weight gain in mice; signs of correlated canalised response. *Genetics Selection Evolution* 40:279–294.
- Ibáñez-Escriche, N., L. Varona, D. Sorensen, and J. Noguera. 2008. A study of heterogeneity of environmental variance for slaughter weight in pigs. *Animal* 2(1).

## J

- Jang, Y., Y. Ma, and M. Lindemann. 2014. Intrauterine position affects fetal weight and crown-rump length throughout gestation. *J. Anim. Sci.* 92(10):4400–4406.
- Jiao, S., C. Maltecca, K. Gray, and J. Cassady. 2014. Feed intake, average daily gain, feed efficiency, and real-time ultrasound traits in Duroc pigs: II. Genomewide association. *J. Anim. Sci.* 92:2846–2860.
- Jinks, J., and H. Pooni. 1988. The genetic basis of environmental sensitivity. In *Proceedings of the Second International Conference on Quantitative Genetics: 31 May - 5 June 1987; Raleigh*. Edited by Weir BS, Eisen EJ, Goodman MM, Namkoong G. North Carolina State University; 1988:505–522.
- Johnson, R. K., M. K. Nielsen, and D. S. Casey. 1999. Responses in ovulation rate, embryonal survival, and litter traits in swine to 14 generations of selection to increase litter size. *J. Anim. Sci.* 77:541–557.
- Johnson, Z. B., J. J. Chewning, and R. A. Nugent 3rd. 2002. Maternal effects on traits measured during postweaning performance test of swine from four breeds. *J. Anim. Sci.* 80:1470–1477.



### K

- Kanis, E., M. Van Pelt, P. Bonekamp, and E. Knol. 2006. Is within-family variation in carcass weight of pigs heritable? In: Proceedings of the 8th World Congress on Genetics Applied to Livestock Production, Belo Horizonte, Minas Gerais, Brazil, 13-18 August, 2006. p 06-23.
- Kapell, D. N. R. G., C. J. Ashworth, P. W. Knap, and R. Roehe. 2011. Genetic parameters for piglet survival, litter size and birth weight or its variation within litter in sire and dam lines using Bayesian analysis. *Livest. Sci.* 115:215–224.
- Kass, R. E., and A. E. Raftery. 1995. Bayes factors. *Journal of the american statistical association* 90:773-795.
- Kaufmann, D., A. Hofer, J. Bidanel, and N. Künzi. 2000. Genetic parameters for individual birth and weaning weight and for litter size of Large White pigs. *J. Anim. Breed. Genet.* 117:121–128.
- Kind, K. L., C. T. Roberts, A. I. Sohlstrom, A. Katsman, P. M. Clifton, J. S. Robinson, and J. A. Owens. 2005. Chronic maternal feed restriction impairs growth but increases adiposity of the fetal guinea pig. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* 288:119–126.
- Kirkwood, R., and A. Zanella. 2005. Influence of gestation housing on sow welfare and productivity. National Pork Board Final Report. National Pork Board (NPB) is a quasigovernmental body of the United States government located in Des Moines, Iowa. NPB is the publisher of the report.
- Knap, P., and G. Su. 2008. Genotype by environment interaction for litter size in pigs as quantified by reaction norms analysis.
- Knol, E. F. 2001. Genetic Aspects of Piglet Survival. PhD Thesis. Wageningen University, Wageningen.
- Knol, E. F., P. Mathur, and G. Foxcroft. 2010. Birth phenotypes in commercial sows: Origins and implications for future genetic selection and management. . In: *Adv. Pork Prod.* 21:1-10.
- Koketsu, Y., and G. Dial. 1997. Factors influencing the postweaning reproductive performance of sows on commercial farms. *Theriogenology* 47:1445–1461.
- Kongsted, A. G. 2004. Stress and fear as possible mediators of reproduction problems in group housed sows: A review. *Acta Agric. Scand., Sect. A* 54:58–66.
- Kruse, S., I. Traulsen, and J. Krieter. 2011. Analysis of water, feed intake and performance of lactating sows. *Livest. Sci.* 135(2):177-183.

- Kuhlers, D., K. Nadarajah, S. Jungst, B. Anderson, and B. Gamble. 2003. Genetic selection for lean feed conversion in a closed line of duroc pigs. *Livest. Prod. Sci.* 84:75-82.

## L

- Lawlor, P. G., and P. B. Lynch. 2005. Effect of sow feed intake during gestation on the growth performance of progeny to slaughter. *Archiv Tierz. Dummerstorf* 48:48–55.
- Lee, Y., and J. Nelder. 2006. Double hierarchical generalized linear models. *J. Roy. Stat. Soc. C-App.* 55:139-185.
- Lund, A. A., D. M. Rhoads, A. L. Lund, R. L. Cerny, and T. E. Elthon. 2001. In vivo modifications of the maize mitochondrial small heat stress protein, HSP22. *Journal of Biological Chemistry* 276:29924-29929.
- Lynch, M., and B. Walsh. 1998. *Genetics and analysis of quantitative traits*. 1st edn. Sinauer, Sunderland, MA.

