

ORIGINAL ARTICLE

Breeding for low body weight in Goettingen minipigsF. Köhn¹, A.R. Sharifi¹, H. Täubert¹, Š. Malovrh² & H. Simianer¹¹ Institute of Animal Breeding and Genetics, Georg-August-University, Göttingen, Germany² Animal Science Department, Biotechnical Faculty, University of Ljubljana, Domžale, Ljubljana, Slovenia**Keywords**

body weight; genetic parameters; Goettingen minipig; growth curve; selection.

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Summary

The Goettingen minipig is a laboratory animal with increasing popularity in medical research. To get a genetically smaller minipig, a new breeding scheme with a focus on weight reduction has to be developed. Therefore, 19 505 body weight measurements of 3461 Goettingen minipigs were analysed with multiple trait models and random regression models (RRM) for the estimation of genetic parameters. Heritabilities were moderate with slightly higher values estimated with the RRM. Genetic correlations between body weight measurements at different ages were decreasing with increasing time lag between the measurements. An operational breeding goal for relative weight reduction RWR is suggested in which the weight reduction in each age class is expressed as per cent of the actual body weight and is weighted according to the proportion of animals sold in this age class. Expected genetic progress was calculated for two different selection ages (80 and 150 days). Selection at age 150 days leads to an expected genetic progress of 3.9 % RWR per year. And it is shown how the selection for RWR will modify the shape of the growth curve. On the basis of these results, a new breeding scheme with a focus on weight reduction can be implemented, which also has to account for correlated undesirable effects, like decline of fertility and increased rate of inbreeding.

Introduction

Animal models are essential for assessing the safety of new pharmaceuticals or new surgical techniques. Usually, two different species have to be used as toxicological models in pharmacology, a rodent like mice or rats and a non-rodent species. As a non-rodent species, pigs have many advantages compared with dogs, which are at the moment still the most widely used non-rodent species in medical research. Pigs show high similarities to humans concerning the cardiovascular system, the gastro-intestinal tract, the lung, kidney, liver, the immune system, and the skin and skeleton (Holtz & Bollen 1999). A main point which makes the pig more advantageous than the dog is that the pigs are usually not used as pets and therefore the emotional barrier to use pigs in

medical experiments is much lower than in dogs (Gad 2007). As pigs are difficult to handle because of their large size, special small pig breeds were developed to facilitate the handling. The Goettingen minipig was bred at the University of Goettingen in the 1960s. It combines the advantageous characteristics of pigs with a small size and therefore is of increasing popularity as an animal model for pharmaceutical and toxicological studies.

In drug development and testing, the test compounds always are administered per kilogram body weight. Because especially in the early phases of testing the cost per weight unit of compound may be extremely high, a low body weight of an experimental animal is very desirable and in many cases will be the dominating criterion for the choice of the species to be used. As the average adult body weight

of a Goettingen minipig is 35–45 kg (Bollen *et al.* 1998) compared with that of the adult body weight of the often used beagle dog of 18 kg, this difference may abolish the otherwise more attractive features of the Goettingen minipig, especially its similarity to humans in many biological criteria. This similarity is still given even so the body weight difference between humans and minipigs is increased after breeding for a smaller minipig. However, for analysing special diseases like obesity or diabetes Goettingen minipigs with typical characteristics for the certain disease can be provided.

Besides the Goettingen minipig base population in Germany, there are two populations in Denmark and one in the USA. In neither of the populations selection for low body weight is carried out at the moment, despite the customers' demand for an even smaller minipig for easy handling and low costs of dosing, feeding and housing. As previous studies showed, it is in principle possible to select for a genetically small minipig (Brandt *et al.* 1997).

Objectives for breeding differ in many ways between Goettingen minipigs and slaughter pigs (and most of the other farm animals). The most obvious difference is that in the minipig the objective is to reduce the weight gain per time unit, whereas in the meat producing species higher daily gains are desirable. Another special characteristic is that Goettingen minipigs are sold at all ages, from weaned piglets to adult animals, depending on the specific research topic of the end user. Although most minipigs used in toxicology and drug testing (which is the main use) are purchased at age 4–6 months, significant numbers are sold in other age groups. Also, the time span of the minipigs used in experiments varies from a few days to long-term studies over 1 year or more. The third characteristic is that it is virtually impossible to assign a reasonable economic weight to the body weight. While in some fields of application (like experimental surgery) body weight is essentially meaningless as long as it stays within a given wide range, a weight reduction of 1 kg in the early phase of toxicology trials may literally save thousands of euros (strongly depending on the cost of the synthesis of the compound to be tested). If compound availability is a quantitative problem, smaller animals requiring lower doses will even reduce the time to market for the drug to be developed which can have an enormous economic impact.

