Macro-environmental sensitivity for growth rate in Danish Duroc pigs is under genetic control¹

Mette D. Madsen,^{*,2} Per Madsen,^{*} Bjarne Nielsen,[†] Torsten N. Kristensen,^{‡,§} Just Jensen,^{*} and Mahmoud Shirali^{*,•}

^{*}Department of Molecular Biology and Genetics, Aarhus University, Tjele 8830, Denmark; [†]SEGES, Pig Research Centre, Copenhagen 1609, Denmark; [‡]Department of Bioscience – Genetics, Ecology and Evolution, Aarhus University, Aarhus 8000, Denmark; and [§]Department of Chemistry and Bioscience, Aalborg University, Aalborg 9220, Denmark

ABSTRACT: The aim of this study was to examine (i) the genetic variation in macro-environmental sensitivity (macro-ES) for ADG in Danish Duroc pigs, (ii) the genetic heterogeneity among sexes, and (iii) residual variance heterogeneity among herds. Record of ADG for 32,297 boars (19 herds) and 42,724 gilts (16 herds) was used for analysis. The data were provided by the National Danish Pig Research Centre. The analysis was performed by fitting univariate reaction norm models with the herd-year-month on test (HYM) effect as environmental covariates and herd-specific residual variance for boars and gilts separately under a Bayesian setting. The environmental covariate was inferred simultaneously with other parameters of the model. Gibbs sampling was used to sample model dispersion and location parameters. The posterior means and highest posterior density intervals of the additive genetic variance, genetic correlations for ADG, and heritability were calculated over the continuous environmental range of $-3\sigma_h$ to $+3\sigma_h$ (SD of the HYM effect). The coheritability of ADG at the average environmental level and ADG in the environments along the $-3\sigma_h$ to $+3\sigma_h$ environmental gradient were also calculated. The

analysis showed significant variation in macro-ES, revealing genotype by environment interactions ($G \times E$) for ADG. The presence of $G \times E$ resulted in changes in additive genetic variance and heritability across the $-3\sigma_h$ to $+3\sigma_h$ range. The genetic correlations were high and positive between ADG in environments differing by $1\sigma_h$ units or less and decreased to moderately positive between ADG in the extreme environments in both sexes. The coheritability of ADG in the environment at the average level and the $-3\sigma_h$ environment for boars were greater than the heritability in the environment at the average level, while it was less for gilts. The coheritability of ADG in the environment at the average level and the $+3\sigma_h$ environment for boars was less than heritability in the environment at the average level, while it was either the same or greater for gilts, depending on the residual variance. Boars had larger additive genetic and residual variances than gilts. Heterogeneity of residual variances across herds was shown for both sexes. In conclusion, this study shows the presence of macro-ES, genetic variance heterogeneity among sexes for ADG in pigs, and residual variance heterogeneity across herds.

Key words: Bayesian analysis, heterogeneous variance, macro-environmental sensitivity, pigs, reaction norms

¹This research was financed by funding from the Danish Natural Science Research Council through a Sapere Aude stipend (DFF: grant no. 4002-00036), the Center for Genomic Selection in Animals and Plants (GenSAP) funded by Innovation Fund Denmark (grant no. 0603-00519B), and the Grønt Udviklings- og Demonstrationsprogram (GUDP) project from the Ministry of Environment and Food of

Denmark (GUDP: grant no. 34009-14-0849). Authors disclose no potential or actual conflict of interest related to the research presented in the manuscript.

²Corresponding author: mette.madsen@mbg.au.dk

Received May 29, 2018.

Accepted September 22, 2018.

© The Author(s) 2018. Published by Oxford University Press on behalf of the American Society of Animal Science. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.

J. Anim. Sci. 2018.96:4967–4977

doi: 10.1093/jas/sky376

INTRODUCTION

Phenotypic responses to environments are partly determined by the macro-environmental sensitivity (**macro-ES**) which can be under genetic control. Therefore, animals can exhibit different environmental sensitivity due to genotype by environment interactions ($G \times E$) for a given trait. Statistical models commonly used for genetic evaluation in animal breeding do not consider variation in macro-ES. Disregarding the presence of $G \times E$ can lead to selection of animals with large macro-ES resulting in nonuniform performance across environments. In this sense, macro-ES is a nuisance, as the selection response across environments will differ from the expected. However, if the population parameters for macro-ES are modeled as a function of the environment, as can be done using reaction norm models, macro-ES becomes a valuable tool to select for more uniform production across different environmental conditions (Mulder, 2016). Another potential problem in estimating variance components is related to ignoring the heterogeneity of genetic variances among sexes in statistical models. For pigs, Nielsen et al. (2018) found different genetic variances for ADG in boars and gilts with a genetic correlation of 0.88. Considering this heterogeneity in statistical models can potentially increase the prediction ability for ADG (Nielsen et al., 2018). The aim of this study was to investigate and quantify: (i) genetic variation in macro-ES for ADG in pure-bred Danish Duroc pigs, (ii) heterogeneity in residual variance across different herds, and (iii) variance heterogeneity between boars and gilts.

MATERIAL AND METHODS

Animal Care and Use Committee approval was not obtained for this study because the data were obtained from an existing database of performance records from Danish pig breeding herds.

