

Use of causative variants and SNP weighting in a single-step GBLUP context

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A O T E A C E N T R E , A U C K L A N D , N E W Z E A L A N D

Motivation

- Decreasing costs of whole genome sequence
- Revived interest in causative variants for prediction
- Several authors are finding and using causative variants
 - No improvement :
 - Binsbergen et al., 2015 and Erbe et al., 2016
 - Up to 5% improvement:
 - Brondum et al. 2015 and Vanraden et al., 2017

Motivation

- ssGBLUP was able to reach accuracies close to 1 with simulated causative variants
 - When priori used for weights were the simulated QTN effects
- GWA estimated weights had limited impact
 - GWA Methodology – no limitation in minimum and maximum weights

Objective

- Test different SNP weighting methods in GBLUP and ssGBLUP in field data which includes causative variants.

Field Data

- 4M Records for Stature
- 3M Cows
- 4.6M Animals in pedigree
- $h^2=0.44$
- 27k Genotyped Sires
 - 54k SNP
 - 54k SNP + 17k Causative Variants (VanRaden et al., 2017)

Analysis

- **GBLUP**

- Multi-step approach
- Daughter deviation as phenotypes
- Genomic Relationship Matrix
- Homogeneous or heterogeneous residual variance

- **ssGBLUP**

- Same model as national evaluation for type traits
- No deregressions
- Matrix combining pedigree and genomic information (**H**)

Weighted Genomic relationship matrix

$$\mathbf{G} = \mathbf{ZDZ}' \frac{\sigma_s^2}{\sigma_a^2} = \frac{\mathbf{ZDZ}'}{\sum_i 2p_i q_i}$$

- Default

- $\hat{d}_i = 1$

- Linear weights

- $\hat{d}_i = \hat{u}_i^2$

- Non-linear A weights

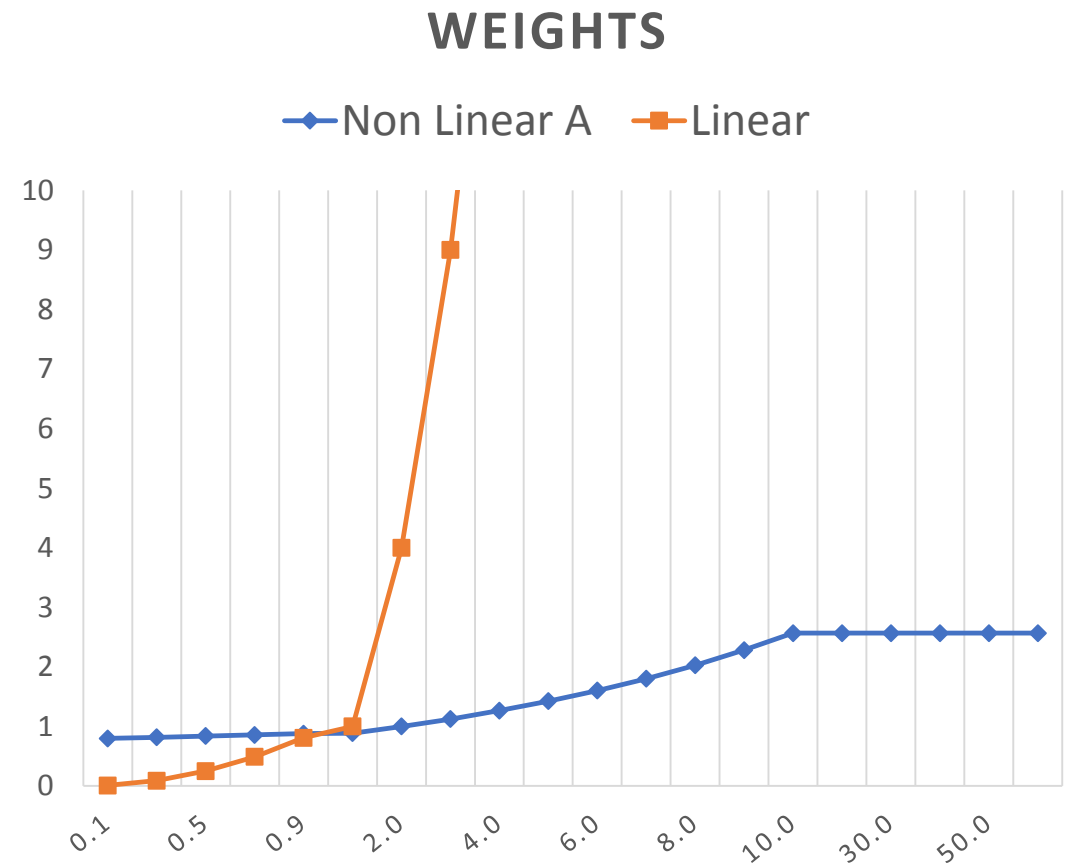
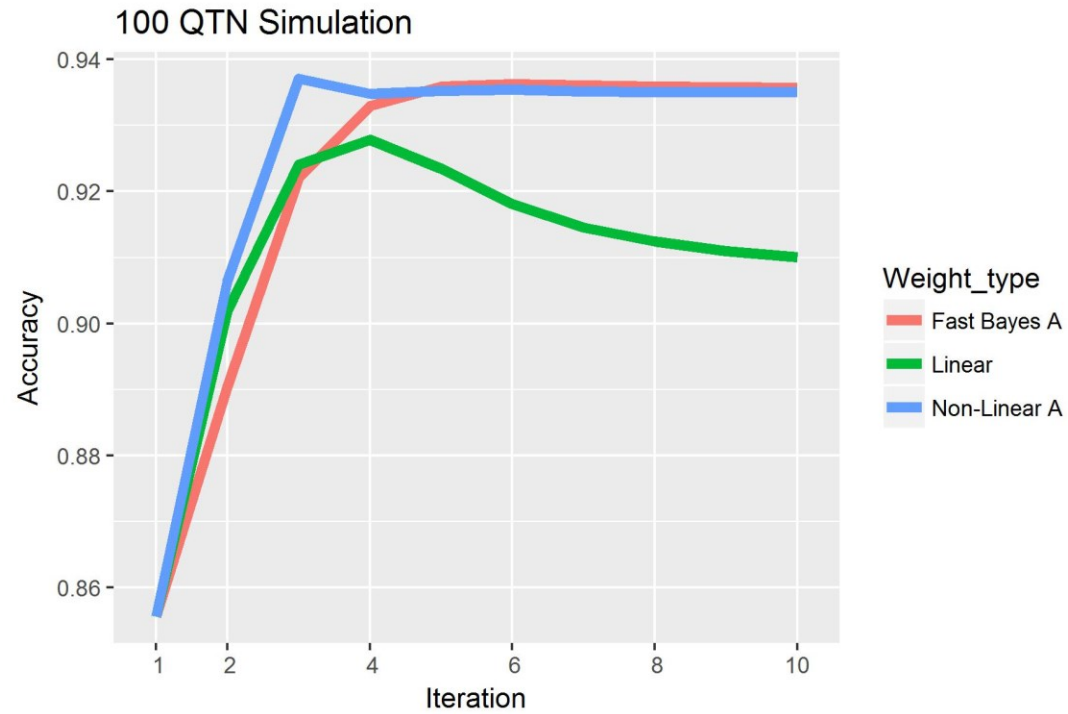
- $\hat{d}_i = 1.125 \frac{|\hat{u}_i|}{sd(u)}^{-2}$