The aims of this study were the estimation of genetic parameters, the prediction of breeding values for body weight and the calculation of genetic progress dependent on the age at selection. Genetic

parameters were estimated using multiple trait models (MTM) and random regression models (RRM).

While it is obvious that a smaller minipig would be advantageous in many applications, the definition of an operational breeding goal needs to be discussed and a suggestion will be made in this study. Based on this composite breeding objective, we estimate the achievable genetic gain per year and discuss different aspects and eventual obstacles of a practical implementation of the suggested breeding scheme.

Data 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. Both units are completely separated from each other, both physically and genetically. Analysed body weights were measured from 1995 to 2005. The minipigs were weighed routinely at birth, then at weaning (age 21–28 days) and again at age 8 weeks, before leaving the rearing unit. Later, all minipigs were weighed once each month, and each minipig was weighed before it was sold. Because minipigs are sold for different purposes at very different ages, the number of available measurements per pig varies considerably.

In total, the original dataset contained 199 764 body weight measurements of 33 749 animals. Because of scarcity, body weights measured after 700 days of age were excluded from analyses. Outliers of the data set were also excluded using the studentized residual as an analyser for the influence of every single observation on the parameter estimates of a normal regression (Belsley *et al.* 1980). This resulted in 180 092 body weight measurements of 32 510 animals.

A data set with a focus on 30–700 days of age was extracted out of this data for the analysis with RRM and MTM. The body weights from day 0 to day 29 were excluded, because of an influence by the parity and the lactation length of the sow. These body weights cannot be classified as independent body weight traits like those after weaning because of the mentioned influence of parity and lactation effects. As shown by Oldigs (1986), birth and weaning weights cannot be used for the prediction of weights at later ages. Compared with the previous study, where genetic parameters for a time period of 30–400 days were estimated (Köhn *et al.* 2007b), the time period up to 700 days was chosen in this study to get additional genetic parameters for body weight at later ages and to analyse the genetic correlations

Table 1 Age classes, age range (in days), number (n) of records, mean body weight (in kg) and variance of body weight (in kg²) per age class

Age class	Age range (in days)	n	Mean weight (in kg)	Variance of weight (in kg ²)
45	30–60	3043	3.28	1.08
80	61–100	3031	5.30	1.65
150	101–200	3448	8.93	4.53
250	201–300	3268	15.71	9.38
350	301–400	3049	22.52	12.13
450	401–500	1842	27.96	11.29
550	501–600	1134	31.98	10.80
650	601–700	690	34.86	10.98

between body weight measurements at early and later ages. These estimates are needed to build up a breeding scheme which considers also body weight in older minipigs. The observed time period is the main time period to select minipigs for breeding, whereas an early selection is desirable, because most of the minipigs that are sold at 3–6 months of age are not longer available for breeding.

Variances of residuals were heterogeneous and changes in the residual variances with age were modelled as a step function with different age classes (Köhn *et al.* 2007b). Within every age class equal residual variance was assumed. Table 1 gives an overview of the eight age classes that were built for the consideration of heterogeneous residual variances. Preliminary analyses with completely unstructured data and data sets with <5 measurements per animal resulted in no convergence for RRM; thus every animal was required to have at least five weight measurements with only one measurement per age class. Animals with <5 body weight measurements were excluded from the analysis. The body weight measured at an age that was closest to the average age per age class was accounted for in the analysis. This resulted in 19 505 records of 3461 animals. Each measurement per age class was treated as a different trait resulting in a MTM with eight traits. The complete pedigree contained 35 066 animals. The 3461 animals that were included in this study were offspring of 295 sires and 794 dams.

