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Using mechanistic animal growth models to estimate genetic parameters of biological traits

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Mechanistic animal growth models can incorporate a description of the genotype as represented by underlying biological traits that aim to specify the animal's genetic potential for performance, independent from the environmental factors captured by the models. It can be argued that these traits may therefore be more closely associated to genetic potential, or components of genetic merit that are more robust across environments, than the environmentally dependent phenotypic traits currently used for genetic evaluation. The prediction of merit for underlying biological traits can be valuable for breeding and development of selection strategies across environments.

Model inversion has been identified as a valid method for obtaining estimates of phenotypic and genetic components of the biological traits representing the genotype in the mechanistic model. The present study shows how these estimates were obtained for two existing pig breeds based on genetic and phenotypic components of existing performance trait records. Some of the resulting parameter estimates associated with each breed differ substantially, implying that the genetic differences between the breeds are represented in the underlying biological traits. The estimated heritabilities for the genetic potentials for growth, carcass composition and feed efficiency as represented by biological traits exceed the heritability estimates of related phenotypic traits that are currently used in evaluation processes for both breeds. The estimated heritabilities for maintenance energy requirements are however relatively small, suggesting that traits associated with basic survival processes have low heritability, provided that maintenance processes are appropriately represented by the model.

The results of this study suggest that mechanistic animal growth models can be useful to animal breeding through the introduction of new biological traits that are less influenced by environmental factors than phenotypic traits currently used. Potential value comes from the estimation of underlying biological trait components and the explicit description of their expression across a range of environments as predicted by the model equations.

Keywords: biological traits, genetic parameters, mechanistic models, pigs

Introduction

Successful breeding strategies rely on their ability to identify animals whose genetic merit provides their offspring with the ability to perform better than their competitors across the prevailing range of environments. It is generally accepted that the expression of genes varies between environments and between growth stages, with at least partly different genes involved, and consequently that the genetic correlation of observable performance traits between environments and different growth stages is generally not unity. This genotype by environment interaction (G × E) imposes difficulties for the traditional methods of estimating genetic merit when specified in terms of observable traits, since these generally assume a unit genetic correlation across environments. Statistical methods exist, such as covariance functions, that can deal with non-unity genetic correlations, but they rely on measurements from multiple environments, which are often difficult to obtain.

Mechanistic growth models build upon an alternative description of the genotype by using traits that are considered more closely related to the underlying biology (and hence to the genes) and more likely to be stable across a range of environments than the observable traits currently used in genetic evaluation. These characteristics make the model's underlying biological traits potentially useful

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predictors for genetic merit and promising traits for DNA marker development. Although the potential benefits from implementing traits derived from biological production functions into breeding programs have long been recognised (e.g. Fowler *et al*., 1976), their representation in current selection objectives is sparse. The most likely reason for this is the difficulty of measuring these traits in live animals and in obtaining accurate estimates of the genetic parameters of these traits.

The present study explores the potential value of using the underlying biological traits derived from a mechanistic pig growth model for animal breeding purposes. This is done by (i) illuminating the theoretical concepts that imply that these underlying traits are closely related to the biology and likely to be more stable across environments than conventionally used phenotypic traits, by (ii) presenting a method for estimating variance components and phenotypic means of these traits, and by (iii) comparing the estimated genetic and environmental components of these traits associated with two genetically different commercial breeds and by comparing them with the corresponding components of more conventional phenotypic traits.

Materials and methods

Knap's mechanistic pig growth model

Model concepts. The mechanistic model used in this study is a predictive, semi-stochastic model for the performance for a population of pigs (Knap, 1999, 2000b and 2000c). Like many mechanistic pig growth models currently used in science and industry, the model builds upon the principles developed by Whittemore and Fawcett (1976), Whittemore (1983), Moughan and Verstegen (1988), Black *et al.* (1995) and Emmans and Kyriazakis (1997), which can be summarised as follows: the genotype is characterised by biological traits assumed to represent its genetic potential, defined as the animal's biological upper limit for growth and for its ability to cope with various kinds of stressors. These upper limits refer to hypothetical optimal environmental conditions in which the genetic potential can be fully expressed. Knap *et al.* (2003) demonstrated that these conditions generally differ between different traits and that the conditions in research or commercial farms are generally suboptimal for at least one of the biological traits describing the genetic potential. By definition, the genetic potentials are assumed independent of the environmental conditions that are included in the model. The interactions between the traits representing the genetic potentials and the prevailing physiological, nutritional, social and environmental constraints are described by a system of mathematical equations that integrate the present knowledge about the metabolic and physiological processes involved in pig growth. Model outputs are simultaneous predictions for various observable phenotypic performance traits (e.g. body weight, feed intake, body composition, etc.). Some of these traits serve as inputs to the statistical methods currently used for genetic evaluations.

Model description. In addition to a description of the genotype in the form of biological traits representing genetic potentials, the mechanistic model uses as inputs the pigs' initial body weight, as well as a description of the diet composition, and the physical and social environment.

Based on the provided pigs' initial body weight the model first calculates the chemical composition of the pig in terms of protein, lipid, ash and water mass at the start of the simulation period according to the rules of Emmans and Fisher (1996) and Emmans and Kyriazakis (1995). The pig genotype is characterised by three Gompertz function parameters P_{mat}, L_{mat} and B, which specify the animal's potential for protein (Prot) and lipid (Lip) mass growth in optimal environmental conditions according to

$$d(\text{Prot})/dt = \text{Prot} \times B \times \ln(P_{mat}/\text{Prot}) \quad (1)$$

$$d(\text{Lip})/dt = \text{Lip} \times B \times \ln(L_{mat}/\text{Lip}) \quad (2)$$

where the same rate parameter B is used for protein and lipid retention, assuming thus full allometry between body protein and lipid. The different asymptotes P_{mat} and L_{mat}, correspond to protein and lipid mass at maturity. Protein and lipid growth constitute two of the resource demanding processes; all others are characterised as maintenance processes, which are also considered as genotype dependent.