Data

Average daily gain in the growing–finishing period (30 to 100 kg BW) was recorded for 32,297 Danish Duroc boars with a mean of 1,184 g d⁻¹ and SD of 123 g d⁻¹ from 19 nucleus herds and 42,724 Danish Duroc gilts with a mean of 1,117 g d⁻¹ and SD of 108 g d⁻¹ from 16 nucleus herds. The

recording was part of the routine Danish pig breeding program led by the Danish Pig Research Centre, SEGES (<http://www.pigresearchcentre.dk/>). The pedigree for animals with records was traced three generations back and included 91,141 animals.

Statistical Analysis

We used the reaction norm analysis with simultaneously inferred environmental covariates under a Bayesian setting developed by Su et al. (2006) as implemented in the DMU software (Madsen and Jensen, 2013). Posterior distributions of all location and dispersion parameters were sampled using Gibbs sampling. Gibbs sampling was run for 2.1 million rounds with the first 100k considered as burn-in and an interleaving of 200 resulting in 10k samples (i) for posterior analysis. Convergence to the posterior distribution of model parameters and derived population parameters was evaluated using the boa package (Smith, 2016) in R program (R Core Team, 2018).

Univariate animal reaction norm models with simultaneously inferred environmental covariates following Su et al. (2006), and including heterogeneous residual variance, were analyzed for boars and gilts separately:

$$y = Xb + Za_0 + Ha^* + Wh + Vp + Ll + e \quad (1)$$

where y was the vector of observations for ADG in either boars or gilts, b contains effects of year of birth and “fixed” regression on start BW as a deviation from 30 kg (mean 0.08, SD 1.9 in both sexes). The additive genetic effect of each animal was modeled as an intercept and a slope, where a_0 was the vector of intercepts and a^* was the vector of slopes. The vectors h , p , and l contained the random effects of herd-year-month on test (HYM), group (defined as a group of animals housed simultaneously in the same pen), and litter, respectively. Descriptive statistics for HYM, group, and litter are found in Table 1. The vector of random residuals (e) for ADG was heterogeneous in 19 herd classes for boars and 16 herd classes for gilts. Matrices X , Z , W , V , and L were the corresponding incidence matrices for b , a_0 , h , p , and l , respectively. The corresponding design matrix for a^* was H , which contained the values of the environmental covariate. Each row of H in sample i (H_i) had one

Table 1. Number of levels and mean (SD), minimum and maximum number of animals per level for herd-year-month on test (HYM), group and litter for boars and gilts

		Boars			Gilts		
		HYM	Group	Litter	HYM	Group	Litter
Levels		1,212	3,398	13,802	1,280	4,200	14,973
Animals per level	Mean	27 (16)	10 (2)	2 (1)	33 (21)	10 (2)	3 (2)
	Min	2	1	1	3	1	1
	Max	103	15	10	139	15	14

nonzero element equal to the HYM effect of the HYM in which the specific animal was reared. The HYM effects used in $\mathbf{H}_i$ were the current value of HYM effects obtained in sample $i - 1$ ($\mathbf{h}_{i-1}$). Thus, the environmental values of the HYM covariate were modeled simultaneously with the effects and variance parameters. This integrated out the error of estimated HYM effects before including it as an environmental covariate in the model.

The prior of $\mathbf{a}_0$ and $\mathbf{a}^*$ was: $\begin{bmatrix} \mathbf{a}_0 \\ \mathbf{a}^* \end{bmatrix} \sim N(0, \mathbf{G}_0 \otimes \mathbf{A})$,

where $\mathbf{G}_0$ was a 2×2 matrix of additive genetic variances and covariances

$$\mathbf{G}_0 = \begin{bmatrix} \sigma_{a_0}^2 & \sigma_{a_0, a^*} \\ \sigma_{a^*, a_0} & \sigma_{a^*}^2 \end{bmatrix}$$

and $\mathbf{A}$ was the additive genetic relationship matrix. The priors for the vectors $\mathbf{h}$, $\mathbf{p}$, and $\mathbf{l}$ were normally distributed: $\mathbf{h} \sim N(0, \mathbf{I}_h \sigma_h^2)$, $\mathbf{p} \sim N(0, \mathbf{I}_p \sigma_p^2)$, and $\mathbf{l} \sim N(0, \mathbf{I}_l \sigma_l^2)$, where $\mathbf{I}_h$, $\mathbf{I}_p$, and $\mathbf{I}_l$ were the identity matrices and σ_h^2 , σ_p^2 , and σ_l^2 were the variances of the HYM, group, and litter effects, respectively. The prior for the residuals in $\mathbf{e}$ was normally distributed and independent both within and between classes 1 and m , i.e.,

$$\mathbf{e} \sim N\left(0, \begin{bmatrix} \mathbf{I}_1 \sigma_{e1}^2 & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & \mathbf{I}_m \sigma_{em}^2 \end{bmatrix}\right),$$

where $\mathbf{I}_k$ was an identity matrix and σ_{ek}^2 was the residual variance of herd k for $k = 1$ to m . Flat priors were assumed for both “fixed” and variance parameters. This means that the “fixed” effects could be any real value with equal probability, while the values of the variance components could be any semi-positive definite covariance matrix with equal probability.