The multiple trait animal model used was as follows:

$$y_{ijklmn} = \mu_m + S_{im} + U_{jm} + Y_{km} + \sum_{r=1}^{c_m} \beta_{mr} (t_{ijklmn} - \bar{t}_m)^r + a_{ijklmn} + l_{jlm} + e_{ijklmn},$$

where y_{ijklmn} = weight in age class m of animal n within sex i , unit j , birth year k , and litter l ; μ_m =

population mean in age class m ; S_{im} = fixed effect of sex i ; U_{jm} = fixed effect of unit j ; Y_{km} = fixed effect of birth year k ; β_{mr} = fixed regression coefficient for linear ($c_m = 1$) and quadratic ($c_m = 2$) polynomials; $\bar{t}_m$ = average age per age class m ; t_{ijklm} = age at weighing per age class; a_{ijklmn} = random additive-genetic effect for animal n ; l_{jlm} = random common environmental effect for litter l ; and e_{ijklmn} = random measurement error. For the regression on age at weighing per age class, polynomials of different orders of fit were applied. For age classes 45 and 80 quadratic and for age classes 150–650, linear polynomials were used. Higher orders of fit did not achieve a significant influence ($p < 0.001$, F -statistic, SS Type 1).

Legendre polynomials (LP) for the regression on age at weighing were used for modelling the random effects with RRM. For the orthogonal functions, the age at which the body weight was measured had to be rescaled to a standardized age t^* using the formula:

$$t^* = \frac{2(t - t_{\min})}{t_{\max} - t_{\min}} - 1,$$

where $t_{\min}$ is the lowest age, here age 30 days, and $t_{\max}$ is the highest age, here age 700 days. The random regression animal model 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 ; μ = population mean; 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 days; 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 within a litter; and ε_{ijkl} = random measurement error.

After examining different polynomial structures, the regression of the fixed effects sex, unit and birth year was calculated with a polynomial of second order of fit. The random regression coefficients for additive genetic effect, permanent environmental effect and common litter environmental effect were fitted with LP of second order of fit. The best fitting model was detected by comparing the estimated

variances and genetic parameters. It is outlined by Jamrozik & Schaeffer (2002) that different test criteria like Akaike's information criterion or the information criterion based on Bayes statistics rank models in a different way. Because of the fact, that it is unclear which criterion is the best for choosing the best fitting model in this study, the model comparison was carried out by using the estimated variances, variance ratios and genetic parameters only (Meyer 2005).

VCE-5 software (Kovac *et al.* 2002) was used to estimate genetic parameters and breeding values for body weight. Eigenfunctions with corresponding eigenvalues were calculated for the covariance components of the random regression coefficients. Eigenvalues represent the amount of variation explained by the corresponding eigenfunction. Accordingly, a large eigenvalue of the additive genetic effect represents considerable genetic variation for pattern of growth and changes in the growth curve that can be modified by selection (Bermejo *et al.* 2003).

Results

As it is shown in Table 1, the number of analysed records varies just slightly between the first five age classes with a maximum of 3448 records at age 150 days. After age 350 days, the number of records in each age class decreased substantially, reaching a minimum at age 650 days with 690 records.

Heritabilities estimated with MTM showed the highest value of 0.228 (0.220, RRM) at age 150 days (Figure 1). The highest value of 0.222 estimated with RRM was calculated for age 250 days (0.223, MTM). After age 250 days, heritabilities estimated with RRM were slightly higher compared with those estimated with MTM. In Table 2, the heritabilities estimated with MTM and the genetic correlations of MTM and RRM are shown. Standard errors are only provided for estimates of MTM by VCE-5, whereas standard errors for estimates of RRM are not yet available from the used software. All standard errors showed expected values; only in the last age class standard errors for genetic correlations were higher and also the standard error for the heritability was relatively higher than in the other age classes because of a fewer number of analysed records in this age class. Additionally, the heritability was much lower at 650 days in both models.