Ad libitum feed intake is then predicted as the intake required satisfying both the protein and energy needs of the potential growth, as defined by equations (1) and (2), plus maintenance requirements, subject to capacity constraints to feed intake volume. After the decomposition of the consumed feed into its nutrient components, the partitioning of the nutrients into growth and maintenance processes is modelled according to the concepts of Knap and Schrama (1996), with some modifications that take metabolic changes imposed by constraints of the physical environment into account. For example, cold thermoregulatory processes lead to increased feed intake in the model, whereas hot thermoregulatory actions includes reduction of *ad libitum* feed intake as well as reduction in physical activity, increase in body temperature and skin wetting, affecting thus body maintenance requirements.

The model follows these processes to iteratively calculate the actual protein and lipid mass growth on a daily basis for a growth period between 16 and 110 kg body weight, subject to the physical, nutritional and environmental constraints that are captured by the model. Empty body weight, which excludes gut fill and is assumed as 95% of the full body weight, is calculated as the sum of body protein, lipid, ash and water mass. The latter two are determined according to the rules of Emmans and

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Kyriazakis (1995 and 1997):

$$\text{Ash}_t = \text{Ash}_{t-1} + 0.21 \times \text{PR}$$

$$\text{Water} = 3.04 \times \text{Pmat}^{0.145} \times \text{Prot}^{0.855}$$

where PR is the daily protein retention and the subscript t refers to day t.

Backfat depth (BF) is calculated from the whole–body subcutaneous fat depth (FAT) via the regression equation (Knap, 2000c): $\text{BF} = 0.82 \times \text{FAT}^{1.212}$. Estimates of FAT were derived from body weight and volumes and density of the subcutaneous tissue according to

$$\text{FAT} = (3.376 \times p_{P,SCT} \times \text{Prot} + 1.227 \times p_{L,SCT} \times \text{Lip})/0.097 \times \text{BW}^{0.633}$$

where $p_{P,SCT}$ and $p_{L,SCT}$ are the proportions of protein and lipid in subcutaneous tissue, respectively, calculated as $p_{P,SCT} = 0.1285 + 0.00\,286 \times \ln$ (Prot) and $p_{L,SCT} = 0.2260 + 0.1310 \times \ln(\text{Lip})$ (Knap, 2000c).

The multivariate model output includes the average daily feed intake (DFI), the body weight growth rate described by the number of days to reach 110 kg (DAYS) and backfat depth (BF), which were used in this study to derive estimates for the underlying biological trait characteristics.

A more detailed description of the model concepts and the mathematical equations, including a pseudo code, is provided in Knap (1999 and 2000c).

The underlying biological traits representing the model genotype

The model uses four traits to describe the pig's genetic potential for growth and energy efficiency. According to equations (1) and (2) the growth potential is characterised by the three parameters P_{mat}, L_{mat} and B corresponding to protein and lipid mass at maturity and a determinant of the rates of tissue mass retention, respectively.

The parameters are expected to be correlated. For example, 'larger animals will have a lower growth rate relative to body size' (Ferguson *et al.*, 1997), implying thus a negative correlation between B and P_{mat}. According to Emmans (1988), this can be remedied by applying Taylor's scaling rule (Taylor, 1985) to the parameter B to produce the scaled rate parameter $B^* = B \times P_{mat}^{0.27}$, which is theoretically uncorrelated to P_{mat}. Further, the parameter L_{mat} has been replaced by its ratio to P_{mat} to produce LP_{mat} (kg/kg), which is assumed to be uncorrelated to both B* and P_{mat}. This leads to three presumed-independent model parameters P_{mat}, LP_{mat} and B*, representing three of the four underlying biological traits describing the animal genotype.

The fourth genotype specific model parameter, MEm_0, relates to the energy requirements of body maintenance processes other than those required for protein turn-over and thermoregulation, which are explicitly captured in the model. These maintenance energy requirements (ME_{maint}) are calculated according to Knap and Schrama (1996) as a simple function of the metabolic body weight ($BW^{0.75}$):

$$ME_{maint} = MEm_0 \times BW^{0.75} \quad (3)$$

ME_{maint} depends on P_{mat}, LP_{mat} and B*, but the genotype specific parameter MEm_0 is assumed uncorrelated to all three growth parameters. From now on, we will refer to ME_{maint}, P_{mat}, LP_{mat} and B* as the four underlying biological traits.

Simulating populations with genetic variation

For simulation, a population of full-sib groups was created, which varied in their values of the four underlying biological traits P_{mat}, L_{mat}, B* and MEm_0. A more complex general pedigree was not adopted as it would only introduce complexities that are unrelated to the validity of any conclusions to be made. The full-sibs were generated from a non-inbred and unrelated base population of n dams and n sires, with the number n chosen according to the criteria outlined below. It was assumed that each founder has a breeding value A for each of the four underlying biological traits, which was sampled from $N(0, \sigma_A^2)$, where the genetic variance $\sigma_A^2 = h^2\sigma_P^2$ is given by the model inputs for the heritability h^2 and phenotypic variation σ_P^2. The simulated population of full-sib groups was generated by mating randomly chosen dams and sire pairs of the base population. Each pair produced n_0 full-sib offspring. The breeding value of each offspring was $\frac{1}{2}(A_{Sire} + A_{Dam})$ plus a Mendelian sampling deviation. The latter term was drawn from a multivariate $N(0, \sqrt{1/2\sigma_A^2})$, which is unaffected by inbreeding due to the short pedigree adopted. The phenotypic value P for each of the four underlying biological traits was obtained using the trait mean, the individual's breeding value and an environmental deviation, sampled from a multivariate normal distribution $N(0, 1 - \sigma_A^2)$ according to:

$$P_i = \mu + A_i + PE_i, \quad (4)$$

where P_i is the phenotype of animal i, μ is the population mean for the trait, and A_i and PE_i are its additive genetic and permanent environmental deviations. According to this decomposition, the value of the underlying biological trait of each animal is specified by the population mean μ, the heritability h^2 and the phenotypic variance σ_P^2. Due to the above described transformations of the underlying biological traits, P_{mat}, L_{mat}, B* and MEm_0 are assumed uncorrelated.