## M

- Mackay, T. F., and R. F. Lyman. 2005. *Drosophila* bristles and the nature of quantitative genetic variation. *Philos. Trans. of the R. Soc. B.* 360(1459):1513-1527.
- McNamara, L., L. Giblin, T. Markham, N. Stickland, D. Berry, J. O'Reilly, P. Lynch, J. Kerry, and P. Lawlor. 2011. Nutritional intervention during gestation alters growth, body composition and gene expression patterns in skeletal muscle of pig offspring. *Animal* 5:1195–1206.
- Merks, J., P. Mathur, and E. Knol. 2012. New phenotypes for new breeding goals in pigs. *animal* 6(4):535-543.
- Milligan, B. N., D. Fraser, and D. L. Kramer. 2001. Birth weight variation in the domestic pig: Effects on offspring survival, weight gain and suckling behaviour. *Appl. Anim. Behav. Sci.* 73:179–191.
- Milligan, B. N., D. Fraser, and D. L. Kramer. 2002. Within-litter birth weight variation in the domestic pig and its relation to pre-weaning survival, weight gain, and variation in weaning weights. *Livest. Prod. Sci.* 76:181–191.
- Mrode, R., and B. Kennedy. 1993. Genetic variation in measures of food efficiency in pigs and their genetic relationships with growth rate and backfat. *Anim. Prod.* 56:225-232.

## References

---

- Muir, W. 2007. Comparison of genomic and traditional BLUP-estimated breeding value accuracy and selection response under alternative trait and genomic parameters. *J. Anim. Breed. Genet.* 124(6):342-355.
- Mulder, H. A., L. Rönnegård, W. F. Fikse, R. F. Veerkamp, and E. Strandberg. 2013b. Estimation of genetic variance for macro- and micro-environmental sensitivity using double hierarchical generalized linear models. *Genet. Sel. Evol.* 45:23.
- Mulder, H. A., P. Bijma, and W. G. Hill. 2007. Prediction of breeding values and selection responses with genetic heterogeneity of environmental variance. *Genetics* 175:1895–1910.
- Mulder, H. A., P. Bijma, and W. G. Hill. 2008. Selection for uniformity in livestock by exploiting genetic heterogeneity of residual variance. *Genet. Sel. Evol.* 40:37–60.
- Mulder, H. A., R. Crump, M. P. L. Calus, and R. F. Veerkamp. 2013a. Unraveling the genetic architecture of environmental variance of somatic cell score using high-density single nucleotide polymorphism and cow data from experimental farms. *J. Dairy Sci.* 96:7306–7317.
- Mulder, H. A., W. G. Hill, A. Vereijken, and R. F. Veerkamp. 2009. Estimation of genetic variation in residual variance in female and male broiler chickens. *Animal* 3:1673-1680.
- Mulder, H. A., W. G. Hill, and E. F. Knol. 2015. Heritable Environmental Variance Causes Non-Linear Relationships Between Traits: Application to Birth Weight and Stillbirth of Pigs. *Genetics*:10.1534/genetics.114.173070.
- Musser, R., D. Davis, M. Tokach, J. Nelssen, S. Dritz, and R. Goodband. 2006. Effects of high feed intake during early gestation on sow performance and offspring growth and carcass characteristics. *Anim. Feed Sci. Technol.* 127:187–199.
- Mwanza, A., P. Englund, H. Kindahl, N. Lundeheim, and S. Einarsson. 2000. Effects of postovulatory food deprivation on the hormonal profiles, activity of the oviduct and ova transport in sows. *Anim. Reprod. Sci.* 59:185–199.

## N

- Nelson, R. M., M. E. Pettersson, X. Li, and Ö. Carlborg. 2013. Variance Heterogeneity in *Saccharomyces cerevisiae* Expression Data:Trans-Regulation and Epistasis. *PloS one* 8 (11):e79507.
- Neugebauer, N., H. Luther, and N. Reinsch. 2010. Parent-of-origin effects cause genetic variation in pig performance traits. *Animal* 4:672–681.

- Nielsen, B., G. Su, M. S. Lund, and P. Madsen. 2013. Selection for increased number of piglets at d 5 after farrowing has increased litter size and reduced piglet mortality. *J. Anim. Sci.* 91(6):2575-2582.
- Nikolaev, A. Y., M. Li, N. Puskas, J. Qin, and W. Gu. 2003. Parc: a cytoplasmic anchor for p53. *Cell* 112:29-40.
- Nissen, P. M., V. O. Danielsen, P. F. Jorgensen, and N. Oksbjerg. 2003. Increased maternal nutrition of sows has no beneficial effects on muscle fiber number or postnatal growth and has no impact on the meat quality of the offspring. *J. Anim. Sci.* 81:3018–3027.

## O

- Omtvedt, I., C. Stanislaw, and J. Whatley. 1965. Relationship of gestation length, age and weight at breeding, and gestation gain to sow productivity at farrowing. *J. Anim. Sci.* 24:531–535.
- Onteru, S. B. Fan, M. T. Nikkilä, D. J. Garrick, K.J. Stalder, and M. F. Rothschild. 2011. Whole-genome association analyses for lifetime reproductive traits in the pig. *J. Anim. Sci.* 89(4):988-995.
- Oostindjer, M., H. van den Brand, B. Kemp, and J. E. Bolhuis. 2011. Effects of environmental enrichment and loose housing of lactating sows on piglet behaviour before and after weaning. *App. Anim. Behav. Sci.* 134(1):31-41.
- Ordas, B., R. A. Malvar, and W. G. Hill. 2008. Genetic variation and quantitative trait loci associated with developmental stability and the environmental correlation between traits in maize. *Genetics research* 90(5):385-395.