The variance proportion of the common litter effect decreased with age in both models (Figure 1). The proportion of the residual variance estimated

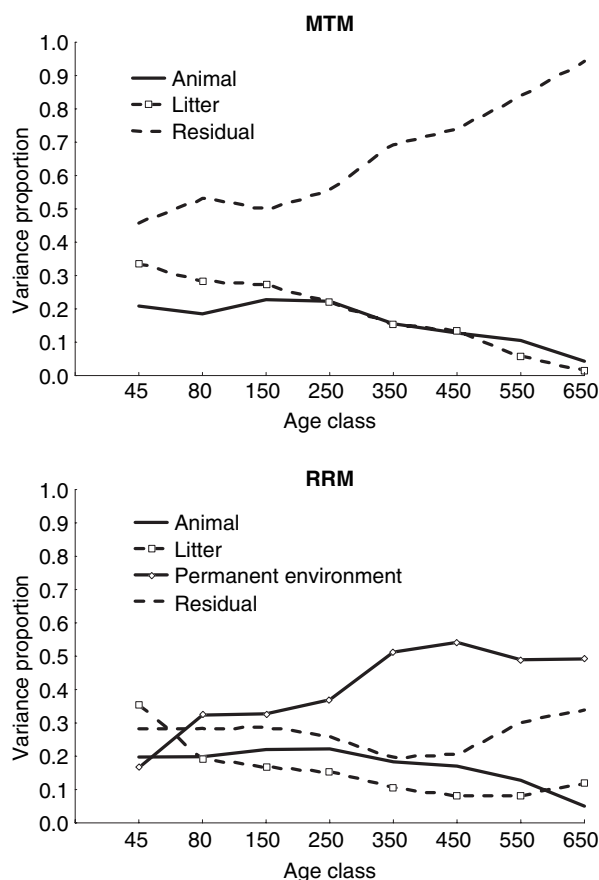


Figure 1 Variance proportions of random and residual effects estimated with multiple trait models (MTM) and random regression models (RRM).

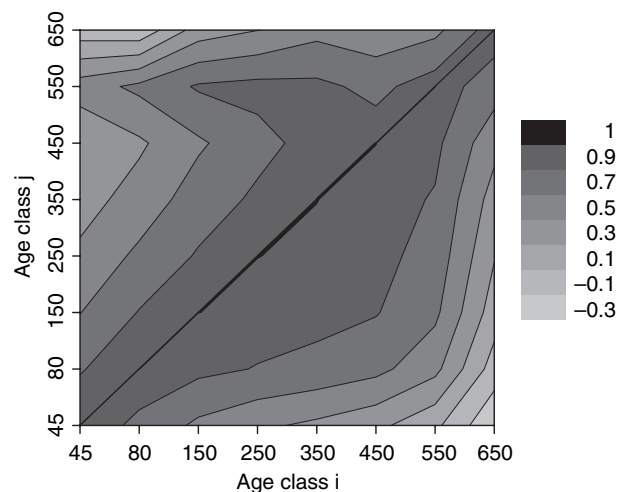
with MTM showed a constant increase throughout the whole examined time period. The RRM estimated a more or less constant proportion of the residual variance, whereas the variance proportion of the permanent environmental effect increased over the whole time range.

The genetic correlations between body weight measurements in different age classes showed an expected decrease with increasing distance between the age classes (Figure 2). Even negative correlations were estimated between age 45 and age 80 days and 650 days; however these estimates are based on a very limited number of observations. Correlations estimated with MTM showed unexpected higher values between age 550 days and age 45–250 days.

The analysis of eigenfunctions and their associated eigenvalues led to the result that the first eigenfunction with an eigenvalue of 85.55 % had the highest proportion of genetic variation compared with the second and third eigenfunction with 13.98 % and 0.47 % respectively (results not shown). The first

Table 2 Heritabilities (diagonal, estimated with multiple trait model) and genetic correlations estimated with multiple trait model (above diagonal) and with random regression model (below diagonal)

Age class	45	80	150	250	350	450	550	650
45	0.209 ± 0.020	0.889 ± 0.072	0.695 ± 0.059	0.539 ± 0.052	0.420 ± 0.053	0.317 ± 0.051	0.601 ± 0.073	-0.018 ± 0.077
80	0.861	0.185 ± 0.015	0.909 ± 0.066	0.743 ± 0.059	0.581 ± 0.059	0.468 ± 0.058	0.747 ± 0.081	-0.052 ± 0.080
150	0.658	0.949	0.228 ± 0.016	0.920 ± 0.066	0.798 ± 0.068	0.670 ± 0.066	0.924 ± 0.090	0.395 ± 0.100
250	0.539	0.891	0.988	0.223 ± 0.018	0.934 ± 0.082	0.839 ± 0.082	0.959 ± 0.100	0.496 ± 0.121
350	0.457	0.840	0.965	0.993	0.156 ± 0.016	0.970 ± 0.095	0.945 ± 0.104	0.639 ± 0.142
450	0.353	0.759	0.912	0.960	0.986	0.128 ± 0.014	0.846 ± 0.102	0.567 ± 0.138
550	0.148	0.557	0.745	0.824	0.883	0.949	0.105 ± 0.014	0.647 ± 0.158
650	-0.275	0.008	0.200	0.313	0.417	0.561	0.794	0.043 ± 0.013