The simulated population for which model predictions are generated consists thus of $n \times n_0$ full-sibs, with between animal variation in the four underlying biological traits. The variation in the underlying biological traits leads to variation in (and covariation between) the phenotypic model output traits for feed intake, growth rate and body composition, for which means, genetic and phenotypic variances and covariances were calculated via sib analysis (e.g. Cameron (1997) chapter 5) based on the decomposition in equation (4).

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The data

Records describing feed consumption, growth rate and body composition average were obtained in terms of daily feed intake (DFI) between weaning and 110 kg body weight, pig age (DAYS) and backfat depth (BF) at 110 kg body weight for 13 268 pigs with four-generation pedigree information of two PIC pig lines. From these records estimates of line specific trait means and heritabilities for these traits as well as genetic and phenotypic correlations between the three traits were derived (Table 1, 'Data' values). Line A is a dam line selected mainly for good reproductive performance, high robustness, and fast growth; Line B is a sire line selected mainly for high feed efficiency and leanness. Line differences in these characteristics are reflected by the differences in the phenotypic means of the three performance traits and – to a lesser degree - in the heritabilities and genetic/phenotypic correlations of the phenotypic traits (Table 1). Animals were kept in normal performance test conditions (indoors, temperate climate, partly slatted floors, about 10 animals per single-sex group, unrestricted feeding) with electronic feed intake recording. Animals were fed a diet containing 14.80 MJ digestible energy, 0.207 kg crude protein and 0.015 kg lysine per kg feed up to 60 kg body weight. For higher body weights, digestible energy, crude protein and lysine were set to 14.90 MJ/kg, 0.192 kg/kg and 0.0127 kg/kg, respectively. The variance components in Table 1 were estimated (PIC-USA, unpublished) using VCE-v3 (Groeneveld, 1996) on data sets with 16 854 (5322 for DFI) records for line A and 6414 (2070 for DFI) records for line B, with a four-generation pedigree for both lines.

Estimating means and variance components for the underlying biological traits using model inversion

Direct measurements of the underlying biological model traits are difficult to obtain in practice. Therefore the genetic and phenotypic characteristics of the recorded performance traits DAYS, DFI and BF listed in Table 1 were used to infer estimates for the components μ, h^2 and σ_P^2 of the underlying biological traits. For the remainder of this paper the inference of the components of the underlying biological traits from observed measures of performance traits is denoted as *model inversion process*. The model is 'inverted' in the sense that the conventional model input traits (the underlying biological traits) are treated as model outputs that need to be determined through the inversion process, and the parameters of the conventional model output traits are treated as known inputs. Various methods exist to carry out the inversion process, ranging from Bayesian inference methods (Tarantola, 1987) to the analytical and numerical methods presented by Doeschl-Wilson *et al.* (2006). Here, the inversion process was carried out by a computational algorithm which determined the components μ, h^2 and σ_P^2 of the underlying biological traits that correspond to performance predictions for DAYS, DFI and BF at 110 kg body weight with statistical properties most similar to those derived from the collected records shown in Table 1. In more detail, each iteration in the computational algorithm provides parameter estimates for the underlying biological trait components which the model then uses to generate a population of full-sib groups as outlined above. Consequently, the performance of these pigs is simulated, producing simultaneous predictions for

Table 1 *Genetic correlations (upper triangle of unshaded area), heritabilities (diagonal of white area) and phenotypic correlations (lower triangle of unshaded area), as well as phenotypic means (shaded area) for the two PIC lines, A (Table 1a) and B (Table 1b) as estimated from data analysis (DATA) and predicted from model inversion (MODEL)*[†]

	Data/Model	Days to 110 kg	DFI (kg/day)	BF (mm)
(a) Line A				
Days to 110 kg	Data	0.373 (0.044)	−0.740 (0.092)	−0.047 (0.066)
	Model	0.375 (0.002)	−0.700 (0.008)	−0.047 (0.0002)
DFI	Data	−0.437 (0.011)	0.267 (0.063)	0.410 (0.118)
	Model	−0.454 (0.003)	0.257 (0.015)	0.411 (0.003)
BF	Data	−0.040 (0.009)	0.233 (0.010)	0.480 (0.040)
	Model	−0.040 (0.0001)	0.233 (0.0009)	0.482 (0.0035)
Phenotypic means	Data	155 (0.097)	2.33 (0.004)	10.70 (0.021)
	Model	154 (0.75)	2.13 (0.014)	11.56 (0.087)
(b) Line B				
Days to 110 kg	Data	0.396 (0.059)	−0.735 (0.116)	−0.042 (0.095)
	Model	0.400 (0.0016)	−0.704 (0.008)	−0.042 (0.0002)
DFI	Data	−0.438 (0.018)	0.267 (0.070)	0.411 (0.148)
	Model	−0.452 (0.0027)	0.257 (0.0014)	0.401 (0.0044)
BF	Data	−0.044 (0.010)	0.238 (0.022)	0.550 (0.061)
	Model	−0.045 (0.0006)	0.242 (0.002)	0.556 (0.008)
Phenotypic means	Data	174 (0.170)	2.00 (0.007)	11.00 (0.031)
	Model	175 (0.845)	1.97 (0.010)	11.23 (0.123)

[†] The 'model' results are the means of 15 independent optimisation runs per PIC line with different random number sequences for producing the pig populations and different initial values in the optimization algorithm. The standard errors of the estimates are shown in brackets. Note that these cannot be directly compared with the corresponding standard errors from the data analysis. DFI = daily feed intake; BF = backfat depth.