Model Dispersion and Derived Parameters

All 10k samples from the posterior distribution of model parameters were analyzed, and the posterior means and 95% highest posterior density

(HPD) regions were calculated for each parameter. In addition, a genetic covariance matrix of dimension 61×61 covering the range from -3 SD units of the HYM effect (σ_h) to $+3\sigma_h$ of sample i with 0.1 unit intervals (resulting in 61 intervals) was computed for each sample using the following equation:

$$\mathbf{G}_i = \mathbf{k}_i \mathbf{G}_0 \mathbf{k}_i' \quad (2)$$

where $\mathbf{k}_i$ was a 61×2 matrix of standardized HYM effects with the first column containing values of ones for the intercept and the second column containing the environmental gradient in the range $-3\sigma_h$ to $+3\sigma_h$ of sample i

$$\mathbf{k}_i = \begin{bmatrix} 1 & -3\sigma_{h_i} \\ \vdots & \vdots \\ 1 & +3\sigma_{h_i} \end{bmatrix}.$$

The matrix $\mathbf{G}_{0i}$ was sample i of the genetic covariance matrix ($\mathbf{G}_0$). The diagonal elements of $\mathbf{G}_i$ were the additive genetic variances for each given level of the standardized environmental gradient, and the off-diagonal elements were additive genetic covariances between different levels of the environmental gradient. The average additive genetic variance ($\bar{\sigma}_a^2$) was calculated as the average of the posterior means of additive genetic variance for the 61 intervals across the environmental gradient $-3\sigma_h$ to $+3\sigma_h$ units.

The additive genetic correlations between ADG at different environmental gradients ($r_{a,ij}$) were obtained from the correlation matrix computed from $\mathbf{G}_i$.

The heritability of ADG at environmental level (j) was calculated for each herd (k) using the following equation:

$$h_{jk_i}^2 = \frac{\sigma_{a,ji}^2}{\sigma_{a,ji}^2 + \sigma_{p_i}^2 + \sigma_{l_i}^2 + \sigma_{ek_i}^2} \quad (3)$$

where $\sigma_{a,ji}^2$ was the additive genetic variance at environmental level j in sample i (element jj in $\mathbf{G}_i$), $\sigma_{p_i}^2$ and $\sigma_{l_i}^2$ were the variances of the group effects and litter effects, respectively, in sample i , and $\sigma_{ek_i}^2$

was the residual variance of herd k in sample i . The average heritability ($\bar{h}^2$) was calculated as the average of the posterior means of heritability for the 61 intervals across the environmental gradient $-3\sigma_h$ to $+3\sigma_h$ units using the averaged posterior mean of the residual variance across the m herds.

The coheritability illustrates the possible response to selection in one trait when selecting on a correlated trait (Falconer and Mackay, 1996). In the current study, the focus was on the response in ADG at the average environmental level, when selection was on records from different environmental levels. The coheritability was, therefore, calculated between the performance in the environment at the average environmental level and the performance across the environmental gradient from $-3\sigma_{h_i}$ to $+3\sigma_{h_i}$ units:

$$\text{ch}_{m,j_{ki}} = h_{m_{ki}} \times h_{j_{ki}} \times r_{a_{m,j_i}} \quad (4)$$

where $h_{m_{ki}}$ and $h_{j_{ki}}$ were the square roots of the heritability in the environment at the average environmental level and at environmental level j , respectively, in herd k in sample i . $r_{a_{m,j_i}}$ was the correlation between ADG in the environment at the average environmental level and at environmental level j in sample i .

Cross-validation

In order to examine if the model with simultaneously inferred environmental covariates has higher predictive ability for EBVs than a model with known environmental covariates based on phenotypic HYM means, cross-validation was conducted for the two models. The only difference between the models was the method in obtaining the environmental covariate. The phenotypic means of each HYM ranged from 833 to 1,460 g d⁻¹ (mean 1,157 g d⁻¹, SD 81 g d⁻¹) in boars and from 730 to 1,409 g d⁻¹ (mean 1,137 g d⁻¹, SD 75 g d⁻¹) in gilts. The validation dataset was defined as animals born in 2017. For both models, EBVs were predicted base on the full data set and on a reduced dataset, where the records for the validation animals were excluded. The prediction ability was evaluated as the correlations between the EBVs for the validation animals predicted from the full and the reduced dataset. The bias of the two models were assessed by regressing the EBVs of the validation animals predicted from the full model on the EBVs of the validation animals predicted from the reduced model. Regression coefficients differing from 1 indicate bias.

RESULTS

The analysis showed significant additive genetic variance of macro-ES for both sexes (Table 2). The posterior mean of additive genetic variance for the intercept was 4% greater for boars than for gilts, while for slope it was 42% lower for boars than for gilts. The differences were not statistically significant since the HPD regions overlapped. The genetic correlations between intercepts and slopes were slightly negative for boars and positive for gilts, but not statistically different from zero in either sex. The average additive genetic variance was 10% greater for boars than for gilts. The average heritability was 12% less in boars compared to gilts. The average residual variance was 30% larger in boars than gilts, and had non-overlapping HPD regions.

Genetic Variances for Macro-ES

The posterior mean of the additive genetic variance changed for both boars and gilts when environments deviated from the mean (Figure 1). The increases in the genetic variance were not symmetric around the environment at the average level and there was a slight initial decrease for boars as the environment moves toward $+1\sigma_h$ units and for gilts as the environment moved toward $-1\sigma_h$. For boars, the additive genetic variance increased more when the environment was $-3\sigma_h$ units than $+3\sigma_h$ units.

