Single-step genomic BLUP for national beef cattle evaluation in US: from initial developments to final implementation

D.A.L. Lourenco[1], S. Tsuruta[1], B.O. Fragomeni[1], Y. Masuda[1], I. Aguilar[2], A. Legarra[3], S. Miller[4], D. Moser[4] & I. Misztal[1]

[1] *University of Georgia, Department of Animal and Dairy Science, 30602 Athens, GA, USA*
danilino@uga.edu *(Corresponding Author)*
[2] *Instituto Nacional de Investigacion Agropecuaria, Canelones, Uruguay 90200*
[3] *Institut National de la Recherche Agronomique, UMR1388 GenPhySE, Castanet Tolosan, France 31326*
[4] *Angus Genetics Inc., St. Joseph, MO 64506*

Summary

The objective of this study was to implement single-step genomic BLUP (ssGBLUP) for national Angus cattle evaluation in the US. National evaluations include a variety of models with several linear and categorical traits, maternal effects, multibreed data, and a large number of genotyped animals. For the initial investigation, we used a dataset from 2014 that comprised over 8 million animals, 6 million birth weight (BW) and weaning weight (WW) records, 3.4 million post-weaning gain (PWG) records, and genotypes for 52k animals. A dataset from 2017 was later used that included 335k genotyped animals. The ability to predict future performance of young animals was investigated when using regular BLUP and ssGBLUP. Because of the increasing number of genotyped animals and the high computing cost to invert the genomic relationship matrix (**G**), the algorithm for proven and young (APY) was used to approximate the inverse of **G**. The APY uses recursions on a small subset of genotyped animals, called core. We further tested the feasibility of having daily interim genomic predictions for newly-genotyped animals based on SNP effects derived from the previous official ssGBLUP evaluation. In addition, we extended all models used in traditional evaluations to ssGBLUP, and compared genetic trends from traditional BLUP, ssGBLUP, and a multistep method that was implemented for the American Angus genomic evaluation in 2009. A new algorithm to approximate accuracy of GEBV for large genomic data was also developed. On average, the increase in ability to predict future performance, for BW, WW, and PWG, with ssGBLUP was 25% in the 2014 data and 36% in the 2017 data, compared to the traditional BLUP. The ssGBLUP with APY was as accurate as the regular ssGBLUP when the number of core animals was at least 10,000, independently of which animals were in the core group. Interim predictions derived from ssGBLUP provided accurate genomic values for newly-genotyped animals. Genetic trends for ssGBLUP and BLUP were similar, revealing overestimation in multistep evaluations, especially for traits with less phenotypes. Single-step GBLUP became a reality for American Angus evaluation and its implementation process resulted in successful updates in methodology, making this approach mature for national beef cattle evaluation.

Keywords: algorithm for proven and young, Angus, genomic selection, indirect prediction

Introduction

The use of genomic information for selection purposes in livestock breeding became possible in 2009. Since then, mainly two methods have been developed: multistep and single-step genomic BLUP (ssGBLUP; Aguilar et al., 2010). The first has some advantages when only EBV and genotypes are available; the later can use genotypes, phenotypes, and pedigree jointly when not all animals are genotyped, which is the truth for all species. The American Angus Association implemented multistep genomic evaluation in 2009, using a correlated approach described by Kachman (2008). In this approach, direct genomic values (DGV) calculated based on SNP effects are used as phenotypic information together with the trait phenotype in a 2-trait model. If the traditional evaluation uses a 4-trait model, the correlated approach requires an 8-trait model. As the DGV is assumed to have heritability > 0.99, genetic correlations can be overestimated indicating the genomic information is explaining more of the genetic variance than expected, which can inflate genomic EBV (GEBV).

In ssGBLUP, the genomic information is used to modify the pedigree relationship matrix (**A**). In this way, SNP markers directly change relationships among genotyped animals, and indirectly change between genotyped and ungenotyped, and among ungenotyped animals. This helps to increase accuracy of GEBV for all animals and makes ssGBLUP a simpler method for genomic evaluations. The simplicity and potentially higher accuracy helped ssGBLUP to become the current method of choice for genomic evaluation.

