

Modifying Growth Curve Parameters By Multitrait Genomic Selection

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Introduction

Selection for growth rate is one of the main objectives in meat production species. However, selection for growth rate increases adult weight, which can be a problem when maintenance costs are important. Selection for growth rate keeping constant adult weight can also be a problem because birth weight increases with growth rate and the species can have birth difficulties. An alternative may be to modify the whole growth curve of the animal. Growth curves describe the entire growth process in terms of few parameters having a biological interpretation (Blasco (2003)). It is possible to modify the shape of an animal's growth curve by selection, keeping adult and birth weight within reasonable limits. However, growth curves require, in order to be fitted with some accuracy, data of weights at different ages that are frequently difficult or expensive to measure, particularly mature weights. Several authors (Muir (2007); Goddard and Hayes (2007)) have pointed out that genomic selection can be a solution for traits difficult to measure. The objective of this study is to examine by simulation the possibility of using genomic selection for changing the whole growth curve of an animal, acting simultaneously on the three parameters of a Gompertz growth curve.

Material and methods

Simulated data. A training rabbit population of 1000 individuals was simulated using features from a growth analysis of rabbit data carried out by Blasco et al. (2003) and Piles et al. (2003). For each rabbit, 40 weights (one by week) were simulated. A hierarchical model was employed to simulate the growth curve of each animal. Gompertz curve, well suited for rabbits (Blasco et al. (1992)), was used as the nonlinear function describing rabbits growth.

$$y_{ij}=a_i \exp(-b_i \exp(-k_i t_j)) + \varepsilon_{ij}$$

where y_{ij} is the observed weight of individual i at age j , a_i can be interpreted as the mature weight, maintained independently of short-term fluctuations, b_i is a time scale parameter related to the initial weight, k_i is a parameter related to the rate of maturing, and ε_{ij} is the fitting error, independently and normally distributed among individuals. The fitting error variance ($\sigma_\varepsilon^2=1000$) was considered to be constant for all ij .

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In a second stage of the hierarchical model, parameters a , b , and k were calculated as the sum of the QTL-genotype effects of an individual plus an overall mean and a residual effect sampled from a multivariate normal distribution $N(\mathbf{0}, \mathbf{I} \otimes \mathbf{R})$ where \mathbf{R} is a 3x3 (co)variance matrix between the residuals, and \mathbf{I} is a identity matrix. We considered parameters a , b , and k as three different traits of an individual. Each parameter of the growth curve was regulated by 60 biallelic QTL with the same effect. A simulated scenario with pleiotropy was considered for the genetic relationship between the Gompertz parameters, with genetic correlations $r(a,b)=-0.50$, $r(a,k)=-0.70$, $r(b,k)=0.40$. In our model, genetic correlations are generated by having common QTL alleles acting on different parameters. Phenotypic values of the parameters were assumed to be residually correlated with values $r_e(a,b)=-0.30$, $r_e(a,k)=-0.44$, $r_e(b,k)=0.65$.

Structured of simulated populations. In all simulations, we worked with a simplified model with only of 5 chromosomes of 1 Morgan with 10,000 SNPs each one. The parameters were regulated by 60 biallelic QTL. A uniform distribution between 0 and 1 was used to sample the absolute value of the all QTL effects. The phenotypic trait was simulated under additive gene action. In all populations LD was simulated by mutation (2.5×10^{-5}) and drift. In order to generate LD by drift, 1000 generations of random mating were simulated with an effective population of 100. After this period, the population was expanded to 1000 individuals where QTL effects were rescaled to set the heritability of the parameters a , b , and k to 0.5, 0.3 and 0.2, respectively. In generation 1001 phenotype and genotype were recorded and the genome-assisted breeding values (GEBVs) were estimated. In the following 9 generations (1001-1009) 100 males and 100 females were selected and mated according to an index composed by the estimated GEBVs. 1000 segregation SNPs (minor allele frequency > 0.05) from the generation 1001 were chosen for the analysis. Validation criterion was the accuracy of estimated breeding values for the generations 1001-1010, calculated as the correlation between true and estimated breeding values. Each simulated data set and its corresponding analysis was replicated 25 times. Four criteria were used to select the parents in the last 9 generations; smallest GEBVs for a (\hat{u}_a) and b (\hat{u}_b) the greatest for k (\hat{u}_k) and the smallest value of the standardized index $I = -\hat{u}_a/\sigma_{ua} - \hat{u}_b/\sigma_{ub} + \hat{u}_k/\sigma_{uk}$.

Statistical analyses. A Bayesian hierarchical model was used to estimate the GEBVs of generation 1001. The growth model used was the same as the Gompertz model simulated. As the QTLs of each individual are unknown, the genetic values of the parameters are not defined by the sum of the QTL effects but by the sum of the SNP marker effects. Thus, the estimated parameters $\theta^s = [\mathbf{a}^s, \mathbf{b}^s, \mathbf{k}^s]$ are now

$$\theta_i = \mu + u_i + e_i = \mu + \sum_{j=1}^{j=1000} X_{ij} \beta_j$$

where X_{ij} (0, 1, or 2) is the marker effect of locus j for individual i , and β_j is the vector of the allele substitution effect of the locus j in the training population. A prior distribution $N(\mathbf{0}, \mathbf{I} \otimes \mathbf{G}_0)$ was assumed for the locus effects, where \mathbf{G}_0 is the locus effects (co)variance matrix between the parameters and \mathbf{I} is the identity matrix. Prior distributions for the nuisance parameters, (co)variance matrices, and parameters of fitting errors models were flat with

limits in order to guarantee proper posterior distributions. Fully conditional posterior distributions of all unknowns of the Gompertz model were equivalent to the ones described by Blasco et al. (2003).