Table 2. Posterior means and 95% highest posterior density regions in brackets of the additive genetic variance of the intercept ($\sigma_{a_0}^2$) and slope (σ_a^2), the genetic correlation between these (r_{a_0,a^*}), the variance of the HYM effect σ_h^2 , the average additive genetic variance ($\bar{\sigma}_a^2$), the average heritability ($\bar{h}^2$) and the average residual variance ($\bar{\sigma}_e^2$) of ADG in boars and gilts

	Boars	Gilts
$\sigma_{a_0}^2$	1,385 (1,114 to 1,677)	1,333 (1,139 to 1,536)
σ_a^2	0.014 (0.001 to 0.020)	0.024 (0.009 to 0.041)
r_{a_0,a^*}	-0.227 (-0.518 to 0.062)	0.144 (-0.035 to 0.356)
σ_h^2	5,076 (4,381 to 5,764)	3,755 (3,219 to 4,302)
$\bar{\sigma}_a^2$	1,599 (1,175 to 2,047)	1,611 (1,270 to 1,966)
$\bar{h}^2$	0.18 (0.14 to 0.22)	0.22 (0.18 to 0.26)
$\bar{\sigma}_e^2$	5,627 (4,785 to 6,554)	4,339 (3,917 to 4,781)

In gilts, the increase was greater when the environment deviated with $+3\sigma_h$ units than $-3\sigma_h$ units. The posterior mean was 29% greater for boars than gilts in the environment deviating with $-3\sigma_h$ units, while it was 32% less in the environment deviating with $3\sigma_h$ units. The HPD regions overlapped for additive genetic variance in boars and gilts.

Genetic Correlations Between Environments

The posterior mean of the genetic correlations between ADG in the environment at the average environmental level and ADG in the remaining environments was positive and high (Figure 2). Average daily gain in the extreme environment of $-3\sigma_h$ units showed a reduction in the genetic correlation from positive and high to positive and moderate when the environmental deviation was increased. This was also observed for ADG in the extreme environment of $+3\sigma_h$ units. The patterns of the genetic correlations were similar in boars and gilts.

Heterogeneous Residual Variance

The residual variance was heterogeneous among the herds for both sexes (Figure 3). The posterior mean for the largest residual variances was 1.8 times greater than the smallest residual variance in boars (herd 17 compared to herd 15), while in gilts it was 2.5 times greater than the smallest residual variance (herd 10 compared to herd 15). Boars had greater posterior means for residual variances than gilts in the 15 herds that reared both sexes. The HPD regions did not overlap between sexes for 10 out of the 15 herds that reared both sexes.

Heritability

The heritability of ADG increased from low to moderate when the environment deviated from the average environmental level for both boars and gilts (Figure 4). For boars, the heritability increased more in poor environments ($-3\sigma_h$) than in good

Figure 1. Posterior means and 95% highest posterior density (HPD) regions of the additive genetic variance over standardized units of the environmental effect range from $-3\sigma_h$ to $+3\sigma_h$ (SD of the herd-year-month on test, HYM, effect) units for boars (left) and gilts (right).

Figure 2. Posterior means of the additive genetic correlation between ADG in the -3 (dashed line), 0 (solid line) or $+3\sigma_h$ (SD of the HYM effect) unit environment and the environments in the range of $-3\sigma_h$ and $+3\sigma_h$ units for boars (left) and gilts (right).

Figure 3. Posterior means for the residual variance in each herd for boars (black) and gilts (red). Error bars indicate the highest posterior density regions.

Figure 4. Posterior means of the heritability calculated using the smallest (solid line) and largest (dashed line) residual variances (σ_e^2) for boars (left) and gilts (right) over the environmental range $-3\sigma_h$ to $+3\sigma_h$ (SD of the HYM effect) units.

environments ($+3\sigma_h$) for both the herds with the smallest and largest residual variance. For gilts, the heritability increased more when the environment deviated positively ($+3\sigma_h$) than when the environment deviated negatively ($-3\sigma_h$) for both the herd with the smallest and largest residual variance. The heritability of ADG in the environment at the average environmental level was 7% less in boars than gilts for the herd with the largest residual variance and 26% less in boars than gilts in the herd with the smallest residual variance. The posterior means of heritability of ADG at the average environmental level for boars and gilts had overlapping HPD regions.

Coheritability of Predicting ADG in the Average Environment

The posterior mean of the $ch_{m,j}$ changed for both boars and gilts when j ranged from $-3\sigma_h$ to $+3\sigma_h$ (Figure 5). For boars, $ch_{m,j}$ was greater than the heritability in the environment at the average level in poor environments ($j = -3\sigma_h$) and less in good environments ($j = +3\sigma_h$) for both the herd with the smallest and largest residual variance. For gilts, $ch_{m,j}$ was less than the heritability in the environment at the average level in poor environments ($j = -3\sigma_h$) and greater in good environments

Figure 5. Posterior means and 95% highest posterior density bands of the coheritability for the herds with the smallest (solid line) and largest (dashed line) residual variances (σ_e^2) between an environment at the average environmental level and the environments deviating between $-3\sigma_h$ and $+3\sigma_h$ (SD of the herd-year-month on test effect) units for boars (left) and gilts (right).