To avoid overestimation and fluctuations on GEBV, the American Angus Association decided to change the genomic method used for their national cattle evaluation. The tests with ssGBLUP started in 2015 and involved a variety of models with several linear and categorical traits, maternal effects, EBV from Red Angus as external information, and a large number of genotyped animals. This required a considerable amount of changes in the algorithms and software. The objective of this study was to implement ssGBLUP for American Angus national evaluation, describing the issues along the implementation process.

Material and methods

Data

Datasets were provided by the American Angus Association (AAA). For the initial investigation on predictive ability, we used a dataset from 2014 that comprised over 8 million animals, 6 million weaning weight (BW) and weaning weight (WW) records, 3.4 million post-weaning gain (PWG), and genotypes for 52k animals. A dataset from 2017 was later used that included over 10 million animals, 8 million records for BW and WW, 4.2 million records for PWG, and 335k genotyped animals. The animals were genotyped/imputed for 54,609 SNP from the BovineSNP50k v2 chip (Illumina Inc., San Diego, CA). After quality control, 38,528 and 39,759 SNP remained in the 2014 and 2017 datasets, respectively. Subsets of the 2017 data were used to evaluate an algorithm to approximate accuracy of GEBV. Additional traits used for the investigation of genetic trends are in Table 1.

Table 1. Number of records and animals in the pedigree for the investigation of genetic trends

TRAIT	Phenotypes	Animals in Pedigree
Scrotal Circumference (SC)	833k	1.96M

| Carcass Weight (CWT) | 105k | 2.54M |
| Marbling (MARB) | 105k | 2.53M |

Models and computations

Models used for genomic evaluations in ssGBLUP were the same as in traditional evaluations and have been described in Lourenco et al. (2015a). Predictive ability for direct effect was calculated as a correlation between adjusted phenotypes (i.e., phenotypes adjusted by all fixed effects in the model) and (G)EBV for 18.7k young genotyped animals born in 2013 (dataset 2014) and in 2016 (dataset 2017). For the maternal effect, adjusted phenotypes were correlated with the total maternal (G)EBV of the dam, which was calculated by adding 0.5 of the direct (G)EBV of the dam to the her maternal (G)EBV.

As the number of genotyped animals is growing fast for the American Angus population, the algorithm for proven and young (APY; Misztal et al., 2014) was tested with different numbers of core animals that varied from 2k to 15k randomly chosen (without replicates) or proven animals. The ideal number of core animals was additionally computed as the number of the largest eigenvalues explaining 98% of the variation in the genomic relationship matrix (**G**). The ability to predict GEBV was compared between ssGBLUP using regular $\mathbf{G}^{-1}$ and APY $\mathbf{G}^{-1}$.

Interim predictions were computed for the 18.7k young genotyped animals using SNP effects back-solved from ssGBLUP GEBV (Wang et al., 2012), assuming those young animals were not in the evaluation. The evaluations included 2k, 8k, or 33k genotyped animals and all phenotypes and pedigree available. Genomic EBV was computed either as DGV or as an index combining parent average (PA) and DGV.

For the multistep method, GEBV were calculated using the correlated approach as described by Kachman (2008), using molecular breeding values (MBV) and trait phenotypes in a multiple-trait model. Correlations between GEBV from this approach and ssGBLUP were calculated and genetic trends were compared with traditional trends.

All computations were done using the BLUPf90 software suite (Misztal et al., 2016), that underwent several modifications to account for a large number of genotyped animals and to reduce computing efforts.

Results and discussion

Ability to predict future performance

Predictive ability for 18.7k young animals that had phenotypes removed from the evaluations is shown in Table 2. For the direct effects, the average increase in ability to predict future performance with ssGBLUP was 25% in the 2014 data and 36% in the 2017 data, compared to the traditional BLUP. This increase reflects the impact of adding about 283k genotyped animals to the genomic evaluations. For the maternal effect, predictive ability increased 8% and 10% for the 2014 and 2017 datasets, respectively. Among BW, WW, and PWG, the greatest predictive ability was observed for BW. Previous studies showed that prediction accuracies or predictive ability are biased downward by selection (Bijma, 2012; Lourenco et al., 2015b). In addition, although the number of animals used for validation was the same, the groups were different in 2014 and 2017.