## P

- Pardo, C., J. Bérard, M. Kreuzer, and G. Bee. 2013. Intrauterine crowding impairs formation and growth of secondary myofibers in pigs. *animal* 7(3):430-438.
- Paré, G., N. R. Cook, P. M. Ridker, and D. I. Chasman. 2010. On the use of variance per genotype as a tool to identify quantitative trait interaction effects:a report from the Women's Genome Health Study. *PLoS genetics* 6(6):e1000981.
- Perry, G. M., K. W. Nehrke, D. A. Bushinsky, R. Reid, K. L. Lewandowski, P. Hueber, and S. J. Scheinman. 2012. Sex modifies genetic effects on residual variance in urinary calcium excretion in rat (*Rattus norvegicus*). *Genetics* 191(3):1003-1013.

## References

---

- Plummer, M., N. Best, K. Cowles, and K. Vines. 2006. CODA: Convergence diagnosis and output analysis for MCMC. *R news* 6:7-11.
- Queitsch, C., T. A. Sangster, and S. Lindquist. 2002. Hsp90 as a capacitor of phenotypic variation. *Nature* 417:618-624.

## R

- Ramos, A. M., R. P. M. A. Crooijmans, A. N. Affara, A. J. Amaral, A. L. Archibald, J. E. Beever, C. Bendixen, C. Churcher, R. Clark, and P. Dehais. 2009. Design of a high density SNP genotyping assay in the pig using SNPs identified and characterized by next generation sequencing technology. *PloS one* 4:e6524.
- Rashidi, H., H. Mulder, P. Mathur, J. van Arendonk, and E. Knol. 2014. Variation among sows in response to porcine reproductive and respiratory syndrome. *J. Anim. Sci.* 92:95-105.
- Ravelli, A. C. J., J. H. P. van der Meulen, C. Osmond, D. J. P. Barker, and O. P. Bleker. 1999. Obesity at the age of 50 y in men and women exposed to famine prenatally. *Am. J. Clin. Nutr.* 70:811-816.
- Razdan, P., P. Tummaruk, H. Kindahl, H. Rodriguez-Martinez, F. Hulten, and S. Einarsson. 2004a. Hormonal profiles and embryo survival of sows subjected to induced stress during days 13 and 14 of pregnancy. *Anim. Reprod. Sci.* 81:295-312.
- Razdan, P., P. Tummaruk, H. Kindahl, H. Rodriguez-Martinez, F. Hultén, and S. Einarsson. 2004b. The impact of induced stress during days 13 and 14 of pregnancy on the composition of allantoic fluid and conceptus development in sows. *Theriogenology* 61:757-767.
- Rehfeldt, C., A. Tuchscherer, M. Hartung, and G. Kuhn. 2008. A second look at the influence of birth weight on carcass and meat quality in pigs. *Meat Sci.* 78:170-175.
- Rehfeldt, C., and G. Kuhn. 2006. Consequences of birth weight for postnatal growth performance and carcass quality in pigs as related to myogenesis. *J. Anim. Sci.* 84:113-123.
- Roberts, J., and J. Deen. 1995. Controlling variability of weights in growing pigs. *Comp. Cond. Educ. Pract. Vet.* 17:1308-1311.
- Roehe, R. 1999. Genetic determination of individual birth weight and its association with sow productivity traits using Bayesian analyses. *J. Anim. Sci.* 77:330-343.

- Roehe, R. 1999. Genetic determination of individual birth weight and its association with sow productivity traits using Bayesian analyses. *J. Anim. Sci.* 77:330-343.
- Roehe, R., and B. Kennedy. 1995. Estimation of genetic parameters for litter size in Canadian Yorkshire and Landrace swine with each parity of farrowing treated as a different trait. *J. Anim. Sci.* 73(10):2959-2970.
- Rönnegård, L., and W. Valdar. 2011. Detecting major genetic loci controlling phenotypic variability in experimental crosses. *Genetics* 188(2):435-447.
- Rönnegård, L., and W. Valdar. 2012. Recent developments in statistical methods for detecting genetic loci affecting phenotypic variability. *BMC genetics* 13(1):63.
- Rönnegård, L., M. Felleki, F. Fikse, H. A. Mulder, and E. Strandberg. 2010. Genetic heterogeneity of residual variance estimation of variance components using double hierarchical generalized linear models. *Genet. Sel. Evol.* 42:1-10.
- Rönnegård, L., M. Felleki, W. Fikse, H. Mulder, and E. Strandberg. 2013. Variance component and breeding value estimation for genetic heterogeneity of residual variance in Swedish Holstein dairy cattle. *J. Dairy Sci.* 96:2627-2636.
- Rowe, S. J., I. M. S. White, S. Avendano, W. G. Hill. 2006. Genetic heterogeneity of residual variance in broiler chickens. *Genet. Sel. Evol* 38:617-635.
- Rutherford, S., Y. Hirate, and B. J. Swalla. 2007. The Hsp90 capacitor, developmental remodeling, and evolution: the robustness of gene networks and the curious evolvability of metamorphosis. *Critical reviews in biochemistry and molecular biology* 42:355-372.
- Rydhmer, L., N. Lundeheim, and L. Canario. 2008. Genetic correlations between gestation length, piglet survival and early growth. *Livest. Sci.* 115:287-293.