($j = +3\sigma_h$) in the herd with the largest residual variance. In the herd with the smallest residual variance, $ch_{m,j}$ was less than the heritability in the environment at the average level in poor environments ($j = -3\sigma_h$) units and the same in good environments ($j = +3\sigma_h$).

Cross-validation

The predictive ability for EBVs of the model with simultaneously inferred environmental covariate was greater than for the model with phenotypic means of each HYM as environmental covariate for both direct EBVs and EBVs for macro-ES of ADG for both sexes (Table 3). The model with phenotypic means of each HYM as environmental covariate was significantly biased for both direct and macro-ES EBVs for both sexes (Table 4). Direct EBVs were unbiased for the model with simultaneously inferred environmental covariate in both sexes. Macro-ES EBVs were significantly less biased for females for the model with simultaneously inferred environmental covariate compared to the model with phenotypic means of each HYM as environmental covariate.

DISCUSSION

In this study, the genetic variation in macro-ES for ADG in boars and gilts was investigated using a Bayesian reaction norm model with simultaneously inferred covariates developed by Su et al. (2006). The model accounted for heterogeneity of residual variance for each herd tested. The Bayesian method provided estimates of marginal posterior distributions of the environmental and genetic parameters simultaneously, which is expected to minimize bias in variance estimation (Su et al., 2006).

Table 3. Correlations between the EBVs for the validation animals predicted from the full and the reduced dataset for the model with simultaneously inferred environmental covariate (*I*) and the model with phenotypic means of each HYM as environmental covariate (PM) for boars and gilts

	Boars		Gilts	
	<i>I</i>	PM	<i>I</i>	PM
Direct EBV	0.69	0.59	0.74	0.72
Macro-ES EBV	0.77	0.58	0.90	0.73

Average daily gain in Danish Duroc has previously been analyzed by Shirali et al. (2017), using a model with homogeneous genetic and residual variances across sexes, environments and herds. In the current study, the reaction norm model showed similar average additive genetic variance for boars and average heritability for gilts to the ones reported by Shirali et al. (2017). The significant differences in genetic parameter estimates can be due to differences in the model and dataset used.

Genotype by Environment Interaction

Existence of $G \times E$ for ADG in Danish Duroc boars and gilts was illustrated by significant variation in macro-ES. Li and Hermes (2016) reported significant sire by environment interactions (variance of slope 0.013, SE 0.004) for ADG in Australian Large White, Landrace and Duroc pigs using a sire reaction norm model. The posterior means of the additive genetic variance of slope found in our study were in the same range as values presented by Li and Hermes (2016). The additive genetic correlations between intercept and slope in our study were low and not significantly different from zero in either of the sexes, which means the

Table 4. Regression coefficients (SD) of a linear regression of EBVs for the validation animals predicted from the full dataset on the EBVs for the validation animals predicted from a reduced dataset for the model with simultaneously inferred environmental covariate (*I*) and the model with phenotypic means of each HYM as environmental covariate (PM) for boars and gilts

	Boars		Gilts	
	<i>I</i>	PM	<i>I</i>	PM
Direct EBV	0.98 (0.03)	0.73 (0.03)	1.00 (0.03)	0.73 (0.02)
Macro-ES EBV	0.69 (0.02)	0.70 (0.03)	0.86 (0.01)	0.74 (0.02)

EBV for the additive genetic intercept (direct EBV) cannot be used to predict the EBV for macro-ES (additive genetic slope) or vice versa. This is in agreement with Li and Hermes (2016) who reported low and nonsignificant correlation between sire intercept and slope (-0.16 , SE 0.09). The nonsignificant correlations found in the current study does not support the common hypothesis that greater growth rate is associated with greater sensitivity. Li and Hermes (2016) reached the same conclusion. Thus, macro-ES does not necessarily increase when selecting for ADG (intercept) and it is possible to select on macro-ES of ADG without reducing the progress in ADG. It is important to recognize that the correlation between intercept and slope in a reaction norm model is dependent on the position of the intercept (0 on the environmental scale) and studies using different positions for intercept cannot be compared directly. The current study, as well as Li and Hermes (2016), placed the intercept at the average environmental level.

The significant $G \times E$ causes the additive genetic variance to change as the environment deviated from the environment at the average environmental level. This in turn caused the heritability to change as the environment deviated from the average environmental level. The convex curve of the additive genetic variance and heritability observed in this study is expected. This is due to the covariance function used to calculate the additive genetic variances, which put more emphasis on the additive genetic variance of slope with greater deviations from the mean. This is evident from Eq. 2. If the formula for the j th diagonal elements (additive genetic variances in environment j) in $\mathbf{G}$ is written out it becomes: $\sigma_{a_j}^2 = \sigma_{a_0}^2 + \sigma_a^2 \times h_j^2 + 2\sigma_{a_0a} \times h_j$, where h_j is the j th standardized HYM effect. As the equation includes the covariance between the additive genetic intercept and slope, the minimum of the curvature is not at zero and the increase in additive genetic variance and heritability are not symmetric around zero. The additive genetic variance therefore increased more in boars in the poor environments and more for gilts in the good

environments. Although the curves are forced to be globally convex by the function, if the minimum falls outside the range of the data it is possible to only observe a continuously increasing or decreasing function in the range of the data. In the current study, the minimum of the curve fell within the range from $-3\sigma_h$ to $+3\sigma_h$ units for both sexes. To validate the curves, an analysis was conducted where the environmental gradient was replaced with three categories of HYM effects (bad: $\hat{h} < -1\sigma_h$, average: $-1\sigma_h \leq \hat{h} \leq +1\sigma_h$ and good: $\hat{h} > +1\sigma_h$) using a linear spline and suppressing the intercept. Such a model is basically a multivariate model for the additive genetic part of the model yielding genetic variances and covariances for three “traits” as defined (bad, average, and good). Results showed an increased additive genetic variance in the bad and good environments compared to the average environment (results not shown). This validates that the increase in additive genetic variance obtained from the reaction norm model was not an artifact of the model.