**Figure 2** Genetic correlations between body weight measurements in different age classes estimated with multiple trait models (MTM) (above diagonal) and random regression models (RRM) (below diagonal).

eigenfunction was positive throughout the whole examined time period, which means that a selection on low body weight on the basis of the predicted breeding values at a certain age will change the body weight in the same direction at any age of the trajectory.

Definition of an operational breeding goal

Goettingen minipigs are sold at a highly variable age (from 30 to >700 days) for various purposes. For many experimental uses, a lower body weight at the age of use would be economically advantageous. However, the absolute weight reduction (in grams) is not a good indicator across ages, for example a reduction in 250 g reflects on average a 4.7 % weight reduction of an 80-days-old minipig, whereas it is only on average a 0.7 % reduction of a 650-days-old minipig. In cases where testing compounds are dosed per kilogram body weight, the weight reduction in

Table 3 Number and percentage of sold animals per age class and relative weights in per cent of kg selling weight

Age class	Sold animals	Sold animals (in %)	Relative weight in RWR (in % per kg)
80	0	0	0
150	2426	14.5	1.7
250	8012	47.9	3.0
350	3258	19.5	0.9
450	1837	11.0	0.4
550	799	4.8	0.2
650	394	2.4	0.1
Total	16726	100.0	

per cent clearly is the appropriate economic indicator, because a weight reduction of x % will lead to a dose reduction of x %, and the quantity and price of the (often extremely expensive) testing compound will be reduced by the same percentage.

A second aspect to account for in the breeding objective is the proportion of animals sold in the different age classes. Table 3 shows the difference of the number of animals in the different age classes, for example in age class 150, we had 2426 pigs less than that in age class 80. We assume, that all these animals were sold (a small proportion may have died, but mortality is negligibly low). Relative to all the observed sales in the considered time window 30–700 days, 14.5 % of the sold animals were sold between ages 80 and 150 days. The largest proportion (47.9 %) of animals was sold between ages 150 and 250 days, and almost 20 % are sold when they are older than 1 year.

We define the relative weight reduction (RWR) as composite breeding objective:

$$RWR_i = - \sum_{j=1}^8 \frac{p_j}{y_j} \times a_{ij},$$

where RWR_i is the relative weight reduction of animal i ; p_j is the proportion (in per cent) of animals

sold in time interval j ; $\bar{y}_j$ is the average body weight (in kg) in time interval j ; a_{ij} is the breeding value of animal i for body weight (in kg) in time interval j .

The unit of RWR is per cent, and $RWR_i = 2.3$ means that animal i genetically has 2.3 % less body weight in all age classes where these body weights in each age class are weighted with the probability that a minipig is sold at that age. Positive values of RWR reflect the desired breeding objective, that is a weight reduction in the relevant age classes.

Using this definition, RWR is a linear combination of true (or estimated) breeding values in the eight age classes. In Table 3, the relative weights ($p_j/\bar{y}_j$) for all eight weights are given. Predicted breeding values for RWR were in a range between -18 and +18 % of selling weight from both models. The correlation between RWR breeding values calculated with parameters obtained from MTM and RRM was 0.94.

Estimation of expected genetic gain

The expected genetic progress was assessed using selection index theory (Hazel & Lush 1942) as implemented in the Selection Index Program (Wagenaar *et al.* 1995). The breeding objective was the improvement of RWR. We compared two scenarios of practical relevance: selection at 80 days or selection at 150 days. At 80 days, less information is available than on 150 days, so the accuracy of breeding value estimation at 80 days is lower. On the other hand, the pool of selection candidates is larger, because 14.5 % of the animals are sold between 80 and 150 days. There is no difference in generation interval, because both male and female breeders are used first at an age well above 150 days.