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the traits DAYS, DFI and BF at 110 kg body weight for each simulated animal. This leads to phenotypic means, heritabilities and genetic and phenotypic correlations for these traits that can be compared with those derived from real records. The goodness of fit was evaluated according to the relative prediction error sum of squares (RPESS), defined as

$$\text{RPESS} = \sum_{j=1}^{12} \left(\frac{\hat{y}_j - y_j}{y_j} \right)^2 .$$

Here $\hat{y}_j$ and y_j are the values for the jth statistical measure of the performance traits DAYS, DFI or BF predicted by the model (MODEL in Table 1) and obtained from data analysis (DATA in Table 1), respectively.

In an appropriate linear model, we would have a perfect fit for 12 parameters derived from 12 data points. However, the non-linearity is such that we do not get a perfect fit. The correlated patterns of influence of the input parameters is such that we do not have the full 12 degrees of freedom available to explain the 12 data points, and the ensuing residuals drive the RPESS criterion.

The computational algorithm

The differential evolution (DE) algorithm (Storn and Price, 1997) was used to determine the set of statistical components of the underlying biological traits that minimise the RPESS. The DE is an evolutionary genetic algorithm that has been modified for improved efficiency for complex search spaces. Details of the algorithm are given in Storn and Price (1997). Briefly, the DE algorithm adapts the concepts of evolutionary theory to search efficiently through the multi-dimensional (12D in the present study) parameter space to find the optimum solution. It is an iterative process consisting of many generations. In each generation a number of solutions (12 in the present study) are simultaneously produced, of which the best (according to tournament selection) contribute to the initial estimates of the next generation. Each solution corresponds to a set of estimates for the 12 model parameters. Convergence towards a final solution was assumed if the RPESS of the best solution of a generation did not change by a relative magnitude greater than 10^{-6} in 1000 successive generations.

Numerous case studies have demonstrated that the DE algorithm searches efficiently through large and complex search spaces before reaching the perceived global optimum, overcoming therefore problems of differentiability, non-smooth response surfaces including sharp cliffs and multiple local optima, which are typically associated with agricultural models (Mayer *et al*., 2005). Due to the complex structure of the mechanistic model used in this study, the existence of a globally unique optimal parameter set cannot be guaranteed from mathematical theories. However, insight into the topography of the search space could be obtained by monitoring the RPESS of the fittest candidate per generation over successive generations and by repeating the optimisation process several times for the same animal population, with different initial DE candidates in the first generation of the optimisation algorithm. By tracking the RPESS value it could be determined whether different sets of parameters for the underlying biological traits correspond to similar RPESS values for the predicted performance traits, and how sensitive the RPESS is to changes in these parameter values. The random processes embedded in the DE imply that different search routes are used in different repetitions of the optimisation process applied to the same simulated animal population. If the different optimisation processes associated with different initial candidates converge to the same optimum, the optimum is considered satisfactory.

Stochasticity and population size

The stochastic nature of the mechanistic model implies that its predictions are influenced by the specific random sampling used to generate the simulated animal populations. Two simulations with identical values for all input parameters will thus produce different predictions and possibly different covariance estimates for the performance traits. Likewise, the optimisation process applied to different simulated populations with the same means and covariance estimates in the performance traits may produce different estimates of the statistical measures for the underlying biological traits. The influence of individual random drawings can be reduced by increasing the number of replicates in the simulated population, but this also increases the run time of the model and the statistical calculations. In the inversion process the model is called many thousands of times and numerous statistical calculations must be carried out for every run, mounting up to a considerable computing time for producing the estimates of the specific model parameters. Our simulated populations consisted of 7000 individuals comprising 700 full-sib families with 10 sibs per family (the average number in the populations whose performance trait records were used). For this population structure, the coefficient of variation for the predicted means, variances and heritabilities of the predicted performance traits DAYS, DFI and BF was less than 10%, with an average run time on a standard PC of 7 days per optimisation process, which was considered as a good balance between model run time and variability in the results. For each PIC sire line, the optimisation was repeated 15 times, corresponding to 15 different populations with the same genetic specifications.

Results and discussion

Performance of the optimisation algorithm

In all optimisation runs, convergence was obtained within 10 000 generations in the DE algorithm. For every simulated animal population the optimisation process was repeated three times with different initial values for the parameters in question. For each animal population, the different processes consistently converged to the same

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solution, implying that the algorithm successfully found the global optimum instead of getting stuck at a local RPESS minimum. Tracking the best solution of every generation in the DE algorithm together with its corresponding RPESS provided the necessary evidence that the algorithm searched widely through the parameter space and that the optimum corresponding to each animal population was unique, i.e. that there is no other parameter set outside a given neighbourhood of the optimal set with a RPESS sufficiently similar to the RPESS corresponding to the optimum. More accurately, for every parameter set in the algorithm's search trajectory, for which at least one of the parameters deviated from the optimum by more than 10%, the corresponding RPESS was more than 30% higher than that corresponding to the optimum. It could be easily verified that an RPESS greater than 130% RPESS of the optimum implies a deviation of more than 5% in at least one of the statistical components of the predicted performance traits from that corresponding to the optimum. Thus, any combination of the underlying biological trait parameters for which one parameter deviates more than 10% from the derived optimum value implies a deviation of more than 5% in at least one of the statistical components of the performance traits.