## S

- Sanchez, M.-P., J. Riquet, N. Iannuccelli, J. Gogue, Y. Billon, O. Demeure, J-C Caritez, G. Burgaud, K. Feve, and M. Bonnet. 2006. Effects of quantitative trait loci on chromosomes 1, 2, 4, and 7 on growth, carcass, and meat quality traits in backcross Meishan× Large White pigs. *J. Anim. Sci.* 84:526-537.
- SanCristobal-Gaudy, M., J. M. Elsen, L. Bodin, and C. Chevalet. 1998. Prediction of the response to a selection for canalisation of a continuous trait in animal breeding. *Genet. Sel. Evol.* 30:423-451.

## References

---

- Sangster, T. A., A. Bahrami, A. Wilczek, E. Watanabe, K. Schellenberg, C. McLellan, A. Kelley, S. W. Kong, C. Queitsch, and S. Lindquist. 2007. Phenotypic diversity and altered environmental plasticity in *Arabidopsis thaliana* with reduced Hsp90 levels. *PLoS One* 2:e648.
- Scarlett, D.-J. G., P. M. Herst, and M. V. Berridge. 2005. Multiple proteins with single activities or a single protein with multiple activities: the conundrum of cell surface NADH oxidoreductases. *Biochimica et Biophysica Acta (BBA)-Bioenergetics* 1708:108-119.
- Schinckel, A., M. Einstein, S. Jungst, C. Booher, and S. Newman. 2010. Evaluation of the impact of pig birth weight on grow-finish performance, backfat depth, and loin depth. *Prof. Anim. Sci.* 26:51–69.
- Schneider, J., D. Nonneman, R. Wiedmann, J. Vallet, and G. Rohrer. 2014. Genomewide association and identification of candidate genes for ovulation rate in swine. *J. Anim. Sci.* 92:3792-3803.
- Schukken, Y. H., J. Buurman, R. B. Huirne, A. H. Willemse, J. C. Vernooy, J. Van den Broek, and J. H. Verheijden. 1994. Evaluation of optimal age at first conception in gilts from data collected in commercial swine herds. *J. Anim. Sci.* 72:1387–1392.
- Sell-Kubiak, E., E. Knol, and P. Bijma. 2012. Effect of sow history features on growth and feed intake in grower-finishing pigs. *J. Anim. Sci.* 90:116–126.
- Sell-Kubiak, E., L. H. van der Waaij, P. Bijma. 2013. Effect of gestating sow body condition, feed refusals, and group housing on growth and feed intake in grower–finishing pig. *J. Anim. Sci.* 91:3538-3548.
- Sell-Kubiak, E., P. Bijma, E. F. Knol, and H. A. Mulder. 2015a. Comparison of methods to study variation of traits: application to pigs. *J. Anim. Sci.* doi:10.2527/jas2014-8313.
- Sell-Kubiak, E., S. Wang, E. F. Knol, and H. A. Mulder. 2015b. Genetic analysis of within-litter variation in piglets' birth weight using genomic or pedigree relationship matrices. *J. Anim. Sci.* doi:10.2527/jas2014-8674.
- Shen, X., M. Pettersson, L. Rönnegård, and Ö. Carlborg. 2012. Inheritance beyond plain heritability: variance-controlling genes in *Arabidopsis thaliana*. *PLoS genetics* 8(8):e1002839.
- Solanes, F., K. Grandinson, L. Rydhmer, S. Stern, K. Andersson, and N. Lundeheim. 2004. Direct and maternal influences on the early growth, fattening performance, and carcass traits of pigs. *Livest. Prod. Sci.* 88:199–212.
- Sonesson, A. K., J. Ødegård, and L. Rönnegård. 2013. Genetic heterogeneity of within-family variance of body weight in Atlantic salmon (*Salmo salar*). *Genet. Sel. Evol.* 45:41.

- Sorensen, D., and R. Waagepetersen. 2003. Normal linear models with genetically structured residual variance heterogeneity: a case study. *Genetical research* 82:207-222.
- Spoolder, H., M. Geudeke, C. Van der Peet-Schwering, and N. Soede. 2009. Group housing of sows in early pregnancy: A review of success and risk factors. *Livest. Sci.* 125:1–14.
- Spötter A., and O. Distl. 2006. Genetic approaches to the improvement of fertility traits in the pig. *Vet. J.* 172:234-247.
- Stalder, K., A. Saxton, G. Conatser, and T. Serenius. 2005. Effect of growth and compositional traits on first parity and lifetime reproductive performance in US Landrace sows. *Livest. Prod. Sci.* 97(2):151-159.
- Sterning, M., L. Rydhmer, and L. Eliasson-Selling. 1998. Relationships between age at puberty and interval from weaning to estrus and between estrus signs at puberty and after the first weaning in pigs. *J. Anim. Sci.* 76:353–359.
- Struchalin, M. V., A. Dehghan, J. C. Witteman, C. van Duijn, and Y. S. Aulchenko. 2010. Variance heterogeneity analysis for detection of potentially interacting genetic loci: method and its limitations. *BMC genetics* 11(1):92.
- Suzuki, K., H. Kadowaki, T. Shibata, H. Uchida, and A. Nishida. 2005. Selection for daily gain, loin-eye area, backfat thickness and intramuscular fat based on desired gains over seven generations of Duroc pigs. *Livest. Prod. Sci.* 97:193-202