From the available data, we analysed the average amount of information from the selection candidate and its close relatives when the candidate is 80 or 150 days old. Table 4 contains r_{TI} , the accuracy of breeding values (identical for males and females, because both sexes are selected with the same amount of information), the selection intensities for males (i_m) and females (i_f), and the male (ΔT_m) and female (ΔT_f) generation interval. Selection intensities and generation intervals were calculated from the available data and averaged over the years. The expected genetic progress per year in the trait RWR then was calculated as follows:

$$\frac{\Delta G}{a} = \frac{i_m + i_f}{\Delta T_m + \Delta T_f} \times r_{TI} \times \sigma_A,$$

where σ_A is the additive genetic standard deviation of trait RWR, which was estimated to be 6.69 %.

Table 4 Accuracy of estimated breeding values (r_{TI}), selection intensities for male and female minipigs (i_m, i_f) and generation intervals for male and female minipigs ($\Delta T_m, \Delta T_f$), for the two different selection ages

Parameters	Selection age (in days)	
	80	150
r_{TI}	0.5082	0.5679
i_m	2.27	2.24
i_f	1.73	1.66
ΔT_m	1.67	1.67
ΔT_f	2.12	2.12

For the calculation of the genetic progress which can be realized per age class and over the whole examined time period, results will be shown based only on genetic parameters estimated with the MTM (RRM-based results were very similar).

The expected genetic progress in RWR was 3.6 % when selection was done at 80 days and 3.9 % when selection was done at 150 days respectively. Figure 3 shows the expected absolute weight changes in the different age classes; the difference between selection at ages 80 and 150 days is more distinct after age class 150 days. It becomes evident that selection at 150 days leads to a higher weight reduction throughout all age classes >45 days, especially in the economically most important age class 250 days (where almost 50 % of all animals are sold) and that the weight reduction through later selection is increased by 12 % (-0.647 versus -0.724 kg/year). This result is due to the higher accuracy of the estimated breeding values for selection at 150 days, which dominates the slightly reduced selection intensity.

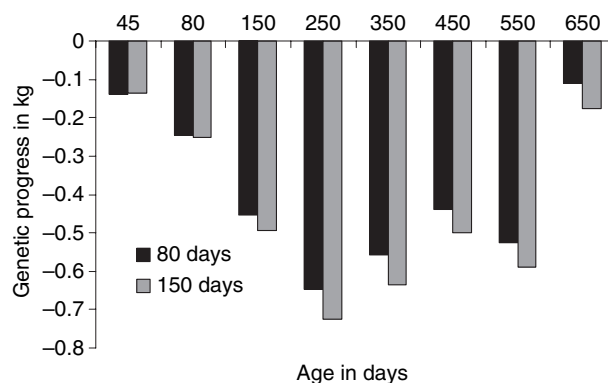


Figure 3 Expected genetic progress per year for the absolute body weight (in kg) calculated for different selection ages [based on results from multiple trait models (MTM)].

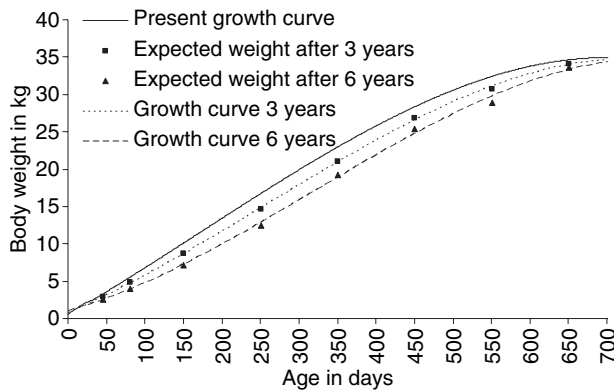


Figure 4 Changes in the current growth curve after 3 and 6 years of selection [based on results from multiple trait models (MTM), selection at 150 days].

