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Modeling genotype-by-environment interaction for reproductive performance in sows across a disease challenge gradient

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Introduction

Porcine Reproductive and Respiratory Syndrome (PRRS) is a viral disease that significantly impacts the global swine industry. The disease causes significant productivity losses, primarily due to reproductive failure in sows and respiratory symptoms in piglets (Zimmerman *et al.,* 2019). This highlights the need to improve disease resilience, defined as the ability of an individual to be minimally affected by the disease or to recover rapidly from it (Berghof *et al.,* 2019).

Several studies have reported changes in genetic parameters and estimated breeding values for reproductive performance before, during, and after a PRRS outbreak, showing genotype-by-environment interactions (GxE) across PRRS outbreak phases (Putz *et al.,* 2019; de Oliveira *et al.,* 2025). This study aimed to investigate GxE effects for reproductive performance traits across an environmental gradient (EG), including natural exposure to PRRS, to better understand the genetic relationship between reproductive performance traits measured under various levels of PRRS virus exposure.

Materials & Methods

Data. Reproductive performance data were available for 16,654 Topigs Norsvin Large White females and 53,157 farrowing events before, during, and after a PRRS outbreak. Data originated from three multiplication farms located in the United States (Farms 1, 2, and 3) and two multiplication farms located in Spain (Farms 4 and 5). Reproductive performance data were available according to each farm's routine data collection process. The traits evaluated in this study included: number of piglets born alive (NBA), number of piglets born mummified (MUM), and number of piglets stillborn (NSB).

Pedigree records were available for all animals, and genotypes for 24,329 genomic markers (after quality control) were available for 3,518 sows and 483 of their 575 sires.

Reaction norm models. A two-step reaction norm model (RNM) was used for this study. In the first step, the estimates of farm-year-week (FYW) for NBA were used to define the EG, as PRRS outbreak decreases NBA (Lewis *et al.,* 2009). The FYW estimates for NBA were obtained using the following model, according to Rashidi *et al.* (2014) and Putz *et al.* (2019):

$$\mathbf{y} = \mathbf{Xb} + \mathbf{Zfyw} + \mathbf{Zsow} + \mathbf{e} \quad (1)$$

where $\mathbf{y}$ is the vector of phenotypic records for NBA; $\mathbf{X}$ is an incidence matrix of fixed effects; $\mathbf{b}$ is the vector of fixed effects, which comprised the effects of parity; $\mathbf{Z}$ is an incidence matrix of random effects; $\mathbf{fyw}$ is the random effect of farm-year-week of the farrowing record, assuming $\mathbf{fyw} \sim N(0, \mathbf{I}\sigma^2_{fyw})$, where $\mathbf{I}$ is an identity matrix and σ^2_{fyw} is the farm-year-week variance; $\mathbf{sow}$ is the random effect of sow, assuming $\mathbf{sow} \sim N(0, \mathbf{I}\sigma^2_{sow})$, where σ^2_{sow} is the sow variance; and $\mathbf{e}$ is the vector of residuals, assuming $\mathbf{e} \sim N(0, \mathbf{I}\sigma^2_{e})$, where σ^2_e is the residual

variance. The FYW estimates were standardized and ranged from -5.23 to 1.72, where values lower than -1.65 were indicative of a PRRS outbreak.

In the second step, RNMs were fitted to analyze NBA, MUM, and NSB by regressing phenotypic records on standardized FYW effects for NBA. The RNM fitted was the following:

