Genetic parameters for body weight of the Goettingen minipig estimated with multiple trait and random regression models

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Introduction

The Goettingen minipig is a laboratory animal which has a widespread popularity in medical and pharmaceutical research because of its shared anatomic and physiologic characteristics with humans. Low body weight of the minipig is a necessary trait because handling in medical experiments is facilitated and also the costs for housing, feeding and dosing are lower. At the moment there is no selection for a low body weight and the genetics of low body weight of Goettingen minipigs at different ages are still unknown.

A popular method to estimate genetic parameters of a trait with repeated measures is the multiple trait model (**MTM**). In this approach, every measurement is treated as a (genetically) different trait. Body weight is a trait where the phenotype of an animal can be represented by a continuous function of time. Thus, this trait is characterized by a trajectory with a theoretically infinite number of measurements. Therefore, a model is appropriate which considers the complex covariance structure. In the infinite-dimensional approach, the covariance structure is modelled as a covariance function (**CF**) (Kirkpatrick et al., 1990). A useful tool for the estimation of CF is the random regression model (**RRM**).

The aims of this study were the estimation of genetic parameters for the trait 'body weight' with multiple trait (**MT**) and random regression (**RR**) analysis and the comparison of these two methods with regard to further routine application for the prediction of breeding values.

Material and methods

Body weight data were provided from Ellegaard Goettingen Minipigs ApS, Denmark, where two subpopulations of the Goettingen minipig base population are housed in two units which are entirely separated from each other. The data were acquired from 1995 to 2005. The minipigs were weighed routinely at various intervals, without a special treatment like fasting before weighing. In total the original dataset contained 199,764 body weight records of 33,749 animals. One data set was prepared out of this data for the MT and RR analysis. This data set focused on the time period from 30 to 400 d of age because of scarcity of body

weight recordings after day 400. The body weights from day 0 to day 29 were also excluded, because they are influenced by the parity and the lactation of the sow and can not be classified as independent body weight traits like those after weaning.

8 age classes were built for the consideration of different traits in the MTM and heterogeneous residual variances in the RRM (Table 1). Every animal considered in this time period had at least 5 weight recordings with only one record per age class. The body weight record that was closest to the average age per age class was accounted for the analysis. This resulted in 38,023 records of 6,713 animals.

Age class	Age range in d	n records	Mean weight in kg	Variance of weight in kg ²
1	30-60	5,792	3.33	1.04
2	61-100	5,761	5.28	1.54
3	101-150	5,855	8.36	3.24
4	151-200	5,821	11.84	5.61
5	201-250	5,639	15.25	7.82
6	251-300	4,105	18.69	9.06
7	301-350	3,012	21.82	10.14
8	351-400	2,038	24.86	10.48

Table 1. Age classes, age range, mean body weight and variance of body weight per age class

The used MTM was as follows:

$$y_{ijklmn} = \mu_n + sex_{in} + unit_{jn} + year_{kn} + \sum_{r=1}^{c_n} \beta_{nr} \left(t_{ijklmn} - \overline{t_n} \right) + a_{ijklmn} + l_{ln} + e_{ijklmn} ,$$

where y_{ijklm} = weight in age class n of animal m within sex i, unit j and birth year k; sex_{in} = fixed effect of sex i; $unit_{jn}$ = fixed effect of unit j; $year_{kn}$ = fixed effect of birth year k; β_{nr} = fixed regression coefficient for linear ($c_n = 1$) and quadratic ($c_n = 2$) polynomials; \bar{t}_n = average age per age class n; t_{ijklm} = age at weighing per age class; a_{ijklm} = random additive-genetic effect for animal m; l_{ln} = random common environmental effect for litter l; and e_{ijklm} = random measurement error. For the regression on age at weighing per age class, polynomials of different orders of fit were applied. For age classes 1 and 2 quadratic and for age classes 3 to 8 linear polynomials were used. Higher orders of fit did not achieve a significant influence (P < 0.001, F-statistic, SS Type 1).