Causes of Macro-ES

Our study found increased additive genetic variance when environments become extreme due to the presence of significant additive genetic variance of macro-ES, as also suggested by studies on *Drosophila* (Ørsted et al., 2018). Wilson et al. (2006) studied birth weight of wild Soay lambs as function of environments and found increased maternal genetic variation in good environments and limited maternal genetic variation in poor environments. The current study showed greater genetic variance in both good and poor environments. Wilson et al. (2006) used random regression to fit the maternal genetic effects as a polynomial function of environmental quality. Environmental quality was defined as the proportion of lambs surviving until October 1 of their birth year standardized to the interval -1 to 1 (Wilson et al., 2006). This way of defining the environmental quality means poor environments impose natural selection on the lambs, which can

decrease the additive genetic variance. Natural selection has been shown to reduce the genetic variance for fledgling body condition in collared flycatchers (*Ficedula albicollis*) (Merilä et al., 2001). In the current study, the environmental span does not include environments poor enough to induce natural selection on the animals, which allows for the observed increase in variation in poor (as well as good) environments. Hoffmann and Merilä (1999) suggested that increased genetic variance in poor environments can arise when resource limitations induce phenotypic differences among genotypes. In the context of our study, highly macro-ES pigs in (extremely) unfavorable environment may suffer more from the poor conditions, such as resource limitations, than the less macro-ES animals increasing the additive genetic variance. The increased additive genetic variance in the (extremely) favorable environments can then be interpreted as the highly macro-ES pigs' greater ability to utilize the good conditions and express their genetic potential than their less macro-ES counter parts.

Heterogeneity Between Sexes

In the current study, we report greater additive genetic variance and residual variances for boars than for gilts and greater posterior mean of heritability for gilts than for boars. Saintilan et al. (2012) reported greater heritability of ADG for gilts than boars in French Large White pigs and Nielsen et al. (2018) reported the same findings for Danish Landrace despite greater additive genetic variance of ADG in boars. Mebratie et al. (2017) found male broiler chicken to have greater additive genetic variance than females and showed that accounting for the heterogeneity in genetic evaluation models may increase the accuracy of ranking of animals. The differences in additive genetic and residual variance between boars and gilts may be due to physiological differences between boars and gilts. Boars grow faster than gilts (Blanchard et al. 1999), which directly affects the variance parameters. Nielsen et al. (2018) analyzed the social genetic effects of Danish Landrace boars and gilts and reported that gilts may be more competitive than boars due to significant unfavorable genetic correlation between direct and social genetic effects for gilts but not for boars. In poor environments, competition would be expected to increase as the animals experience sub-optimal resources, which may have a greater impact on gilts than on boars due to gilts competing more with other gilts than boars. This may be one of the underlying reasons for the greater additive genetic

variance of macro-ES in gilts than in boars. Greater additive genetic variance of macro-ES in gilts than boars indicates more sensitivity to environmental challenges in gilts.

Selection Across Environments

We found moderate positive genetic correlations between ADG in the most extreme environments. Mulder and Bijma (2006) argued that if the genetic correlation between performances in different environments is below 0.6–0.7, then different breeding programs are needed to ensure high selection response in both environments. Following the suggestion by Mulder and Bijma (2006), one should develop different breeding schemes each covering only environments with maximally $3\sigma_h$ units difference for gilts and $4\sigma_h$ units difference for boars. This may not be a practical approach, as the current study demonstrated that the difference in HYM does span the $-3\sigma_h$ to $+3\sigma_h$ units range within many of the herds (results not shown). Considerations of macro-ES in breeding value estimation may make it possible to increase the genetic correlation of ADG in different environments by selecting for reduced macro-ES of ADG. Due to the nonsignificant genetic correlations between additive genetic intercept and slope, selection to reduce macro-ES of ADG should not affect ADG itself.

Aside from the genetic correlations between performances in different environments, the selection response across environments also depends on the heritability in the different environments. If the heritability in environment 1 is greater than the heritability in environment 2, then the difference in heritability may offset a reduction in genetic correlation between the two environments and higher selection response may be obtained in environment 2 through selection in environment 1. This property stems from the coheritability (Falconer and Mackay, 1996), which illustrates the possible response to selection in one trait when selecting on a correlated trait. The correlated response to selection is given by $CR_1 = i_2 \times ch_{1,2} \times \sigma_{P_1}$, where i_2 is the selection pressure on trait 2, $ch_{1,2}$ is the coheritability of the two traits and σ_{P_1} is the phenotypic standard deviation of trait 1 (Falconer and Mackay, 1996). In the current study, the two traits were ADG at the average level and ADG at the deviating environments. The observed reduction in $ch_{m,j}$ in good environments ($j > 0\sigma_h$) for boars and in poor environments ($j < 0\sigma_h$) for gilts is due to less than unity of the genetic correlation between