Sensitivity analysis was carried out to determine the effects of changes in the parameters of the underlying biological traits on the predictions for the genetic and phenotypic parameters of the performance traits DAYS, DFI and BF. In this analysis one parameter was gradually altered at a time, while the others were kept fixed to their optimum (Table 1). As expected, gradual changes in the underlying biological trait parameters led to gradual changes in the phenotypic performance trait parameters, resulting in RPESS values greater than those referring to the optimum. The means of the traits DAYS, DFI and BF were primarily affected by changes in the means of the underlying biological traits. The biggest effect was achieved by altering average B*- a 5% variation in average B* resulted in a 5% variation in the average growth rate (DAYS). Modifying one biological trait parameter by up to 5% affected in most cases simultaneously heritabilities, genetic and phenotypic correlations at the order of magnitude of 10^{-3}. In all cases, the absolute difference was found less than 0.03. Genetic and phenotypic correlations between the traits DAYS and BF were found most sensitive to changes in the biological trait parameters. Overall, the model predictions were found robust to gradual changes in the underlying biological trait parameters.

Estimates of the underlying biological trait components and their implications

Table 2 shows the average values together with standard errors for the 12 parameters specifying the underlying biological traits corresponding to the two PIC lines, obtained from the inversion process. All runs corresponding to different simulated populations from each PIC line produced very similar estimates, which are reflected in the low standard errors. The unanimous results imply that the underlying biological trait values depend little on the simulated population.

The estimates of the means and phenotypic variances for the underlying biological traits P_{mat}, L_{mat}, B* and MEm_0 obtained through the inversion process in this study (Table 2) can be compared with independent estimates obtained from direct measurements in previous empirical experiments, which are summarised in Table 3. However, as pointed out in the footnotes of Table 3, some of the experimental conditions were unlikely to correspond to the optimal conditions required for the full expression of the genetic growth potential and the intrinsic maintenance energy requirements, decreasing thus the confidence in the validity of the empirical estimates.

The average values for the Gompertz parameters LP_{mat} and B*, and for the maintenance energy coefficient MEm_0 obtained through model inversion fall within the range estimated in previous studies (Table 3), with the estimate for LP_{mat} situated towards the lower end of the spectrum and the coefficient MEm_0 slightly exceeding the maximum value of the empirical estimates. The inversion estimate of P_{mat} (above 57 kg) is however considerably higher than the estimates from previous data analyses (below 41 kg). Decreasing P_{mat} in the simulation model to the previous estimates provided in Table 3 and leaving the remaining parameters fixed leads to drastic changes in the estimated average body weight growth (DAYS) and backfat depth (BF) as well as in some of the genetic and phenotypic covariances. The model predictions would thus provide a poor fit to the data used in the optimisation criterion.

Table 2 *Estimates of the mean values and standard errors (in brackets) of the genetic model parameters for the two PIC lines derived by model inversion using the DE algorithms for 15 replications per PIC line*

PIC line[†]	Parameter	P_{mat} (kg)	LP_{mat} (kg/kg)	B* (kg/(day × kg))	MEm_0 (kJ/(day × $kg^{0.75}$))
Line A	Mean (s.e.)	59.395‡(0.328)	1.287** (0.026)	0.032*** (0.0005)	747.9 (1.34)
	h^2 (s.e.)	0.527* (0.029)	0.516 (0.017)	0.445 (0.019)	0.107 (0.006)
	CV (s.e.)	0.053 (0.002)	0.125 (0.004)	0.051 (0.003)	0.083 (0.004)
Line B	Mean (s.e.)	57.499 (0.878)	1.145* (0.040)	0.028* (0.0004)	737.94 (6.847)
	h^2 (s.e.)	0.670* (0.042)	0.517 (0.009)	0.424 (0.020)	0.114 (0.007)
	CV (s.e.)	0.050 (0.004)	0.127 (0.009)	0.049 (0.004)	0.079 (0.005)

[†] Line A was selected for fast growth, robustness, high meat quality, etc. Line B was selected for feed efficiency, leanness, etc.
Superscripts refer to probability levels for significance tests for differences between the PIC lines (‡ $P < 0.1$, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$).

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Table 3 *Estimates of the underlying biological traits used to describe the genetic growth potential in Knap's pig growth model derived from data analysis*

Source[†]	Parameter	P_{mat} (kg)	LP_{mat} (kg/kg)	B* (kg/(day × kg))	MEm_0 (kJ/(day × $kg^{0.75}$))
Ferguson and Gous	Mean	28.4–38.7	2.60–3.89	0.0287–0.0296	–
	CV	0.05	0.10	0.09	–
Knap	Mean	24.5–38.5	0.97–5.16	0.0226–0.0445	489–733[‡]
	CV	0.036–0.549	0.048–0.289	0.045–1.894	0.06–0.15
Knap *et al.*	Mean	27.7–40.7	1.95–3.49	0.0218–0.0348	–
	CV	0.15	0.27	0.14	–

[†] Ferguson and Gous (1993a and b) and Ferguson *et al.* (1997): Regression analysis of repeated measurements from 27 pigs raised under experimental conditions which were likely to allow the expression of the genetic potentials for protein and lipid growth. In their experiments dietary and environmental conditions were carefully balanced, so that protein retention could reach its maximum without causing lipid retention to exceed the animal's intrinsic desire; Knap (2000a and c): Estimates derived from 5 independent data sets including pigs of different breeds and sex. The experimental conditions were likely to differ from those necessary for the full expression of the genetic potentials. Knap *et al.* (2003) D_2O dilution method of data from 14 pigs raised under conditions that were likely to differ from those necessary for the full expression of the genetic potential.
[‡] Estimates were derived from Knap's estimates of MEmaint = $MEm_0 \times BW^{0.75}$ for body weights between 25 and 110 kg under thermoneutral conditions (Knap, 2000c).