To display the expected changes in the growth curve of the current Goettingen minipig population, body weights from age 0 to 700 days were predicted with the polynomial of third order, which was found to give the best fit for the growth curve in Goettingen minipigs (Köhn *et al.* 2007a). Expected weight changes in each age class after 3 and 6 years of selection were subtracted from these body weights. Figure 4 shows the current growth curve and the expected growth curves after 3 and 6 years of selection for body weight reduction, where the resulting values in the eight age classes again were fitted with a third order polynomial. By the suggested breeding scheme and objective, the expected change will be a slower weight development in the first year, while the pigs will grow to roughly the same adult body weight during the second year.

Discussion

A breeding scheme for Goettingen minipigs with a focus on the trait low body weight is a necessary tool for achieving the customers' demand for a phenotypically small minipig. Genetic parameters were estimated in this study to get the basic results for further application. The estimation was carried out by using MTM and RRM. One aim was to find out which model is the more appropriate one for a routine application in an automatic breeding value estimation and selection with a focus on practicability. Further, the best age for selection had to be identified.

Multiple trait model analyses are very common for the estimation of variance components for traits with repeated measurements. The model is able to account for different genetic correlations between

the measurements. A problem is the overparameterization of the covariance matrix if measurements at many different ages exist (Meyer & Hill 1997). Many animals would have missing data for most of the traits if they are randomly measured and not at fixed ages. Thus, a better way is to limit the number of traits by defining time periods (e.g. months) and only take one measurement per time period into account. The disadvantage of this adjustment of age is that the covariance structure is fitted as discontinuous whereas in reality it is continuous. Nowadays, RRM are more and more used for the estimation of genetic parameters of repeatedly measured traits like milk yield or body weight in animals (Albuquerque & Meyer 2001; Huisman *et al.* 2002; Lewis & Brotherstone 2002; Malovrh 2003). The RRM is able to give the covariances of a trait which is measured at different ages as a function of these ages. There is no need for an adjustment of ages with this model, and as a consequence, errors associated with an adjustment are avoided (Albuquerque & Meyer 2001).

On the other hand, it is outlined by Nobre *et al.* (2003) that random regression analysis requires structured data. Otherwise, a bad fit for some curves modelled with RRM may be the consequence. Thus, for the estimation of genetic parameters with RRM on the basis of weight measurements with an uneven distribution as it is given in the original unadjusted data sets with minipig body weights, an adjustment of the results based on estimates from MTM and literature information could be necessary.

The estimation of genetic parameters with RRM of unstructured minipig body weight data failed. A detailed data preparation of every new data set in advance is very labour-intensive and reflects a lack of practicability of the RRM in this specific case. Thus, the MTM seems to be the more appropriate model for a routine and automatic estimation of breeding values.

The estimated heritabilities were moderate to low in this study. Köhn *et al.* (2007b) estimated heritabilities with a RRM in the same range for body weight of Goettingen minipigs in a time period of 30–400 days of age. A maximum value of 0.25 was estimated at age 225 days. Much higher heritabilities for Goettingen minipig body weight, for example 0.77 for age 120 days, were estimated by Oldigs (1986). He measured body weight of 204 Goettingen minipigs at seven different ages including birth weight and estimated the genetic parameters with a sire–dam model. Because of the less number of analysed records, his results seem to be less trustworthy compared with the results of this study. Malovrh

(2003) analysed body weight measurements of 3819 boars of four German pure-bred lines for fattening pigs. The pigs in an age range from 30 to 167 days were weighed six times. An MTM with six traits and an RRM with animal, litter and permanent environment as random effects were applied. In her study, Malovrh (2003) estimated heritabilities with an MTM also including animal and litter as random effects which were a bit higher than in our study. They ranged from 0.363 at 31 days of age to 0.415 at 145 days of age. Heritabilities estimated with RRM were also higher than that in our study and ranged from 0.30 at 31 days of age to 0.40 at 145 days of age.

The changes in variance proportion with decreasing animal and litter effect and increasing permanent environment and residual effects were expected. Up to age 200 days, before the minipigs are used for breeding, a highly standardized environment can be provided. The environmental effects associated with the management practices (e.g. transfer of the sow for mating, transfer of the sow for farrowing) have a bigger influence on the pigs. Thus, the permanent and temporary (residuals) environmental effects increased while the heritability decreased. The genetic correlations between body weights in different age classes showed an expected decrease with increasing time distance between measurements.