For calving ease, predictive ability was obtained only for the 2014 data. Predictive ability for the direct effect was 0.12 for BLUP and 0.13 for ssGBLUP, whereas for maternal

effect it was 0.05 and 0.08 for BLUP and ssGBLUP, respectively. Low predictivity for calving ease may be because of low heritability (0.18 for direct and 0.12 for maternal) and because animals with difficult calving are unlikely to be retained for breeding and therefore would not be genotyped on a regular basis. In fact, only 330 animals out of 95k with difficult calving were genotyped.

Table 2. Predictive ability for direct and maternal effects using datasets from 2014 and 2017.

	2014				2017			
	Direct		Maternal[1]		Direct		Maternal[1]	
Trait[2]	BLUP	ssGBLUP	BLUP	ssGBLUP	BLUP	ssGBLUP	BLUP	ssGBLUP
BW	0.29	0.39	0.25	0.28	0.32	0.47	0.29	0.34
WW	0.34	0.38	0.35	0.36	0.33	0.40	0.31	0.32
PWG	0.23	0.29	-	-	0.25	0.35	-	-

[1] Maternal effect is not considered for post-weaning gain.
[2] BW = birth weight; WW = weaning weight; PWG = post-weaning gain.

Number of core animals in APY

Based on the 2014 dataset, several numbers of core animals were tested in the APY algorithm to construct $\mathbf{G}^{-1}$. Figure 1 shows correlations between post-weaning gain GEBV when using regular and APY ssGBLUP, for the 18.7k young genotyped animals. When the core group was selected based on the accuracy of EBV (Fig. 1A), correlations with regular ssGBLUP increased with the number of core animals and reached 0.99 with at least 8k animals. In the case core animals were randomly sampled (Fig. 1B), 10k was enough to reach correlation of 0.99 with regular ssGBLUP, meaning the number of animals was more important than which animals are in the core group.

Pocrnic et al. (2016) showed that the number of core animals that maximizes the correlation between GEBV from regular and APY ssGBLUP is dependent on the effective population size, and can be calculated as the number of eigenvalues explaining 98 or 99% of the variance of $\mathbf{G}$. Figure 1C shows numbers of eigenvalues explaining 90, 95, 98, and 99% of the variance of $\mathbf{G}$, and correlations between GEBV from regular and APY ssGBLUP (data labels in the plot area). The correlations reached 0.99 when the number of core animals represented eigenvalues explaining 98% of the variance of $\mathbf{G}$ (10.6k).

Using 10k core animals in APY ssGBLUP, for example, only requires the inverse for a block of $\mathbf{G}$ for 10k animals, which has a cubic computing cost (time); additional genotypes require only linear storage and computing cost (time). The APY algorithm drastically reduced computing time and allowed the use of ssGBLUP for American Angus evaluations.

Interim evaluations using ssGBLUP

Genomic evaluations for American Angus are weekly based; however, there may be a need for interim evaluations on a daily basis, especially for young genotyped animals. In addition, some tests for commercial cattle (non-registered) provided by Angus Genetics Inc. (St. Joseph, MO) jointly with Zoetis (Kalamazoo, MI) (e.g., GeneMax) rely on predictions based on SNP effects only (no phenotypes are used). In ssGBLUP, SNP effects can be obtained by backsolving GEBV (Wang et al., 2012; Lourenco et al., 2015). Table 3 shows correlations

between adjusted phenotypes and genomic predictions for 18.7k young genotyped animals from the 2014 data, assuming different numbers of genotyped animals in the evaluation. When the evaluation included a large number of genotyped animals (33k), predictions based only on SNP effects (i.e., DGV) were similar to GEBV and to predictions obtained using an index of PA and DGV. For young animals, interim predictions via SNP effects derived from ssGBLUP seem a viable alternative as it can be done separately from the full evaluation.

Table 3. Predictive ability for interim evaluations based on only SNP effects (DGV), and an index combining PA[1] and DGV[2].

Method	Birth weight			Weaning weight			Post-weaning gain		
	2k	8k	33k	2k	8k	33k	2k	8k	33k
DGV	0.23	0.32	0.37	0.28	0.33	0.37	0.19	0.24	0.29
PA + DGV	0.31	0.35	0.38	0.36	0.37	0.39	0.24	0.26	0.29
GEBV[3]	0.34	0.36	0.39	0.35	0.36	0.38	0.27	0.27	0.29

[1] PA is parent average from traditional EBV.
[2] DGV is the direct genomic value obtained based on SNP effects as Zu, where Z is the matrix of SNP content and u is the SNP effect.
[3] GEBV are genomic estimated breeding values obtained in regular ssGBLUP.