Various reasons could however explain the observed discrepancy in P_{mat} between inversion results and previous estimates. First, the majority of pigs in the experiments that provided the data for the statistical analyses were slaughtered before they reached maturity. The scarcity of data relating to mature animals may have led to poor estimation of the parameter P_{mat} in the statistical analysis (Knap *et al.*, 2003). Second, as Knap (2000a) points out, the steady progression towards larger and leaner animals due to breeding strategies is expected to be reflected by higher values for P_{mat} and lower values of LP_{mat} over time. The data used in the inversion process were generated in 2004, and correspond to pigs that had been selected over many generations for fast growth and leanness. In contrast, the data from which the earlier estimates were derived correspond to pigs of a variety of breeds slaughtered 20 to 7 years earlier. As Figure 1 shows, the estimates for $PD_{max} = P_{mat}/(B_{Gomp} \times e)$ and LP_{mat} derived here follow the trends predicted by Knap (2000a).

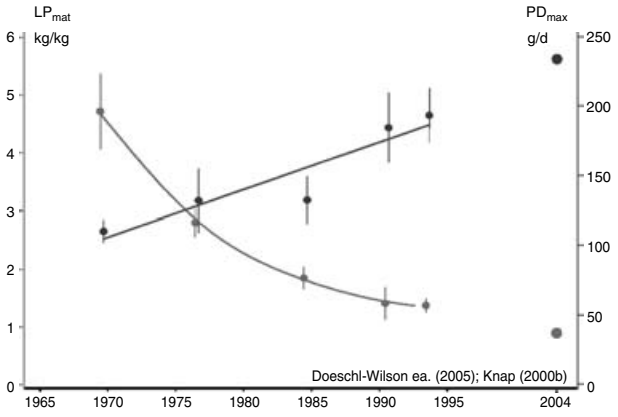

Figure 1 Estimated values and trends for the 1969 to 1993 population averages of the biological traits LP_{mat} and PD_{max} as produced by Knap (2000a), together with the corresponding estimates from the present analysis (2004).

The coefficients of variation in underlying traits estimated by the inversion procedure are between 0.05 and 0.13 for all four traits with LP_{mat} having the highest between animal variation in both PIC lines (Table 2). The estimates agree well with the estimates obtained in previous data analyses. Heritability estimates for the underlying biological traits do not exist from empirical studies since these would require huge experimental settings involving a large number of pedigreed animals.

Except for the maintenance energy coefficient MEm_0, for which the model inversion predicts a low heritability of 0.1, the heritabilities of the three underlying biological traits associated with leanness, growth rate and body composition vary between 0.42 and 0.67 and exceed the heritabilities of the phenotypic traits DAYS, DFI and BF (0.27–0.55) associated with the same characteristics (Table 2) for both PIC lines. The results of the model inversion thus suggest that the underlying biological traits for growth and body composition used in the model are more closely related to the underlying genetic potential for growth and composition than the phenotypic traits DAYS, DFI and BF, since a closer relation to the genetic level is reflected by higher heritabilities.

The estimated heritability of 0.1 of the maintenance energy coefficient MEm_0 is lower than the value of 0.3 obtained by Knap *et al.* (2003) from a literature review. The low value also stands in disagreement to the theory of Glazier (2002), who hypothesised that traits with higher priority (e.g. maintenance) in the resource allocation have also higher heritability than lower priority traits (e.g. growth traits). Model runs with higher MEm_0 heritabilities yield higher values for the predicted heritabilities of DFI and weaker genetic correlations between DFI and DAYS and DFI and BF than those provided by data analysis (Table 1). However heritabilities for processes that are vital for the basic survival are generally low because many generations of natural and artificial selection for these traits have fixed favourable alleles. It is also possible that

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the estimated low heritabilities are partly an artifact of the crude definition of maintenance processes in the model. The term maintenance in the model comprises all physiological and metabolic processes that are not involved in protein or lipid retention, including resting metabolism, hair growth, basic activity, coping with infectious and other stress, etc. Consequently, part of the genetic variation in true maintenance could have been captured by the growth and body composition traits.

Differences between the PIC lines

The relatively high heritabilities of the underlying biological traits used to represent the genotype in the growth model support the contention that these traits may be more closely related to the true genetic potential than the performance traits DAYS, DFI and BF. One would then also expect that the moderate differences in the means and co-variances of the performance traits DAYS, DFI and BF between PIC lines A and B manifest themselves into differences in the genotypic model parameter values. The differences in the estimated genotypic model parameters associated with each line were assessed using the MANOVA option in the SAS procedure PROC GLM (Statistical Analysis Systems Institute, 1999). This was done under the assumption that the line-specific parameter estimates from DATA (Table 1) were made without error, such that sampling error relates only to repeatability of simulated dataset replicates. The analysis revealed a difference ($P < 0.05$) between the estimated parameter sets associated with each line. However, considering each parameter individually, differences with $P < 0.05$ were only found in the mean of LP_{mat} and B* as well as in the heritability of P_{mat} (indicated by ** in Table 3). In addition, the average value for P_{mat} was found different between both lines at $P = 0.057$. The significantly higher values for B* and LP_{mat} for PIC line A *v.* B portray the faster body weight growth rate and lower backfat depth, which characterise PIC line A on a phenotypic level (Table 2). The optimisation results suggest that within-animal variations and heritabilities (with exception of P_{mat}) in the underlying biological traits are similar for both PIC lines.