As shown by Köhn *et al.* (2007a), the Göttingen minipig does not have a sigmoid growth curve, but an almost linear growth curve up to an age of about 500 days, and then the growth curve flattens off. While Oldigs (1986) suggested the trait 'low adult body weight' as breeding objective, we suggest to use RWR, which is an economically weighted average of the proportional reduction in body weight over the relevant age classes. Adult body weight is not a suitable breeding goal, because (i) late body weights have a very low heritability (Figure 1), (ii) more than 80 % of minipigs are sold at an age of less than 1 year, and (iii) using adult body weight would be in conflict with a desired shortening of the generation interval.

In Figure 4, we showed the expected shape of the growth curve after 3 and 6 years of selection for RWR based on the suggested selection scheme (using 150 days breeding values). It becomes clear that the main weight reduction is expected at the economically most relevant age at 250 days, while the final weight (adult body weight) remains almost unchanged.

Figure 4 is based on a linear extrapolation of the theoretically derived genetic trend over several years. While this approach is helpful to understand the effects on the growth curve, it must be seen that the Goettingen minipig may be close to a physiologi-

cal selection limit which may limit the potential to reduce body size by the predicted increment. Therefore, it is necessary to monitor the achieved genetic progress, once the selection scheme is implemented to realize if the expected changes can be achieved.

Body weight is known to have a positive genetic correlation with litter size in pigs (Ferguson *et al.* 1985). We found a correlation between estimated breeding values for litter size (number of piglets born alive) and RWR of -0.197 ($p < 0.0001$), confirming that weight reduction is expected to lead to reduced litter size. Genetic correlations between these traits will be estimated and reported in a separate study. Selection on litter size only in the last 10 years caused a negative genetic trend in RWR of -0.32 % per year, calculated as the linear regression of birth year on RWR (Figure 5).

Before implementation of a new breeding objective, some aspects need to be discussed: given the negative genetic correlation of RWR and litter size. A combined objective would be desirable, avoiding the undesired correlated selection response in fertility when selection focuses exclusively on reduction in body weight. As the absolute economic weights of the different traits can hardly be determined, a possible solution will be to construct a restricted selection index (Kempthorne & Nordskog 1959) to reduce body weight while keeping litter size constant. Expected cost (in terms of a reduction of genetic progress in RWR) will be determined based on the genetic correlations between the trait complexes.

Additional genetic progress could be made if selection intensity was increased and/or generation intervals were minimized. However, as the Goettingen

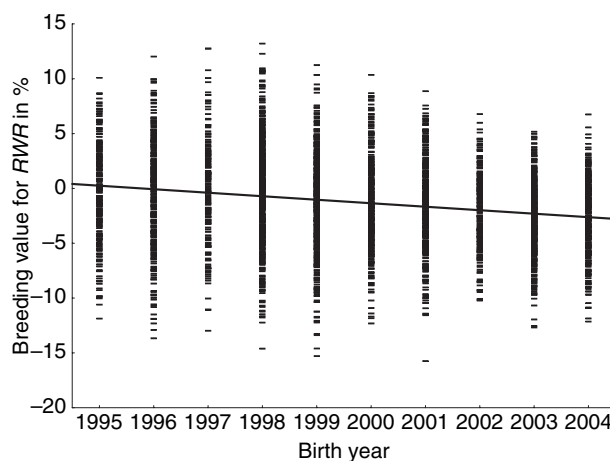


Figure 5 Development of breeding values for relative weight reduction (RWR) (in per cent of selling weight) over the analysed birth years [based on results from multiple trait models (MTM)].

minipig is unique and only exists in four breeding colonies of limited size world wide, avoiding inbreeding and maintaining genetic diversity is an important issue. Effective population size will decrease with increasing selection intensity (Robertson 1961) and the rate of inbreeding (ΔF per year) will increase with a reduction in the generation interval. Therefore, the achievable genetic progress needs to be balanced with an acceptable rate of inbreeding, which can be implemented by using appropriate tools like optimum genetic contribution theory (Meuwissen 1997).

The results show that a further substantial reduction in the body weight of the Goettingen minipig is achievable. Although some of the practical aspects of breeding and use of experimental animals differ clearly from the situation in slaughter pigs or farm animals in general, the well-established animal breeding concepts proved flexible enough to design an efficient breeding programme for Goettingen minipigs.

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