## T

- Takahashi, K. H., L. Rako, T. Takano-Shimizu, A. A. Hoffmann, and S. F. Lee. 2010. Effects of small Hsp genes on developmental stability and microenvironmental canalization. *BMC evolutionary biology* 10:284.
- Taylor, G. R., and S. Hermes. 2005. Breeds of pigs: Large White. Primefact 62. New South Wales Department of Primary Industries: Orange, New South Wales, Australia.
- Tomiyama M., S. K., T. Takagi, and K. Suzuki. 2011. Evaluation of genetic trends and determination of the optimal number of cumulative records of parity required in reproductive traits in a Large White pig population. *J. Anim. Sci.* 82:621-626.
- Tummaruk, P., N. Lundeheim, S. Einarsson, and A. Dalin. 2001. Effect of birth litter size, birth parity number, growth rate, backfat thickness and age at first mating of gilts on their reproductive performance as sows. *Anim. Reprod. Sci.* 66:225–237.



### V

- Van Den Berg, I., S. Fritz, and D. Boichard. 2013. QTL fine mapping with Bayes C ( $\pi$ ): a simulation study. *Genet Sel Evol* 45:10.1186.
- Van der Lende, T., and D. de Jager. 1991. Death risk and preweaning growth rate of piglets in relation to the within-litter weight distribution at birth. *Livest. Prod. Sci.* 28:73–84.
- Van Tienderen, P. H., and H. P. Koelewijn. 1994. Selection on reaction norms, genetic correlations and constraints. *Genetical research* 64:115-125.
- Van Vleck, L. D. 1968. Variation of milk records within paternal-sib groups. *J. Dairy Sci.* 51(9):1465-1470.
- Van Wijk, H. J., D. J. Arts, J. O. Matthews, M. Webster, B. J. Ducro, and E. F. Knol. 2005. Genetic parameters for carcass composition and pork quality estimated in a commercial production chain. *J. Anim. Sci.* 83:324–333.
- Van Wijk, R., J. H. Ovelgönne, E. De Koning, K. Jaarsveld, J. Van Rijn, and F. A. C. Wiegant. 1994. Mild step-down heating causes increased levels of HSP68 and of HSP84 mRNA and enhances thermotolerance. *International journal of hyperthermia* 10:115-125.
- Vandenplas, J., C. Bastin, N. Gengler, and H. Mulder. 2013. Genetic variance in micro-environmental sensitivity for milk and milk quality in walloon Holstein cattle. *J. Dairy Sci.* 96:5977–5990.
- VanRaden, P. 2008. Efficient methods to compute genomic predictions. *J. Dairy Sci.* 91(11):4414-4423.
- Vidović V., D. L., L. Štrbac, V. Višnjić, D. Punoš, R. Šević, J. Krnjajić, and M. Stupar. 2012. Genetic trend for certain traits in pigs using different selection criteria. *Animal Science and Biotechnologies* 45:274-279.

### W

- Weller, J. I. 2009. Quantitative trait loci analysis in animals. CABI Publishing, Wallingford, U.K.
- Wijga, S. 2013. Immunogenetics in dairy cattle: somatic cell count and natural antibody level. PhD Thesis. Wageningen University, Wageningen.
- Wittenburg, D., V. Guiard, F. Teuscher, and N. Reinsch. 2008. Comparison of statistical models to analyse the genetic effect on within-litter variance in pigs. *Animal* 2:1559–1568.
- Wittenburg, D., V. Guiard, F. Teuscher, and N. Reinsch. 2011. Analysis of birth weight variability in pigs with respect to liveborn and total born offspring. *J. Anim. Breed. Genet.* 128:35–43.

- Wolc, A., I. White, S. Avendano, and W. Hill. 2009. Genetic variability in residual variation of body weight and conformation scores in broiler chickens. *Poultry Sci.* 88(6):1156-1161.
- Woolard, J., W-Y Wang, H. S. Bevan, Y. Qiu, L. Morbidelli, R. O. Pritchard-Jones, T-G Cui, M. Sugiono, E. Waine, and R. Perrin. 2004. VEGF165b, an Inhibitory Vascular Endothelial Growth Factor Splice Variant Mechanism of Action, In vivo Effect On Angiogenesis and Endogenous Protein Expression. *Cancer research* 64:7822-7835.

## Y

- Yang, H., P. Eastham, P. Phillips, and C. Whittemore. 1989. Reproductive performance, body weight and body condition of breeding sows with differing body fatness at parturition, differing nutrition during lactation, and differing litter size. *Anim. Sci.* 48:181–201.
- Yang, J., B. Benyamin, B. P. McEvoy, S. Gordon, A. K. Henders, D. R. Nyholt, P. A. Madden, A. C. Heath, N. G. Martin, G. W. Montgomery, M. E. Goddard, and P. M. Visscher. 2010. Common SNPs explain a large proportion of the heritability for human height. *Nature Genet.* 42:565–569.
- Yang, Y., O. F. Christensen, and D. Sorensen. 2011. Use of genomic models to study genetic control of environmental variance. *Genetics research* 93(2):125-138.
- Yang, J. et al. 2012. FTO genotype is associated with phenotypic variability of body mass index. *Nature* 490:267-272.