$$\mathbf{y} = \mathbf{Xb} + \mathbf{Qa} + \mathbf{Zpe} + \mathbf{e} \quad (2)$$

where $\mathbf{y}$ is the vector of phenotypic records; $\mathbf{X}$ is the incidence matrix of fixed effects; $\mathbf{b}$ is the vector of fixed effects, which comprised the effects of parity, contemporary group (defined as the concatenation of farm, year, and season of farrowing), and the outbreak phase (before, during or after the outbreak); $\mathbf{Q}$ is the incidence matrix relating observations to random additive genetic effects; $\mathbf{a}$ is the vector of random additive genetic effects, which includes random intercept ($\mathbf{a_0}$) and random slope ($\mathbf{a_1}$), $\begin{bmatrix}\mathbf{a_0}\\ \mathbf{a_1}\end{bmatrix} \sim \mathrm{N}\left(0, \mathbf{H} \otimes \begin{bmatrix}\sigma^2_{\mathrm{a_0}} & \sigma_{\mathrm{a_0a_1}}\\ \sigma_{\mathrm{a_0a_1}} & \sigma^2_{\mathrm{a_1}}\end{bmatrix}\right)$, where $\mathbf{H}$ is a hybrid relationship matrix combining genotyped and non-genotyped animals, $\sigma^2_{\mathrm{a_0}}$ is the additive genetic variance for the intercept, $\sigma^2_{\mathrm{a_1}}$ is the additive genetic variance for the slope, and $\sigma_{\mathrm{a_0a_1}}$ is the additive genetic covariance between intercept and slope; $\mathbf{Z}$ is the incidence of permanent environment effects; $\mathbf{pe}$ is a vector of random permanent environmental effects, which includes random intercept ($\mathbf{pe_0}$) and random slope ($\mathbf{pe_1}$), with $\begin{bmatrix}\mathbf{pe_0}\\ \mathbf{pe_1}\end{bmatrix} \sim \mathrm{N}\left(0, \mathbf{I} \otimes \begin{bmatrix}\sigma^2_{\mathrm{pe_0}} & \sigma_{\mathrm{pe_0pe_1}}\\ \sigma_{\mathrm{pe_0pe_1}} & \sigma^2_{\mathrm{pe_1}}\end{bmatrix}\right)$, where $\sigma^2_{\mathrm{pe_0}}$ is the permanent environmental variance for the intercept, $\sigma^2_{\mathrm{pe_1}}$ is the permanent environmental variance for the slope, and $\sigma_{\mathrm{pe_0pe_1}}$ is the permanent environmental covariance between intercept and slope, $\mathbf{I}$ is an identity matrix; and $\mathbf{e}$ is the vector of residuals. The vector $\mathbf{e}$ contains the residuals, assumed $\mathbf{e} \sim \mathrm{N}(0, \mathbf{R})$, where $\mathbf{R}$ is diagonal with class-specific residual variances (σ^2_{e}). Residual variances were modeled assuming either homogeneity (M1) or heterogeneity across the environmental gradient (EG). In M1, a single residual variance was assumed for the entire EG range. In the heterogeneous models (M2–M5), residual variances were partitioned into up to five discrete classes defined by cut points along the EG: **M2:** {−Inf, −1.65, Inf}; **M3:** {−Inf, −1.65, −1, Inf}; **M4:** {−Inf, −1.65, −1, 0, Inf}; and **M5:** {−Inf, −1.65, −1, 0, 1, Inf}. Model fit was compared using the Akaike Information Criterion. All models were fitted using the Average Information Restricted Maximum Likelihood (AIREML) algorithm implemented in BLUPF90+ software family (Misztal *et al.,* 2014).

Results

Heterogeneous residual variance structures improved the fit for NBA (assuming two classes of residual variance) and MUM (assuming three classes of residual variance), while a homogeneous residual variance model was best for NSB. Table 1 presents the intercept and slope variance components for additive and permanent environmental effects from the selected RNM per trait, together with class-specific residual variances across the EG.

The heritability estimates for the RNM intercept ranged from 0.04 to 0.07 for NBA, from 0.01 to 0.04 for MUM, and were 0.01 for NSB. The heritability estimates for the RNM slope were 0.01 for NBA, 0.004 to 0.03 for MUM, and 0.08 for NSB. The genetic correlation estimates between intercept and slope for NBA, MUM, and NSB were 0.14 ± 0.13, -0.89 ± 0.02, and -0.23 ± 0.13, respectively. The average heritability across the EG for NBA, MUM, and NSB were 0.08, 0.05, and 0.09, respectively.

Table 1. Variance component estimates (± SE) for the intercept and the slope terms from the selected reaction-norm models per trait in a Large White population.

	Trait[2]		
Variance component[1]	NBA[2]	MUM	NSB
$\hat{\sigma}^2_{a_0}$	0.869 ± 0.088	0.053 ± 0.006	0.226 ± 0.019
$\hat{\sigma}^2_{a_1}$	0.092 ± 0.022	0.047 ± 0.006	0.017 ± 0.005
$\hat{\sigma}_{a_0 a_1}$	0.040 ± 0.034	-0.045 ± 0.005	-0.014 ± 0.007
$\hat{\sigma}^2_{pe_0}$	1.318 ± 0.083	0.167 ± 0.011	0.238 ± 0.017
$\hat{\sigma}^2_{pe_1}$	0.052 ± 0.043	0.268 ± 0.018	0.121 ± 0.007
$\hat{\sigma}_{pe_0 pe_1}$	-0.189 ± 0.043	-0.209 ± 0.014	-0.098 ± 0.009
$\hat{\sigma}^2_e$ class1[3]	18.026 ± 0.042	10.414 ± 0.046	2.409 ± 0.019
$\hat{\sigma}^2_e$ class2	9.899 ± 0.042	5.619 ± 0.046	-
$\hat{\sigma}^2_e$ class3	-	1.101 ± 0.046	-

[1] $\hat{\sigma}^2_{a_0}$: additive genetic variance for the intercept; $\hat{\sigma}^2_{a_1}$: additive genetic variance for the slope, $\hat{\sigma}_{a_0 a_1}$: additive genetic covariance between intercept and slope; $\hat{\sigma}^2_{pe_0}$: permanent environmental variance for the intercept; $\hat{\sigma}^2_{pe_1}$: permanent environmental variance for the slope, $\hat{\sigma}_{pe_0 pe_1}$: permanent environmental covariance between intercept and slope; and $\hat{\sigma}^2_e$: residual variance.
[2] NBA: number of piglets born alive, MUM: number of piglets born mummified, NSB: number of piglets stillborn.
[3] The number of classes shown for each trait corresponds to its selected model. Traits with values only for class 1 indicate homogeneous residual variance (M1). Dashes denote classes not present in the selected model.