Genetic trends and correlations among evaluation methods

The genetic trends for WW, SC, CWT, and MARB are in Figure 2. For WW, all trends were very similar, with a small underestimation for multistep GEBV. Correlations between multistep and ssGBLUP GEBVs for 2,500 young bulls was 0.92. For the traits that had fewer phenotypic records (SC, CWT, and MARB), the trends for multistep GEBV were clearly in a different scale, with an underestimation for older animals and a severe overestimation for the young ones (compared to traditional BLUP). The genetic trends for ssGBLUP and traditional BLUP were coincident for all traits. Correlations between GEBV from multistep and ssGBLUP for 2,500 young bulls were 0.90, 0.73, and 0.86 for SC, CWT, and MARB, respectively. Kuehn et al. (2017) tested multistep and ssGBLUP using data from the U.S. Meat Animal Research Center and reported strong bias for carcass traits with multistep. For CWT, the regression coefficients of traditional EBV on GEBV from multistep and from ssGBLUP were 0.56 and 0.99, respectively (Kuehn et al., 2017).

Issues in the implementation of ssGBLUP for commercial evaluations

Based on the results from Lourenco et al. (2015) and Kuehn et al. (2017), the American Angus Association implemented ssGBLUP officially in July of 2017. Changing the evaluation system from traditional BLUP to ssGBLUP requires a modification in the relationship matrix. The use of a denser relationship matrix can often bring convergence issues. One of the issues faced during the implementation of ssGBLUP for national Angus evaluation in the US was the increased computing time for the calving ease (CE) evaluation. The traditional BLUP evaluation for CE uses BW as a correlated trait, assuming CE categorical and BW continuous in a threshold-linear model. When changing to ssGBLUP, the computing time increased from 12 hours to 4.5 days. This was using a dataset with 7.2 million records for BW, 1.4 million records for CE, 8.5 million animals in the pedigree, and 152k genotyped animals. We increased the number of preconditioned conjugate gradient

iterations from 40 to 200 to solve the mixed model equations, which consequently reduced the number of threshold iterations; in addition, we increased the percentage of the pedigree relationship matrix among genotyped animals (A_{22}) that is blended to G (to avoid singularity problems) from 5% to 15%. After all, the computing time reduced to 19 hours. Another strategy that can be adopted to reduce computing time is to use EBV from traditional evaluation as prior information for the ssGBLUP run.

Another implementation issue was the inclusion of external EBV from Red Angus in the evaluation of growth traits. For traditional evaluations, the external EBV is used as prior information in the right hand side of the mixed model equations, and the reliability is added to the pedigree relationships among external animals in the left hand side of the mixed model equations (Legarra et al., 2000). We changed the computing algorithm to support genomic and external information, and the implementation of a genomic multibreed model increased the computing time only by 2.5 hours, compared to a genomic single-breed model.

The first implementation of ssGBLUP did not consider inbreeding for , but considered for and . Because of that, the coefficients in and were not in the same scale as , and a scaling factor (omega = 0.7) was used to reduce ; this avoided inflation in GEBV. Once inbreeding was considered for , there was no need to use omega different than 1.0 for this population.

Understanding the choice for core animals was not an easy task at the beginning of the implementation of ssGBLUP. Based on the tests, we observed that choosing core animals randomly or based on EBV accuracy resulted in correlations >0.99 between GEBV from regular and APY ssGBLUP, if the core group had a minimum of 10k animals. Bradford et al. (2017) showed random core definition is more robust, especially if the genotyped animals have incomplete pedigree. Less optimal core definitions may cause convergence issues. We chose to select core animals based on EBV accuracy for the official evaluations because all genotyped animals in the Angus database have complete pedigree. Convergence and computing time were monitored when using the two definitions mentioned before; however, no differences were found.

The calculation of SNP effects from GEBV requires saving G^{-1} to disk, because this calculation is done in a standalone software from the BLUPF90 family (postGSf90). With the increasing number of genotyped animals, one solution to speed up the computations is to change the algorithm used in postGSf90, so the APY G^{-1} can be used instead of the regular G^{-1}. However, the number of elements to be saved is still considerably large, because of relationships between core and noncore animals. To overcome this issue, SNP effects were estimated based on the core G^{-1} and compared DGV with the ones obtained using the full G^{-1}. Because correlations were >0.98, only core animals are being used in the estimation of SNP effects.