Results and discussion

The response to selection on the growth curve using the four criteria proposed is showed in figure 1. Most of the effects of all selection criteria are directly correlated to changes in adult weight, even when selection is performed only in parameter k . Reducing adult weight maintaining growth rate seems to be possible, as well as increasing growth rate keeping adult weight within reasonable limits. However, selection for multiple objectives looks more difficult (figure 1d). A second important problem is that the loss of accuracy is high for both the parameter being selected and the parameters that are not selected, due to the relatively high correlation between parameters. Figure 2 shows that accuracy is rapidly lost for all growth curve parameters, requiring a re-evaluation of the associations between SNPs and genes responsible of the response to selection.

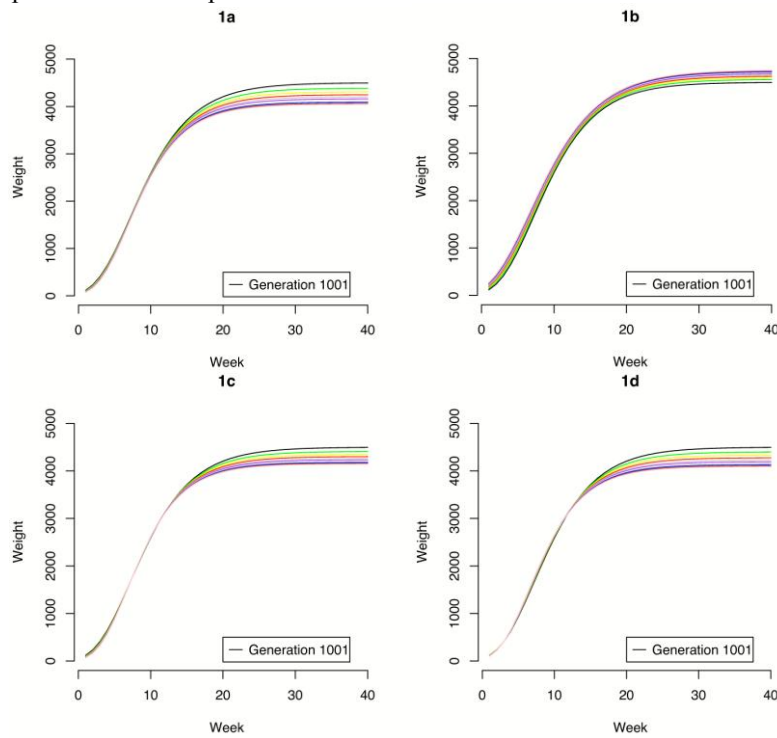


Figure 1: Response to selection. 1a. Selection to decrease parameter a . 1b. Selection to increase parameter b . 1c. Selection to increase parameter k . 1d. Selection for decreasing a typified index including the three parameters a , b , k .

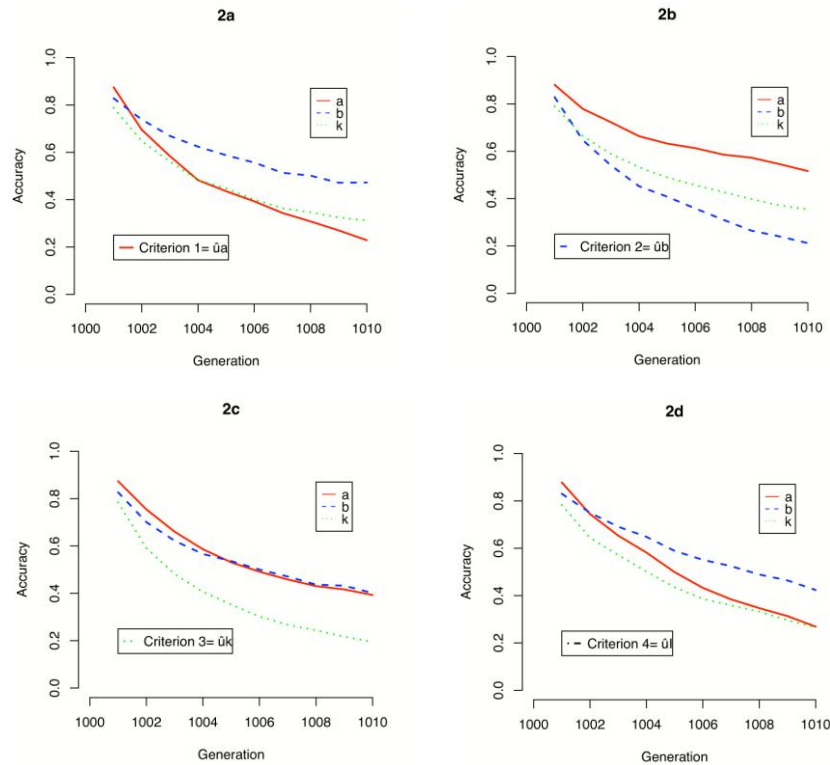


Figure 2: Evolution of accuracy with selection. 2a. Selection to decrease parameter a . 2b. Selection to increase parameter b . 2c. Selection to increase parameter k . 2d. Selection for decreasing a typified index including the three parameters a , b , k .

Conclusion

Genomic selection can be used for changing growth curve parameters, which respectively implies changes in mature weight, birth weight and relative growth rate. These changes are not easy due to the high genetic correlations between growth curve parameters. The easiest change seems to be the reduction of mature weight conserving growth rate for most of the curve or selection for growth rate keeping mature weight within reasonable limits. Applying genomic selection will require a constant re-evaluation of the associations between SNPs and genes determining the curve parameters.

References

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