Model fit and validation

As Table 1 shows, the model predictions for the multiple phenotypic and genetic components of the performance traits DAYS, DFI and BF including their phenotypic and genetic correlations closely match those derived from real measurements. Except for an 8% discrepancy between the predicted and estimated average backfat depth, the predictions generally differ from the data estimates by less than 5%. The low standard errors in the estimates of the genotypic model parameters corresponding to the sampling error derived from different simulated populations (Table 2) are accompanied by low standard errors in the predictions for the statistical measures (Table 1).

The close match between predictions and data estimates in all 12 measures for two different breeds suggests that the growth model is capable of simultaneously accurately predicting several traits up to the level of their co-variation, provided that the genotype and environment are appropriately specified.

However, proper verification that the obtained estimates for the underlying biological trait components are genuine for the corresponding PIC lines requires independent records of these lines derived from different environmental settings or covering different growth stages (the performance trait components listed in Table 1 refer exclusively to data measured at 110 kg body weight). Unfortunately such data do not exist for the PIC lines considered in this study. Therefore validation of the results of the inversion process was restricted to comparing predicted growth trajectories of various performance traits for the simulated PIC lines A and B with those derived from repeated measurements of various PIC cross-breeds for different environmental conditions. It was found that the predicted curves for PIC lines A and B generally matched the cross-breed curves reasonably well, considering the differences in the genetic specifications between the optimised lines and the cross-breeds. For example, as Figure 2 shows, compared with the cross-breeds, the selection lines A and B achieve 110 kg body weight faster, which is accompanied by higher feed consumption during the faster growth period, and are considerably leaner at given body weights. The change in backfat depth with increasing body weight, for which no significant difference was found between the different cross-breeds, was also found not significantly different from that of the PIC lines A and B ($P = 0.7$). In particular, PIC line A, which was selected amongst other criteria for fast growth, has the highest growth rate according to the simulations, whereas PIC line B that was selected amongst others for higher feed efficiency and leanness, has lower feed intake and lower backfat depth for a given body weight than line A (Figure 2).

Implications for animal breeding

In this study attention has been called to a new set of traits emerging from mechanistic animal growth models that are defined as intrinsic drivers of phenotype. The value of traits related to biological models for animal breeding has long been recognised. Fowler *et al.* (1976) investigated the potential of biological models for constructing selection objectives that can be applied to a variety of situations and concluded that these models would exceed classical index construction methods in their ability to provide greater flexibility in a rapidly changing industry. Varona *et al.*'s (1997) seminal paper describes the methodology for estimating genetic and phenotypic relationships between parameters of biological growth functions, which is essential for the integration of these biological traits into breeding programmes. It has been followed by numerous studies of genetic and phenotypic variations and co-variations of traits emerging from a variety of functions

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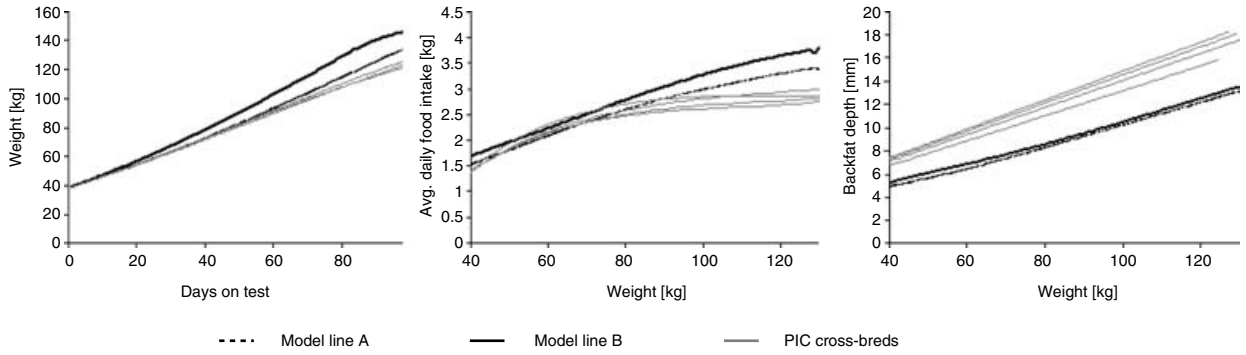

Figure 2 Model predictions for growth rate, average daily feed intake and backfat depth for PIC lines A and B together with statistical curves derived from repeated measurements of pigs from four different cross-bred lines[†]

describing growth for a range of animal species (e.g. Varona *et al.*, 1998; Chang *et al.*, 2001; Fernandez *et al.*, 2002). Further steps have been taken to explore inheritance, effects of selection and evolution of growth function parameters (e.g. Kirkpatrick *et al.*, 1990; Blasco *et al.*, 2003). The implementation of mathematical functions for describing biological processes is not restricted to growth. For example, De Vries and Kanis (1992) proposed the use of a mathematical function for feed intake based on protein retention and minimum lipid to protein retention ratio for optimising selection for feed intake.

Adding biological function parameters as new traits in the selection objective has the advantage that these traits describe a growth trajectory instead of the state of the animal at a specific growth stage, having also a biological interpretation. However, it is also well known that the parameters of the biological production curves depend strongly on the prevailing environmental conditions (e.g. Wood, 1976; McKay, 1992), implying that they need to be re-estimated whenever the environmental conditions change.

