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A decade of untangling the genetic background of litter size phenotypic variability in pigs

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Introduction

Litter size (LS) is a key trait for the efficiency of pig production and breeding. The profitability of pig farming is determined by the pounds of pork marked from a sow during each year of her productive life (Merks *et al*., 2012; Baxter *et al*., 2013). Thus, any deviation from the expected number of piglets in successive parities concerns farmers. As average litter size increases, greater variation among litters is observed, which is associated with a genetic correlation of approximately 0.5 between litter size and its variability (estimated from the residual variance in a classical animal model). Ignoring this relationship will lead to further increases in differences between litters of individual sows, especially if selection pressure toward larger litters continues to intensify. One approach to reducing variability is to study the genetic basis of phenotypic variance, which includes the genetic component of residual variance (Hill and Mulder, 2010). Although heritability of variability is low (0.001–0.05; e.g. Ibáñez-Escriche *et al*., 2008; Mulder *et al*., 2013; Sonesson *et al*., 2013), it remains biologically meaningful. Understanding variability requires quantitative genetics and genomic tools. Although many QTL for litter size exist, vQTL for variability were not documented until recently. The concept of vQTL (Rönnegård and Valdar, 2011) aligns with earlier findings in plants, animals, and humans (e.g. Mackay and Lyman, 2005; Shen *et al*., 2012; Yang *et al*., 2012; Mulder *et al*., 2013). Identifying vQTL is essential for understanding resilience to environmental stressors such as diseases or heat stress (e.g. Sangster *et al*., 2007). Thus, the aim of this work is to explore knowledge of phenotypic variability in LS and to identify the optimal litter size.

Materials & Methods

The phenotypic data used in the presented studies consisted of: Large White (LW) and Landrace (LN) data from multiplication farms of Topigs Norsvin obtained in 2000-2023, and Polish local Złotnicka White (ZW) and Spotted (ZS) breeds from the herd books of Poznan University of Life Sciences collected in 1950-2022. Also, the genotypes were available for a selected subset of Large White (60K and 660K SNP chip) and Landrace (660K SNP chip) pigs. To thoroughly evaluate the background of litter size variability, a number of statistical analyses were used, including the classical Animal model, a double hierarchical generalised linear model (DHGLM), the log-variance of residuals (LnVar), random regression, genome-wide association studies (GWAS), and simulations of breeding programs.

Results & Discussion

Litter size variability DHGLM vs LnVar. The DHGLM has been shown to be a highly reliable tool to estimate the litter size variability phenotype (Sell-Kubiak *et al*., 2015;2022a), and the level of genetic correlation between the mean and variability of litter size is 0.5. This level of correlation allows to design the breeding program in a way that variability is reduced while litter size is kept at a stable level or even increased. Since DHGLM is a rather complicated algorithm, a simpler method based on the log-variance of residuals (LnVar) from the Animal model for litter size was also evaluated as a potential approach to estimate the variability phenotype. Evidence included lower correlations between breeding values from

2021 and those from Sell-Kubiak *et al*. (2015) (0.73 for LnVar vs. 0.86 for DHGLM), reduced accuracy of breeding values, and poorer prediction for animals without phenotypes. Even though Sell Kubiak *et al*. (2022a) demonstrated on LW data that DHGLM provides more accurate estimates than LnVar, the use of the latter is more straightforward and still widely used. Extended analysis of LnVar's by Dobrzański *et al*. (2020) showed, on the same data, that LnVar derived from different levels of complication in the model terms represents genetically identical traits, confirming that simplified models can reliably assess variability. However, Cieleń *et al*. (2023) reported, based on Landrace data, that the Box-Cox transformation alters the variance components of LnVar for litter size when at least a small deviation from the Normal distribution is observed in the data. In analyses of the Polish ZW and ZS pigs, a decline in mean litter size with stable variability was reported (Sell Kubiak *et al*., 2025). This suggests an inbreeding depression, which should be further investigated and better monitored in the genetic resource conservation program managing the Złotnicka pig population.

Other variability sources across parities. Further work focused on examining possible genetic background in the expected level of average litter size across parities i.e. "parity curve". This was done using random regression with Legendre polynomials (Sell Kubiak *et al*., 2019). Accounting for "parity curve" in the litter size model showed that genetic variance and heritability increase from the second parity onward, and that the first parity is genetically distinct from later parities. Also, the simulations demonstrated that modifying the parity curve through selection is either infeasible or reduces overall mean litter size, indicating that the curve cannot be used to decrease variability between parities. However, not every litter size fits the "parity curve". Such cases were examined by studying the genetics behind second litter syndrome (SLS). It was demonstrated that SLS occurrence is driven by management factors rather than genetics, with heritability estimates reflecting only variability around the parity curve (Sell Kubiak *et al*., 2021).

