

Breeding and Genetics: Genomic Methods and GWAS

461 Exact P -values for large-scale single-step genome-wide association using the BLUPF90 software suite. D. Lourenco^{*1}, I. Aguilar², Y. Masuda¹, I. Misztal¹, and A. Legarra³, ¹University of Georgia, Athens, GA, ²INIA, Las Brujas, Canelones, Uruguay, ³INRA, Castanet Tolosan, France.

Single-step genomic BLUP (ssGBLUP) is a method that combines all sources of information in a single analysis to compute genomic EBV (GEBV). For single-step genome-wide association studies (ssGWAS), GEBV are back-solved to SNP effects, and those effects are converted to proportion of explained additive genetic variance. Thus far, no formal framework for hypothesis test is currently present in ssGWAS from the BLUPF90 software suite. Our objective was to implement P -values for ssGWAS and to apply the method to a large dairy cattle population. P -values were obtained based on the prediction error (co)variance for SNP, which uses the inverse of the coefficient matrix for genotyped animals and formulas to compute SNP effects. Six steps are needed for the calculation of P -values: 1) factorize and invert the LHS of ssGBLUP; 2) solve MME using sparse Cholesky factor; 3) extract the LHS⁻¹ for genotyped animals; 4) back-solve GEBV to SNP effects; 5) obtain the prediction error covariance for SNP effects; 6) calculate P -values using the cumulative standard normal function of SNP effect divided by standard deviation of SNP effect. The US Holstein data used in this study consisted of almost 800k udder depth records for 500k cows. Pedigree information was available for 1.3M animals, of which 8,802 sires were genotyped. The model contained the same effects as the official model used for linear type trait evaluation in the US; however, in a single-trait setup. Computation of P required 20Gb of memory and no inflation was observed. The SNP passing the Bonferroni threshold of 6.1 in the $-\log_{10}$ scale were the same as those that explained the highest proportion of additive genetic variance. The exact P -value for ssGWAS is a very general and efficient strategy for QTL detection and test. It can be used in complex data sets such as the ones used in animal breeding, where only a proportion of pedigreed animals are genotyped. The BLUPF90 software suite is now equipped with the P -value calculation tool.

Key Words: genome-wide association studies (GWAS), single-step genomic BLUP (ssGBLUP), significance test

462 Genomic predictions using more markers and gene tests. G. R. Wiggins², P. M. VanRaden¹, D. J. Null¹, and J. B. Cole^{*1}, ¹USDA Animal Genomics and Improvement Laboratory, Beltsville, MD, ²Council on Dairy Cattle Breeding, Bowie, MD.

The number of markers used in US genomic predictions increased to 79,276 (or 80K) in December 2018 from the previous 60,671 (60K) used since 2014. The revised list includes more exact gene tests, removes poorer-quality markers, adds new variants from DNA sequence or high-density chips with larger effects on traits, and improves marker order using the new ARS-UCD1.2 reference map. Missing alleles were imputed for Holsteins by (1) imputing all bulls and their ancestors and (2) using those haplotypes as priors to impute the remaining 2 million females, which required 9 d to compute with 25 processors and 270 GB of memory. The 80K list increased computing times for other key programs by about 30%. Important variants now included directly (e.g., in *DGATI*, *ABCG2*, β -casein, and β -lactoglobulin) had large effects on yield traits and the net merit index. Of the top 5 effects for each of 41 traits, only 34% were from the original 50,000-marker list for Holsteins, 55% for Jerseys, 53% for Brown Swiss, 33% for Ayrshires, and 38%

for Guernseys. For Holsteins, a new sequence marker on chromosome 3 had the largest effect on final score, foot angle, feet-and-legs score, and rear legs (rear view). Gene tests for cholesterol deficiency, complex vertebral malformation, brachyspina, and calpain had large effects on somatic cell score, udder cleft, protein yield, and gestation length, respectively. For Jerseys, *bGHR* had a large effect on productive life. Genomic predictions improved more for breeds with larger reference populations. Individual predictions changed most for animals less related to the US population, with less complete pedigrees, or genotyped with lowest density chips. After excluding older cows genotyped using 3,000 markers and imputed dams, correlations of 80K with 60K predictions were about 0.99 for Jersey, Holstein, and Guernsey yield traits but higher for Ayrshires and Brown Swiss. Correlations for many other traits were lower. For Holsteins, correlations averaged a little less than 0.99 for the 6 new health traits and slightly less than 0.98 for type and calving traits. Reliability is expected to increase by 1 to 3 percentage points.

Key Words: genomic prediction, gene test, sequence

463 Validation of genomic predictions for linear type traits in US Holsteins using over 2 million genotyped animals. S. Tsuruta^{*1}, D. A. L. Lourenco¹, Y. Masuda¹, I. Misztal¹, and T. J. Lawlor², ¹University of Georgia, Athens, GA, ²Holstein Association USA, Brattleboro, VT.

As accumulating more genotypes, the validation of genomic predictions can be more reliable. In our previous studies, 0.5 million genotyped Holsteins were used to predict genomic (G)PTA. Today, genotypes for over 2 million Holsteins are available, meaning that more genotyped young animals can be used for validation. The objective of this study was to investigate biases in GPTA for young genotyped bulls and verify that the method with a single-step genomic BLUP that has been used in our studies is reliable. Phenotypes for 18 linear type traits used in 2018 genetic evaluation were provided by Holstein Association USA, and genotypes in 2018 were provided by the Council on Dairy Cattle Breeding. The full data set consisted of 10,946,264 records up to 2018 calving, 13,591,145 animals in the pedigree, and 2,334,951 genotyped animals with 80K SNP. Young genotyped bulls with no daughters in 2014 and with at least 50 daughters in 2018 were used to calculate regression coefficients (b_1) of GPTA in 2014 on daughter yield deviations in 2018 as an indicator of inflation or deflation of GPTA. Coefficients of determination (R^2) were used to compare accuracies in parent averages and GPTA. The BLUP90IOD2 program was used to predict GPTA in 2014 and in 2018 with the single-step genomic BLUP using the algorithm of proven and young animals. Genetic trends were also calculated to detect the bias in GPTA. All results from this study were compared with the results from our previous study that used phenotypes and genotypes as of 2014. The model included inbreeding in the pedigree-based relationships and estimable unknown parent groups to reduce inflation and minimize biases in GPTA as suggested in our previous studies. Inflation or deflation (b_1) in GTPA was within 1.0 ± 0.1 on average, depending on the trait, but more stable than the previous results. Genetic trends verified that the model used in this study was unbiased. More young genotyped bulls could provide more stable and reliable results for the validation of GPTA. Convergence via BLUP90IOD2 was reached in 3