The novelty of the present study is that the considered biological traits emerge from mechanistic models for animal performance instead of from single production functions. The benefit of using the more complex model is that it integrates the present knowledge of the biology of pig performance containing descriptions of the relevant metabolic and physiological processes and of the environmental influences on these. Because the influence of various environmental factors on animal performance is explicitly captured by the model equations, the biological traits can be defined as independent of these factors. The mechanistic model intends to 'soak up' all the interactions into the model main effects that are combined non-linearly to give the phenotype. Of course we cannot claim to have captured all possible factors and interactions, so we will not obtain a perfect fit across environments. The biological traits emerging from mechanistic models have however, next to the above described benefits of traits related to single biological production functions, the additional advantage of being independent from a range of environmental factors. This increases their validity across a range of environments and would make redundant the re-estimation of the trait values in environments that differ in these factors. Having only a single environment to test, we cannot test to what extent the estimated biological trait components are independent from the environment. But compared with conventional estimation methods for genetic value, the mechanistic model gives environmental effects the chance to explain differences in the phenotype between environments and even some G × E effects managed purely by the biological correctness of the model, which we have limited power to test – but the concept is made. For appropriate mechanistic models, the availability of records over different ages across the growth trajectory could partly substitute for lack of phenotypic information across different environments. However, it does not eliminate the need for information across environments. A powerful solution would be to collect records over different ages and to subject one individual to more than one environment during the growth performance test.

Since the traits considered here are defined to represent the underlying biology, direct measurements of these traits are often difficult to obtain in practice. Nevertheless, accurate estimates of the trait values are crucial for accurate model predictions and thus for the appropriate application of mechanistic models to breeding purposes. We have shown how realistic and unique estimates of phenotypic and genetic components of these biological traits can be derived from those of recorded performance traits that are represented as outputs of the mechanistic model. We further found that genetic differences between two breeds that for many generations had been selected according to different breeding goals are reflected in the biological traits. In addition, the underlying biological traits related to growth and body composition were found to have higher

[†]Cross breds were expected to have slower growth, higher or similar feed intake and larger backfat depth than the pure-bred lines.

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heritabilities than performance traits corresponding to growth and body composition. These properties combined provide some scientific evidence for the theoretical inference of a close association of these traits to the genetic makeup of the animals and may encourage further consideration of these traits for genetic improvement.

In this study, simulated populations with a simple balanced pedigree structure (full-sibs) have been used to derive the estimates for the underlying biological trait components, since the more complex pedigree structures of real animal populations would complicate the estimation of genetic and phenotypic variance and covariance components without increasing the accuracy (and meaningfulness) of the estimates. The approach presented here was not designed to and cannot produce estimates of these traits for individual animals of real pig populations. If the biological traits however were to be integrated into genetic evaluation programs in the future, estimates of their values for specific animal populations could be derived by adapting the methods of Varona *et al.* (1997) to the corresponding mechanistic growth model. Also, in the decomposition of the phenotype (equation (4)) several other possible variance components, including those given by random environmental effects, have been ignored. Inclusion of additional variance (and co-variance) components would be theoretically possible, but would increase the number of parameters to be estimated and therefore require most likely additional information to obtain robust solutions in the inversion process.

By integrating mechanistic models into the genetic evaluation methodology, several shortcomings of the current methods for predicting genetic merit may be overcome. First, regression models, which lie at the heart of current breeding value estimation, are designed to fit a specific data set rather than to represent the underlying biological processes. This approach usually results in useful statistics (estimated breeding values, EBVs) appropriate for the prevailing conditions. However, it provides a narrow scope of use; in particular, empirical models assume simple linear relationships between (combinations of) individual model components, which are renowned to cause problems when extrapolating to conditions not covered in the data. In order to avoid unexpected poor performance in environments that differ from the data conditions, new data need to be produced and the covariances required for the EBVs need to be re-estimated whenever the production conditions change. This is not always feasible at the commercial level.

Second, genetic markers and quantitative trait loci (QTL) have proved valid contributions to the description of the animal's true genetic merit, since they refer directly to the animal's intrinsic capacities in the prevailing environment. However, in order to be useful for breeding purposes, their association with the phenotypic performance traits of interest needs to be established in each environment and genetic background. In addition to the risk that this association is not sufficiently strong to translate into a significant genetic gain, current methods for determining the genotype-phenotype association generally lack the ability to quantify how gene expression varies across different environments and during different growth stages (Ma *et al.*, 2002). Encapsulating both, validity across a range of environments and describing the processes along part of or the entire growth trajectory, the biological traits of mechanistic growth models may add value to marker development.

It can be speculated that the underlying crux of these shortcomings of the current methods for estimating genetic merit is their lack of integrating knowledge of the biochemical, metabolic and physiological mechanisms that determine how the genetic merit may be expressed in the prevailing conditions. In contrast, mechanistic animal growth models aim to describe the metabolic and physiological pathways that link the genotype with predictions for phenotypic performance traits. As a consequence of the explicit description of the interactions between genetic potential and physiological and environmental constraints in the growth models, the mechanistic models are expected to be more able to provide for proper extrapolation outside the data range.

Conclusions

This paper suggests a novel use of mechanistic growth models for estimating genetic components of biological traits that could be advantageous for animal breeding. The biological traits specified as input parameters of mechanistic growth models are considered as intrinsic drivers of the observed phenotype. They are considered less dependent on the environment, as environmental factors are also fitted in these models.

It is therefore suggested that implementation of these traits into breeding programs would reduce the deleterious impact of G × E, and give more robust genetic gains across environments. For example, genetic gain made under favourable nucleus environments would give better correlated responses under less favourable commercial conditions that involve poorer nutrition, greater temperature stress, etc.

Implementation of biological traits into breeding programs requires the prediction of these traits for selection candidates, and this depends on having appropriate observed traits and the prevailing environmental conditions recorded. Further implications would follow for QTL mapping and/or marker association studies on the new set of traits. Such associations may well be stronger than for the more easily measured but less heritable observed traits – conditions that are conducive to more efficient marker-assisted selection programmes.

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