## Z

- Zhang, X., and D. Mosser. 2008. Macrophage activation by endogenous danger signals. *The Journal of pathology* 214:161-178.



## **Curriculum Vitae**



Ewa Sell-Kubiak was born on 20th of March 1984 in Poznań, Poland. In June 2003 she graduated St. Maria Magdalena High School in Poznań. The following October, Ewa started Biotechnology MSc Program at the Poznań University of Life Sciences. After choosing specialization in Biotechnology in Animal Breeding, Ewa obtained the Koepon Foundation scholarship to follow the MSc program in Animal Breeding and Genetics at Wageningen University, which she started in September 2007. In 2009 she graduated from both Wageningen University and Poznań University of Life Sciences. Her MSc thesis entitled: "Two-stage procedure to detect QTL for health traits in Dutch dairy cattle" won The Best MSc Thesis Award in Animal Sciences in Poland in 2011. In November 2009, Ewa was accepted as a PhD candidate at the Animal Breeding and Genomics Center at Wageningen University. She worked on a project on "Genetics of social interactions in livestock: Improving health, welfare, and productivity in laying hens and pigs", and focused on the random variance and improvement of uniformity in reproduction and production traits in pigs. The results of the project are presented in this thesis. Currently Ewa writes her own research proposal as she plans to continue her scientific carrier at Poznań University of Life Sciences.



## **Publications**



### Peered reviewed papers

- Sell-Kubiak, E., S. Wang, E. F. Knol, H. A. Mulder. 2015. Genetic analysis of within-litter variation in piglets' birth weight using genomic or pedigree relationship matrices. *J. Anim. Sci.* doi:10.2527/jas2014-8674.
- Sell-Kubiak, E., P. Bijma, E. F. Knol, H. A. Mulder. 2015. Comparison of methods to study variation of traits: application to pigs. *J. Anim. Sci.* doi:10.2527/jas2014-8313.
- Proskura, W., Cichoń, D. Grzesiak, W. Zaborski, D. Sell-Kubiak, E., Cheng, Y. H., & Dybus, A. 2014. Single Nucleotide Polymorphism in the LDHA Gene as a Potential Marker for the Racing Performance of Pigeons. *J. Poult. Sci.* 51(4):364-368.
- Sell-Kubiak, E., L. H. van der Waaij, P. Bijma. 2013. Effect of gestating sow body condition, feed refusals, and group housing on growth and feed intake in grower–finishing pig. *J. Anim. Sci.* 2013 91(8):3538-3548.
- Sell-Kubiak, E., E. F. Knol, P. Bijma. 2012. Effect of sow history features on growth and feed intake in grow-finish pigs. *J. Anim. Sci.* 90(1):116–126.

### Manuscripts in preparation

- Sell-Kubiak, E., N. Duijvesteijn, M. S. Lopes, E. F. Knol, P. Bijma, H. A. Mulder. Genome-wide association study reveals novel loci for litter size and its variability in pigs.

### Literature reviews

- Sell-Kubiak, E., Hodowla i chów trzody chlewnej w Holandii. *Animal Production review* (in press).
- Sell-Kubiak, E., T. Szwaczkowski. 2014. Czy grupowe utrzymanie loch prośnych ma wpływ na ich potomstwo? *Animal Production Review.* 2:20-22.

**Conference proceedings**

- Sell-Kubiak, E., M. S. Lopes, N. Duijvesteijn, E. F. Knol, P. Bijma, H. A. Mulder. 2015. New genomic regions associated with litter size and its variation in pigs. Book of Abstracts of the EAAP, Warsaw, Poland.
- Sell-Kubiak, E., P. Bijma, E. F. Knol and H. A. Mulder. 2014. Genetic analysis of birth weight uniformity in pigs: comparison of methods. Proceedings of the 10th World Congress on Genetics Applied in Livestock Production, Vancouver, Canada.
- Sell-Kubiak, E., P. Bijma, E. F. Knol and H. A. Mulder. 2013. Zróżnicowanie masy urodzeniowej prosiąt w krzyżówkach dwóch linii czystych. IV Polish Congress of Genetics, Poznań, Poland.
- Sell-Kubiak, E., Van der Waaij, E. H. and Bijma, P. 2013. Gestation features of group-housed sows affecting growth rate and feed intake in finishers. Book of Abstracts of the EAAP, Nantes, France.
- Sell-Kubiak, E., Knol, E. F., Bijma, P. and Mulder, H. A. 2013. Within-litter variation in piglet's birth weight in reciprocal crosses. Book of Abstracts of the EAAP, Nantes, France.
- Sell-Kubiak, E., E. F. Knol, and P. Bijma. 2011. Effect of sow history features on growth and feed intake in finishers. Book of abstracts of The Annual Meeting of Polish Society for Animal Production, Poznań, Poland.
- Sell-Kubiak, E., E. F. Knol, and P. Bijma. 2011. Sow history features affecting growth and feed intake in finishers. Book of Abstracts of the EAAP, Stavanger, Norway.
- Sell-Kubiak, E., T. C. W. Ploegaert, G. C. B. Schopen, H. K. Parmentier, E. Tijhaar, J. A. M. van Arendonk, H. Bovenhuis and J. J. van der Poel. 2010. QTL affecting innate immunity in Dutch dairy cattle. Proceedings of the 9th World Congress on Genetics Applied in Livestock Production, Leipzig, Germany.