Figure 1 shows pairwise genetic correlations between EG levels for each trait. Across traits, the genetic correlation estimates declined as the distance between EG levels increased, with correlations near zero when contrasting PRRS-affected weeks (FYW < −1.64) with positive FYW values, for almost all traits (Figure 1). Notably, for MUM, contrasts between negative FYW and FYW > 1 yielded negative genetic correlation estimates (Figure 1). These results indicate re-ranking across environments, especially for PRRS-free vs. PRRS-challenged conditions.

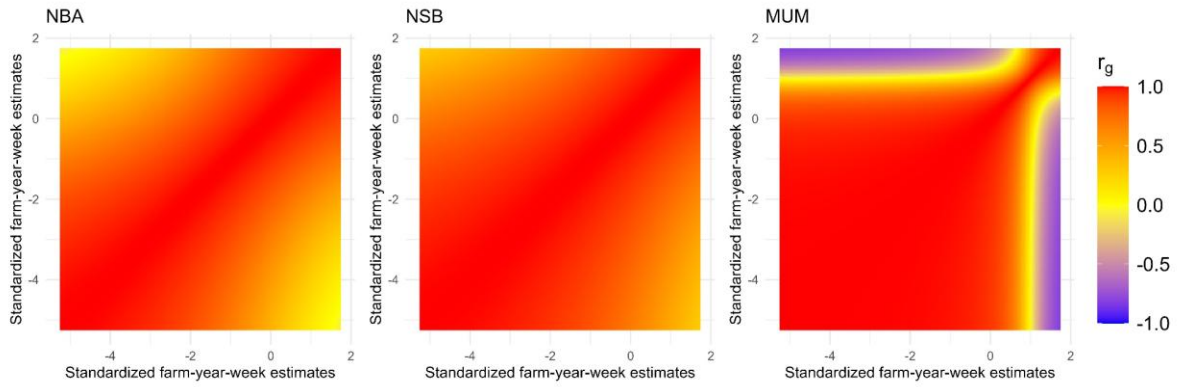

Figure 1. Heatmap of genetic correlations across environmental gradient levels for each reproductive trait. NBA: number of piglets born alive; NSB: number of piglets stillborn; MUM: number of mummified piglets.

Discussion

Based on the RNM approach, we estimated an intercept and a slope for each animal. As the EG was centered to zero, the intercept represents expected performance in the average environment, while the slope reflects the individual's sensitivity to environmental variation (Hayes *et al.,* 2016). We used this approach to investigate GxE for reproductive performance

traits measured under various levels of PRRS exposure. Our results show that the genetic correlation between intercept and slope for NBA was low (0.14 ± 0.13), suggesting that the genetic mechanisms underlying average reproductive performance are largely independent from those influencing environmental sensitivity. This implies that it is possible to genetically select animals with flatter slopes (i.e., more resilient to PRRS) without compromising overall reproductive performance under PRRS-free conditions. Additionally, we found a favorable, negative, and moderate-to-high genetic correlation between intercept and slope for MUM, indicating that animals with lower average mummified piglets tend to be more resilient to PRRS challenge.

The estimates of genetic correlations between EG levels revealed low correlations between the PRRS-free and PRRS-challenged phases. This is consistent with previous findings (Putz *et al.,* 2019; de Oliveira *et al.,* 2025), which reported similar patterns of genetic correlations between healthy and diseased phases. These results indicate potential re-ranking of animals across EG levels, meaning that top-performing individuals under PRRS-free conditions may not be the top performers under PRRS challenged conditions. This is consistent with the GxE interaction pattern previously described by de Oliveira *et al.* (2025).

Conclusions

Our findings provide strong evidence of GxE for reproductive performance traits under the presence versus absence of PRRS, resulting in meaningful re-ranking of animals across environmental conditions. To maximize genetic improvement across environments, incorporating data from farms with PRRS-challenged conditions would be advantageous. Furthermore, our results indicate that the inclusion of the RNM slope as a novel indicator trait for PRRS resilience in selection indexes should be considered, as it would enable simultaneous improvement of reproductive performance under both PRRS-challenged and non-challenged conditions. Additionally, sows with lower average numbers of mummified piglets tend to exhibit greater resilience to PRRS challenges.

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