One of the benefits of using genomic information is to increase breeding value accuracy. Accuracies are calculated based on prediction error variance (PEV) and can be obtained from the inverse of the coefficient matrix (diagonal of . If the number of animals in the pedigree is large, the inverse is not computationally feasible and an approximation has to be used. For ssGBLUP, A^{-1} is replaced by the inverse of the realized relationship matrix (H^{-1}) that contains pedigree and genomic relationships. Therefore, approximating accuracy of GEBV requires the calculation of contributions due to phenotypes, pedigree, and genomic relationships. An algorithm to approximate genomic contributions was developed based on diagonals of G and the average traditional accuracy for genotyped animals. The increase in computing time was irrelevant, comparing to the approximation based on pedigree and phenotypes only. Correlations between accuracy from the new algorithm and true accuracy from PEV were higher than 0.85 for growth traits, using a sample dataset.

Conclusion

Several issues were raised during the initial tests with single-step GBLUP for beef cattle genomic evaluation; however, all of them were solved. This method is more stable and less biased than the multistep method previously used for American Angus evaluation. In addition, changes in the traditional models are not needed during the implementation of single-step, as the main changes are in the relationship matrix and in the algorithms. To account for the increasing number of genotyped animals, the algorithm for proven and young can be successfully used. This algorithm drastically reduces computing time and enables genomic evaluations for millions of genotyped animals. When interim predictions are part of the evaluation system, GEBV from single-step can be used for the estimation of SNP effects and, consequently, calculation of direct genomic values for young genotyped animals. The full implementation of single-step GBLUP by the American Angus Association in July of 2017 shows this method is mature for beef cattle national evaluation.

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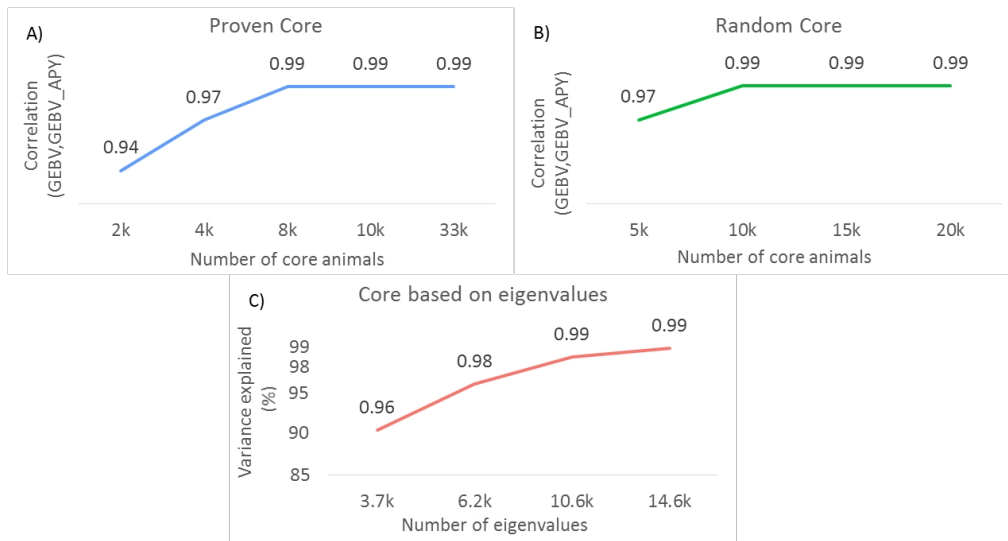
Figure 1. Correlation between GEBV from regular ssGBLUP (GEBV) and APY ssGBLUP (GEBV_APY) for post-weaning gain for 18.7k young genotyped animals. A: core animals selected based on the accuracy of EBV; B: core animals selected randomly; C: number of core animals selected based on the number of eigenvalues explaining 90, 95, 98, and 99% of the variance of G matrix. The data labels in the plot area the correlation between GEBV and GEBV_APY.

Figure 2. Genetic trends for ssGBLUP, multistep, and traditional evaluation using all animals. A: weaning weight; B: scrotal circumference; C: carcass weight; D: marbling.

Trends for carcass traits do not reflect recent model changes adopted by Angus Genetics Inc. (St. Joseph, MO).