## **Training and Supervision Plan**

## Training and Supervision Plan



### The Basic Package (3 ECTS)

WIAS Introduction Course)	2009
Course on philosophy of science and and ethics	2011

### Scientific Exposure (18 ECTS)

#### *International conferences*

9 <sup>th</sup> WCGALP, Leipzig (Germany), 1-6.08.2010	2010
62 <sup>nd</sup> EAAP, Stavanger (Norway), 29.08-2.09.2011	2011
76 <sup>th</sup> Meeting of Polish Society for Animal Production, Poznań (Poland), 13-16.09.2011	2011
62 <sup>nd</sup> EAAP, Nantes (France), 26-30.08.2013	2013
IV Polish Congress on Genetics, Poznań (Poland), 10-13.09.2013	2013
10 <sup>th</sup> WCGALP, Vancouver (Canada), 17-22.08.2014	2014

#### *Seminars and workshops*

Seminar 'Developments in genome-wide evaluation and genomic selection', Wageningen	2009
WIAS Science Day	2010-2015
Seminar 'Genomics and Animal Breeding', Wageningen	2011
Seminar, 'Learning how to eat like a pig', Wageningen	2011
Symposium, 'Genetics of social life: Agriculture meets evolutionary biology', Wageningen	2013
Seminar, 'Genomic selection for novel traits', Wageningen	2013

#### *Presentations*

9 <sup>th</sup> WCGALP, Leipzig (Germany) - oral presentation	2010
62 <sup>nd</sup> EAAP, Stavanger (Norway) - oral presentation	2011
76 <sup>th</sup> Meeting of Polish Society for Animal Production, Poznań (Poland) - oral presentation, 1 <sup>st</sup> price winner	2011
WIAS Science Day2013 - oral presentation	2013
64 <sup>nd</sup> EAAP, Nantes (France) - oral presentation I, 1 <sup>st</sup> price winner	2013

## Training and supervision plan

---

64 <sup>nd</sup> EAAP, Nantes (France) - oral presentation II	2013
IV Polish Congress on Genetics, Poznań (Poland) - oral presentation	2013
10 <sup>th</sup> WCGALP, Vancouver (Canada) - oral presentation	2014

### **In-Depth Studies (10 ECTS)**

#### ***Disciplinary and interdisciplinary courses***

Genomic Selection by Ben Hayes	2010
Quantitative genetics by Bruce Walsh	2010
Genomic Selection in Livestock	2011

#### ***PhD students' discussion groups***

Quantitative Genetics Discussion Group (weekly meetings), ABGC

### **Professional Skills Support Courses (7 ECTS)**

Techniques for Writing and Presenting a Scientific Paper	2011
Project and Time Management	2011
Social Dutch for Employees	2013
Writing Grant Proposals	2015

### **Didactic Skills Training (4 ECTS)**

#### ***Supervising practicals and excursions***

Reviewing Student Proposals for Research Master Cluster	2010-2011
Supervising practicals of Modern Statistics for Life Sciences	2013

#### ***Supervising theses***

Minor thesis	2013
--------------	------

### **Management Skills Training (2 ECTS)**

#### ***Organization of seminars and courses***

Organizing the Quantitative genetics course by Bruce Walsh	2010
--	------

### **Education and training total**

**44 ECTS**



## **Acknowledgments**





Writing these acknowledgments was a bitter-sweet experience. The reason for it, is not the time to say “thank you”, but the time to say “good-bye” to the Netherlands and all of my Dutch and non-Dutch friends that I have met here... But even the best things sometime have to come to an end☺  
The PhD time was a wild ride with many up’s and down’s and I could not have done it without help of others. Thank you all for that!

I would not be here if it was not for Johan van Arendonk and Piter Bijma letting me join the “Social interaction” project.

Johan – thank you for the insightful comments and discussions about my papers and thesis. It was always a valuable contribution needed for development of my work. I highly value this guidance! Thank you also for your support for all of my plans throughout the PhD and help with all the formalities related to them. It made stressful times a bit easier.

Piter – it was great to have you as my supervisor! You are a fantastic teacher and you always know what your students are missing. Thank you for all the time you had for me to clarify, discuss and plan. Really appreciate that you were always there to support my scientific progress and to help with all the non-scientific issues that could disturb this process. I am glad, our cooperation worked out so well, even though I successfully avoided long-distance “fietsen” and the only thing you seem to know about Poland is “kluski”☺

But my thesis committee does not end here, there are two more members that greatly contributed to my work: Egbert Knol and Han Mulder.

Egbert – thank you for your endless research ideas! If it was not for them, none of the papers in this thesis would have been written☺ Thank you for sharing your pig knowledge, for all the discussions and making me think more about practical aspects of pig breeding. I highly value what I have learned from you!