Genome-wide association studies. The study by Sell-Kubiak *et al*. (2015) was the first to perform a genome-wide association study (GWAS) targeting litter size variability using 2,067 genotyped animals (40,969 SNPs after quality control). The analyses identified candidate genes on chromosome 7, with *HSPCB* being the most promising. This gene encodes a heat-shock protein acting as a molecular chaperone under stress conditions and is homologous to *Hsp90*, known in *Drosophila* and *Arabidopsis* for stabilising morphological traits. Advances in technology later enabled the GWAS for litter size variability to be repeated on ~12,000 genotyped sows (Sell-Kubiak *et al*., 2022a). Despite methodological differences between DHGLM and LnVar, the GWAS for both traits pointed to the same major region: a SNP on chromosome 7 located in a regulatory intron identified by Genomic Evolutionary Rate Profiling (GERP). Linkage disequilibrium between SNPs identified in 2015 and 2022 was 0.11, reinforcing chromosome 7 as the principal region controlling litter-size variability and supporting DHGLM as the preferred analytical approach. However, it became later clear that chromosome 7 is breed-specific. The study by Cieleń *et al*. (2023) was the first to assess phenotypic and genomic variability of litter size before and after Box–Cox transformation in Landrace pigs. GWAS detected 14 SNPs for LnVar_TNB and eight for LnVar_bcTNB, with promising candidate genes including *STAG3* (chromosome 3; gametogenesis), *ESRRG* (chromosome 10; placental development), and, from post-GWAS analysis, *MFN1* (chromosome 13; embryonic development). The results showed that the Box-Cox transformation substantially altered the SNPs associated with the studied traits, with only partial overlap between traits. Taking into account the breed differences, but at the same time very high number of GWAS studies performed for litter size related traits, previously published SNP associations were integrated in a comprehensive meta-analysis (Sell-Kubiak *et al*.,

2022b). The meta-analysis combined associations for five traits: total number born (TNB), number born alive (NBA), stillborn (SB), litter weight (LWT), and corpus luteum number (CLN). Only 21 of 233 previously reported candidate genes appeared in more than one population or trait. *PRKD1*, associated with SB and TNB and involved in angiogenesis, emerged as the strongest candidate. The results indicated a highly polygenic nature of reproductive traits and the scarcity of pleiotropic genes. The meta-GWAS identified two novel SNPs: one on chromosome 14 in *FAM13C*, and one on chromosome 9 in *AGMO*. Functional analysis highlighted *SOSTDC1*, linked to reduced male fertility in rats, suggesting that boars may influence litter size more than previously assumed.

Maximum vs optimum. Pig breeding has reached a stage where litter size, birth weight, and uniformity require a balanced approach to ensure the welfare of sows and piglets. Increasing litter sizes also makes piglet rearing more challenging. Therefore, Sell-Kubiak (2021) defined and analysed traits describing the maximum litter size and maximum litter weight achieved by a sow. Maximum values showed much higher heritability than classical analyses (i.e., using all available observations) or mean values, suggesting a faster response to selection. However, maximum-value traits are associated with a higher risk of stillborn piglets (though not with the maximum number born alive) and increased variability in all reproductive traits. Thus, maximum values should be considered indicators of sow potential rather than traits included in breeding indices. Although selection to increase both litter size and birth weight is genetically feasible, intensifying selection using "maximum values" is not advisable. For welfare and management reasons (costs of very small and extremely large litters, e.g., sow culling and piglet survival), selection should instead aim for a balance between mean reproductive traits and variability, achievable only through a well-designed breeding program.

Sire effect in reproduction traits. With extensive experience in adapting the animal model for variance-component analysis, attention was drawn to the fact that, in some pig breeds, the sire effect in the model accounted for a larger proportion of variance than expected given breeding practice, which attributes reproductive traits primarily to females. Reproductive traits such as litter size, number born, or litter weight are typically assigned to sows. In the review by Cieleń and Sell-Kubiak (2024), the biological and genetic importance of boar effects in pig breeding was highlighted, including boar reproductive biology, genetic and non-genetic sire effects in models used for estimating breeding values for traits measured in females, and genes involved in male reproduction. Key boar traits influencing reproductive success were described, including sexual maturity, semen quality, and testicular parameters, along with the environmental factors that affect them (e.g., feed and temperature). The main part of the review detailed the genetics of boar reproductive traits, including heritability estimates, and direct genetic correlations with female reproductive traits. Genetic and non-genetic sire effects accounted for 1–4.5% and 1–2% of total phenotypic variance, respectively, depending on breed and trait. The review also summarized candidate genes and confirmed mutations affecting male reproductive success: *IGF2, Tgm8, ESR1, ZSWIM7,* and *ELMO1*. Overall, boar effects on litter traits should not be ignored, as they contribute to female reproductive success.

Conclusions

Reproductive performance in pigs emerges from a complex interaction of genetic mechanisms, modelling choices, and management conditions, and this work shows that meaningful progress requires integrating all three dimensions. Robust statistical approaches such as DHGLM provide the most reliable insight into litter size variability, while simpler methods, though convenient, can distort genetic signals and differ across breeds. Genomic analyses confirm that variability is highly polygenic and population-specific, with limited overlap of candidate genes,

reinforcing the need for tailored evaluations rather than universal markers. Patterns across parities reveal that reproductive biology is not uniform throughout a sow's life, and deviations such as second litter syndrome stem largely from management rather than genetics. Although maximum reproductive values show strong genetic potential, their biological costs make them unsuitable as direct selection targets, underscoring the importance of balanced breeding goals that improve both mean performance and uniformity. The growing evidence for meaningful sire contributions further underscores the need to incorporate male effects into reproductive evaluations.

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