For the analysis with RRM, Legendre polynomials (**LP**) for the regression on age at weighing were used for modelling the random effects. Therefore, the age at which the body weight recordings were taken had to be rescaled to a standardized age t* for the orthogonal functions,

using the formula (Schaeffer, 2004): $t^* = \frac{2(t - t_{\min})}{(t_{\max} - t_{\min})} - 1$, where t_{\min} is the youngest age, here

30 d of age, and t_{max} is the oldest age, here 400 d of age. The used RRM was:

$$y_{ijkl}(t) = \mu + S_i + U_j + Y_k + \sum_{r=1}^{3} \beta_r t^r + \sum_{s=1}^{s} \alpha_{sijkl} \phi_s(t^*) + \sum_{s=1}^{s} \gamma_{sijkl} \phi_s(t^*) + \sum_{s=1}^{s} \rho_{sj} \phi_s(t^*) + \varepsilon_{ijkl},$$

where $y_{ijkl}(t)$ = weight of animal l at age t within sex i, unit j and birth year k; S_i = fixed effect of sex i; U_j = fixed effect of unit j; Y_k = fixed effect of birth year k; β_r = fixed cubic regression coefficient; t = age in d; t^* = age standardized to the range -1 to 1; ϕ_s = value of the s-th LP at standardized age t^* ; α_{sijkl} = random regression coefficient for additive-genetic effects; γ_{sijkl} = random regression coefficient for permanent environmental effects; ρ_{sj} = random regression coefficient for common environmental effects for litter; and ε_{ijkl} = random measurement error. The estimation of variance components with both models was carried out using the VCE-5 software package (Kovac and Groeneveld, 2002).

Results and discussion

This is the first genetic study made for body weight of the Goettingen minipig in such detail. Additionally, the used data set is unique in pig research due to the high number of animals which had at least five weight recordings over a wide time range.

After examining the estimated variances and variance ratios for all models, the best fitting RRM was the model with a polynomial of third order of fit for the fixed effects and LP of second order of fit for all random effects. The heritabilities estimated with the MTM and RRM were moderate with higher heritabilities estimated with the RRM (Figure 1). The decrease of the estimated heritability at 80 d of age occurs with both models and is due to high residual variance ratios at this age. This can be explained by a lower number of analysed weight recordings in the second age class and a higher variance in weights compared to the first age class. In the study of Malovrh (2003), the heritabilities estimated with a MTM also including animal and litter as random effects were higher than in our study. Additionally, Malovrh (2003) tested the influence of maternal genetic effect on pig growth with the MTM. She found out, that the maternal effect caused only a small proportion of variance compared to the other random effects. Thus, the maternal effect can be neglected in growth studies for pigs if the pigs are weaned at an age of 21 to 28 d. Another important fact is the exclusion of birth weight in the analysis. Implausible values of variance components often occur at

extreme ages like at birth. This is mainly a problem with high order polynomials (Meyer, 2005). Thus, including birth weights increased the order of fit for the best fitting polynomial model in a significant way in the study of Meyer (2001).



Figure 1. Heritabilities for body weight estimated with MTM and RRM.

Phenotypic and genetic correlations between body weights in different age classes estimated with MTM and RRM decreased while the distance between the age classes increased as it was expected (Figure 2).





The estimation of genetic parameters with RRM provides an insight into the effects of selection across the growth trajectory by examining the eigenfunctions and eigenvalues. The

estimates of the first eigenfunction were positive throughout. This indicates that selection between d 30 to d 400 changes the pattern of growth in the same direction, i.e. selection on low body weight at d 30 will also lead to a low body weight at d 400. The first eigenvalue explained 89.93 % of the genetic variation. As it is outlined by Kingsolver et al. (2001) eigenvalues indicate the amount of variance explained by its associated eigenfunction. Thus, a successful selection on low body weight is possible. The second and third eigenfunction explained in total only 10.07 % of the genetic variation and can therefore be neglected.

For the estimation of genetic parameters with RRM on the basis of weight recordings with an uneven distribution as it is given in original, not adjusted data sets with minipig body weights, an adjustment of the results based on estimates from MTM and literature information could be necessary. Another problem is a possible poor fit of growth curves estimated with RRM using LP. LP require large data sets with an almost homogeneous distribution of weight recordings for a successful estimation of variance components (Misztal, 2006).

With regard to a practicable application for the regular estimation of breeding values, the MTM seems to be more robust. However, the RRM is a useful tool for the examination of eigenfunctions. Compared to the MTM, the RRM is a more sophisticated model, but needs well-structured data. Further, for every new data set the best fitting model has to be found. It is therefore more difficult to implement the RRM in a routinely working procedure for the estimation of breeding values. On the basis of these results it is possible to construct a breeding scheme with a focus on the reduction of body weight, through a change of the growth curve.

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