Han – I still cannot believe our collaboration started by a total coincidence during a coffee break! Thank you very much for letting me join you in the search for uniformity☺ I have learned a lot from you! Thank you also for the time you had for me to explain the codes and to discuss all the theory behind it. I appreciate the enthusiasm you have for your work. And I hope our cooperation does not end with this thesis!

Once again: thank you Johan, Piter, Egbert and Han for your supervision!

Over the years I got a lot of support from many people from the Topigs Norsvin Research Center. For this, I would like to thank you all! And a special thank you to:

## Acknowledgments

---

Annemieke, Marcos, Susan and Rob – thank you for your help with the Topigs data!

Egiel – thank you for all the discussion we had while I was writing the general discussion of my thesis. I really appreciate your help!

Naomi and Marcos – thank you for all the time and work you put in helping me with the GWAS paper. I would not have finished it without you!

René – thank you for your help and time during my visits to the Beilen farm.

Thanks to all the staff and fellow PhD students at ABGC. It would not be as fun without you!

Henk, Liesbeth, Henri, Jan, Bart and Pim – thank you for all the discussions over coffee, “mini-lectures” on QDG’s, suggestions to manuscripts “in preparation”, help in solving statistical and programming problems and that it was always possible to just pop up at your offices with questions.

Alex – thank you for rescuing me from all the server and computer related issues, for checking the codes, getting licenses and giving advices for possible solutions.

Ada, Lisette and Monique – Ladies! Thank you very much for all the help I got from you throughout the years. Especially, for all the advices and assistance with the (HR) paper work... You are really the masters in your job!

Katrijn and Naomi – I could not have asked for better roommates for the PhD-time! It was great to discuss with you scientific issues, gossip and share all PhD-writing up’s and down’s. Not to mention all the dinners and parties we had! And surprisingly enough, we still like each other after all this time in one office☺  
@Naomi: thank you for being my paranymph!

Susan and Irene – thank you soooo much for all the support I got and still get from you!! In all different shapes and forms☺ Both of you always know what to say to make me feel better! Thank you A LOT for the time you put in helping me in the last stages of PhD-writing. It meant a great deal to me!

Hamed – I will simply say to you: it is great to have you for a friend! Thank you for taking the job of being my paranymph☺

Nancy and Mathieu – thank you for being the perfect roommates for the last part of my PhD-writing in our Radix’s office. We had some fun times together!  
@Nancy: thank you for being my “spare” paranymph!

Marcin – thanks a lot for being my “statistics-little-helper”! And that I can count on you for any kind of help actually☺ Looking forward to working with in Poznań!

Sandrine – thank you for many great talks we had! And more!

And not to forget about: Andre, Aniek, Bert, Britt, Claudia, Coralia, Dianne, Esther, Gabriel, Gus, Hadi, Hooi Ling, Ilse, Jovana, Juanma, Kimberly, Lucas, Mahlet, Marcos, Mathijs, Mirte, Panya, Sonia, Tessa, Yvonne, and many more... Thank you for helping, partying, car-pooling, discussing, traveling, baby-sitting, gossiping and cooking! It was great to meet you all!!

And of course a big thank you to the all non-work friends and family that had to put up with me throughout the PhD-writing time☺

Bas, Linda and Marcel – thank you for all the dinners (BLM) and parties (LM), and for rescuing us in the times of need (B)!

Kasia and Jonathan – thank you for all the fun we had together in Enschede! You were a very entertaining break from the Wageningen's world☺

Gosia and Przemek – dzięki, że dla całej naszej rodziny byliście odskocznią od chaosu pisanie doktoratu!

Mamo i Tato, nie osiągnęłabym tego celu, gdybyście od zawsze nie wspierali moich wszelkich decyzji (pomimo wątpliwości☺)! Dziękuję wam za to!

Agu i Pio, ogromnie się cieszę, że wyrosliśmy na tak różnych ludzi! Dziękuję za tłumaczenia i korekty językowe oraz za wszelkie rysunki/malunki (szczególnie tę okładkę!).

Kostek and Kajtek, my dearest “side projects”☺ To, że jesteście w naszym życiu, jest najpiękniejszym prezentem od losu! Byliście najwspanialszą odskocznią od PhD-writing jaką mogłam sobie wymarzyć. Kostku masz pełne prawo mówić, że pisałeś ten doktorat ze mną☺

Jasiu, najdroższy... codziennie zdobywasz +100 do „ja to ogarnę, kochanie!”☺ Bez ciebie, twojego wsparcia i pomocy w każdym aspekcie życia nie mogłabym osiągnąć zbyt wiele. A i tak to razem tworzymy najlepszy team na świecie☺ Dziękuję, że jesteś!

*Ewa*



## **Colophon**

## Colophon

The research described in this thesis was financially supported by the Netherlands Organization for Scientific Research (NWO) and by the Dutch Technology Foundation STW (project number: 10477).

The data used in this thesis were provided by Topigs Norsvin Research Center (Beuningen, The Netherlands).

The cover of this thesis was created and designed by Piotr Sell ([www.pcell.it](http://www.pcell.it))

This thesis was printed by GVO drukkers & vormgevers B.V. | Ponsen & Looijen, Ede, the Netherlands.