ADG in different environments. The heritabilities in these environments are not high enough to offset the decline in genetic correlation. Coheritability has previously been shown to decrease with a decreasing genetic correlation between environments for BW in rainbow trout (Sae-Lim et al., 2015). The increase in $ch_{m,j}$ observed in poor environments ($j < 0\sigma_h$) for boars is due to the greater heritabilities in these environments. The consistency or increase for gilts in good environments ($j > 0\sigma_h$) is also due to the greater heritability in these environments, compared to poor environments ($j < 0\sigma_h$). The selection response in the environment at the average level will be increased when selecting boars from the $-3\sigma_h$ units environment, due to the increase in $ch_{m,j}$. Depending on the herd, the selection response will increase or stay the same when selecting gilts from the $+3\sigma_h$ units environment. However, due to the reduced $ch_{m,j}$, selecting boars from the $+3\sigma_h$ units environment and gilts from the $-3\sigma_h$ units environment will reduce the selection response in the environment at the average environmental level. This can be avoided by including both direct and macro-ES EBVs in the selection index. It is, therefore, necessary to consider reaction norms in optimum statistical modeling of ADG in genetic selection programs.

Selection of breeding animals takes place in all nucleus herds. The current study found differences in residual variance among nucleus herds for both boars and gilts. The presence of herd-specific residual variances has previously been shown (Tempelman et al., 2015). The differences in residual variance result in herd-specific heritabilities, meaning that some herds have greater potential selection response. Disregarding heterogeneity of residual variance across herds in statistical models may lead to inaccuracies in prediction of breeding values for animals in herds with more extreme residual variance. The accuracies of EBVs depend on the heritability of the trait of interest. The heritability in herds with a large residual variance may be greater when the residual is considered homogeneous compared to when it is treated as heterogeneous, resulting in inflated accuracies. The opposite holds for herds with low residual variance. Inaccurate EBVs will lead to a reduced selection response. Therefore, considering heterogeneity in residual variance in the statistical model can benefit genetic improvement of traits in breeding programs.

Estimation of the Environmental Covariate

In reaction norm models, the environmental covariates are assumed known, which is not the case

in many circumstances. The environmental covariates therefore have to be estimated. The estimation can be done before inclusion of the environmental covariate in the model, such as the phenotypic mean of the individuals in a particular environment (Calus et al., 2004), preadjusted phenotypic means (Kolmodin et al., 2002), or the least-squared means derived from a model without a reaction norm (Li and Hermes, 2016). However, using any of these methods to obtain the environmental covariate includes a function of the data in the reaction norm model (Kolmodin et al., 2002) and treats the covariate as known. Together these effects result in an understatement of the uncertainty of the model (Su et al., 2006) and lead to inaccuracies due to not accounting for the uncertainty of estimating the environmental covariates. Alternatively, an iterative procedure, where the environmental covariate is updated each iteration, can be used (Calus et al., 2004; Su et al., 2006). Calus et al. (2004) compared a reaction norm model using the phenotypic means of herds as an environmental covariate to a reaction norm model that used the herd effects estimated in the previous iteration as the covariate. They found similar prediction ability between the models. However, their model used the fixed effect directly, without correcting for the error of estimates. This may help explain the differences between their study and the study of Su et al. (2006) who found that simultaneously inferring the environmental values along with other parameters performed better than a model using phenotypic means as environmental covariate. In agreement with the findings of Su et al. (2006), we found greater prediction ability of EBVs for the simultaneously inferred environmental covariate model than a model with phenotypic mean in each HYM as the environmental covariate. We also found no bias of predicting direct EBVs for both sexes and reduced bias of predicting macro-ES EBVs for gilts using the model with simultaneously inferred environmental covariate compared to the model with phenotypic mean in each HYM as the environmental covariate. The greater prediction ability and reduced bias indicate that the Bayesian method integrates out the error in estimating the environmental covariates and therefore increases the accuracy of estimating breeding values.

CONCLUSION

We found significant genetic variance of macro-ES in ADG due to the HYM effect for Danish Duroc boars and gilts, using a univariate reaction norm model with simultaneously inferred environmental covariate and heterogeneous

residual variance. The posterior mean of the additive genetic variance and heritability was increased in the extreme environments. The genetic correlation between intercept and slope was not significantly different from zero and selecting for ADG (intercept) does not necessarily increase macro-ES. The coheritability between performance in the environment at the average environmental level and performance at a different level of the environmental gradient from $-3\sigma_{h_i}$ to $+3\sigma_{h_i}$ units decreased in environments deviating positively for boars and environments deviating negatively for gilts. This was due to the heritability in these environments not being high enough to offset the less than unity genetic correlations between ADG at different levels of the environmental gradient (HYM effects). Variances were different in the two sexes with greater genetic and residual variances in boars than in gilts. The heritability was greater in gilts than boars. The analysis further showed differences in posterior means of the residual variance between herds, showing that consideration of the heterogeneity of the residual variance is relevant for practical breeding. The reaction norm model with simultaneously inferred covariates and heterogeneous residual variance is a feasible approach to estimate genetic parameters considering macro-ES and differences in residual variance among herds.

LITERATURE CITED

- Blanchard, P., M. Ellis, C. Warkup, J. Chadwick, and M. Willis. 1999. The influence of sex (boars and gilts) on growth, carcass and pork eating quality characteristics. *Anim. Sci.* 68:487–493. doi:10.1017/S1357729800050499
- Calus, M. P., P. Bijma, and R. F. Veerkamp. 2004. Effects of data structure on the estimation of covariance functions to describe genotype by environment interactions in a reaction norm model. *Genet. Sel. Evol.* 36:489–507. doi:10.1051/gse:2004013
- Falconer, D. S., and T. F. C. Mackay. 1996. Introduction to quantitative genetics. Essex: Pearson Education Limited.
- Hoffmann, A. A., and J. Merilä. 1999. Heritable variation and evolution under favourable and unfavourable conditions. *Trends Ecol. Evol.* 14:96–101. doi:10.1016/S0169-5347(99)01595-5
- Kolmodin, R., E. Strandberg, P. Madsen, J. Jensen, and H. Jorjani. 2002. Genotype by environment interaction in Nordic dairy cattle studied using reaction norms. *Acta Agric. Scand. A.* 52:11–24.
- Li, L., and S. Hermes. 2016. Evaluation of sire by environment interactions for growth rate and backfat depth using reaction norm models in pigs. *J. Anim. Breed. Genet.* 133:429–440. doi:10.1111/jbg.12207
- Madsen, P., and J. Jensen. 2013. A user's guide to DMU Ver. 6, rel. 5.2. Available from http://dmu.agrsci.dk/DMU/Doc/Current/dmuv6_guide.5.2.pdf (accessed 15 January 2018).
- Mebratie, W., M. Shirali, P. Madsen, R. L. Sapp, R. Hawken, and J. Jensen. 2017. The effect of selection and sex on genetic parameters of body weight at different ages in a commercial broiler chicken population. *Livest. Sci.* 204:78–87. doi:10.1016/j.livsci.2017.08.013
- Merilä, J., L. E. B. Kruuk, and B. C. Sheldon. 2001. Natural selection on the genetical component of variance in body condition in a wild bird population. *J. Evol. Biol.* 14:918–929. doi:10.1046/j.1420-9101.2001.00353.x
- Mulder, H. A. 2016. Genomic selection improves response to selection in resilience by exploiting genotype by environment interactions. *Front. Genet.* 7:178. doi:10.3389/fgene.2016.00178
- Mulder, H. A., and P. Bijma. 2006. Benefits of cooperation between breeding programs in the presence of genotype by environment interaction. *J. Dairy Sci.* 89:1727–1739. doi:10.3168/jds.S0022-0302(06)72241-X
- Nielsen, H. M., B. Ask, and P. Madsen. 2018. Social genetic effects for growth in pigs differ between boars and gilts. *Genet. Sel. Evol.* 50:4. doi:10.1186/s12711-018-0375-0
- Ørsted, M., P. D. Rohde, A. A. Hoffmann, P. Sørensen, and T. N. Kristensen. 2018. Environmental variation partitioned into separate heritable components. *Evolution* 72:136–152. doi:10.1111/evo.13391
- R Core Team. 2018. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing. Available from <https://www.R-project.org/> (accessed 17 May 2018).
- Sae-Lim, P., H. Mulder, B. Gjerde, H. Koskinen, M. Lillehammer, and A. Kause. 2015. Genetics of growth reaction norms in farmed rainbow trout. *PLoS One* 10:e0135133. doi:10.1371/journal.pone.0135133
- Saintilan, R., P. Sellier, Y. Billon, and H. Gilbert. 2012. Genetic correlations between males, females and castrates for residual feed intake, feed conversion ratio, growth rate and carcass composition traits in large white growing pigs. *J. Anim. Breed. Genet.* 129:103–106. doi:10.1111/j.1439-0388.2011.00972.x
- Shirali, M., A. B. Strathe, T. Mark, B. Nielsen, and J. Jensen. 2017. Joint analysis of longitudinal feed intake and single recorded production traits in pigs using a novel horizontal model. *J. Anim. Sci.* 95:1050–1062. doi:10.2527/jas.2016.0606
- Smith, B. J. 2016. boa: an R package for MCMC output convergence assessment and posterior inference. *J. Stat. Softw.* 21:1–37.
- Su, G., P. Madsen, M. S. Lund, D. Sørensen, I. R. Korsgaard, and J. Jensen. 2006. Bayesian analysis of the linear reaction norm model with unknown covariates. *J. Anim. Sci.* 84:1651–1657. doi:10.2527/jas.2005-517
- Tempelman, R. J., D. M. Spurlock, M. Coffey, R. F. Veerkamp, L. E. Armentano, K. A. Weigel, Y. de Haas, C. R. Staples, E. E. Connor, Y. Lu, et al. 2015. Heterogeneity in genetic and nongenetic variation and energy sink relationships for residual feed intake across research stations and countries. *J. Dairy Sci.* 98:2013–2026. doi:10.3168/jds.2014.8510
- Wilson, A. J., J. M. Pemberton, J. G. Pilkington, D. W. Coltman, D. V. Mifsud, T. H. Clutton-Brock, and L. E. Kruuk. 2006. Environmental coupling of selection and heritability limits evolution. *PLoS Biol.* 4:e216. doi:10.1371/journal.pbio.0040216