- Value capped at 10

- Fast-Bayes A

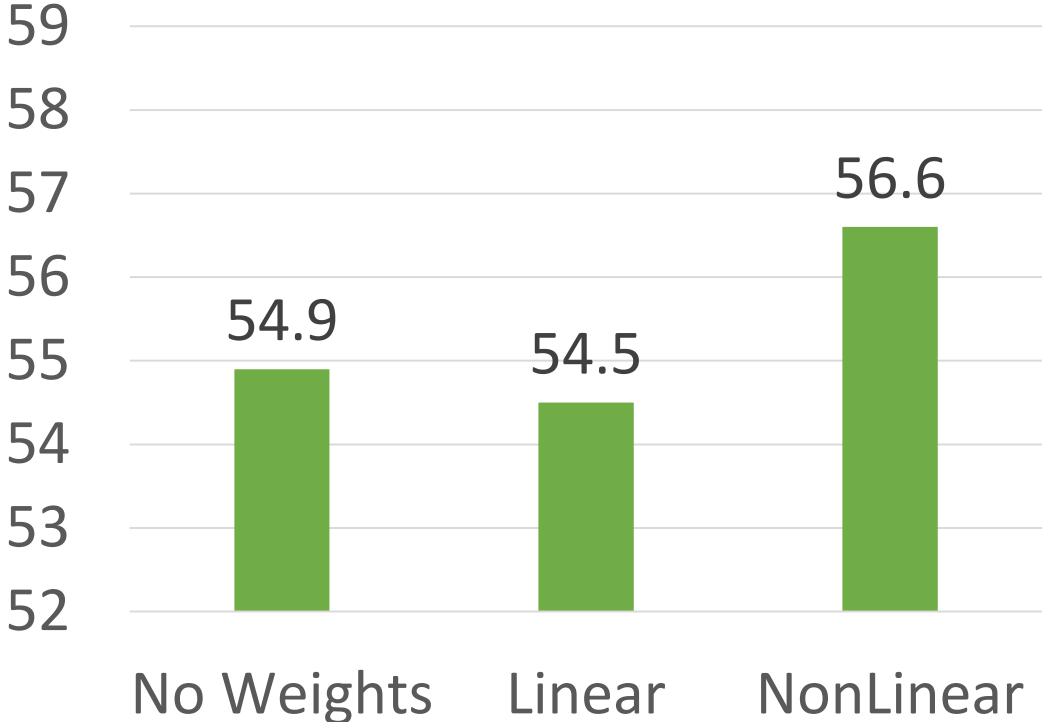
- $\hat{d}_i = \frac{SNP_{eff_i}^2 + df * S^2}{df + 1}$

Weighted

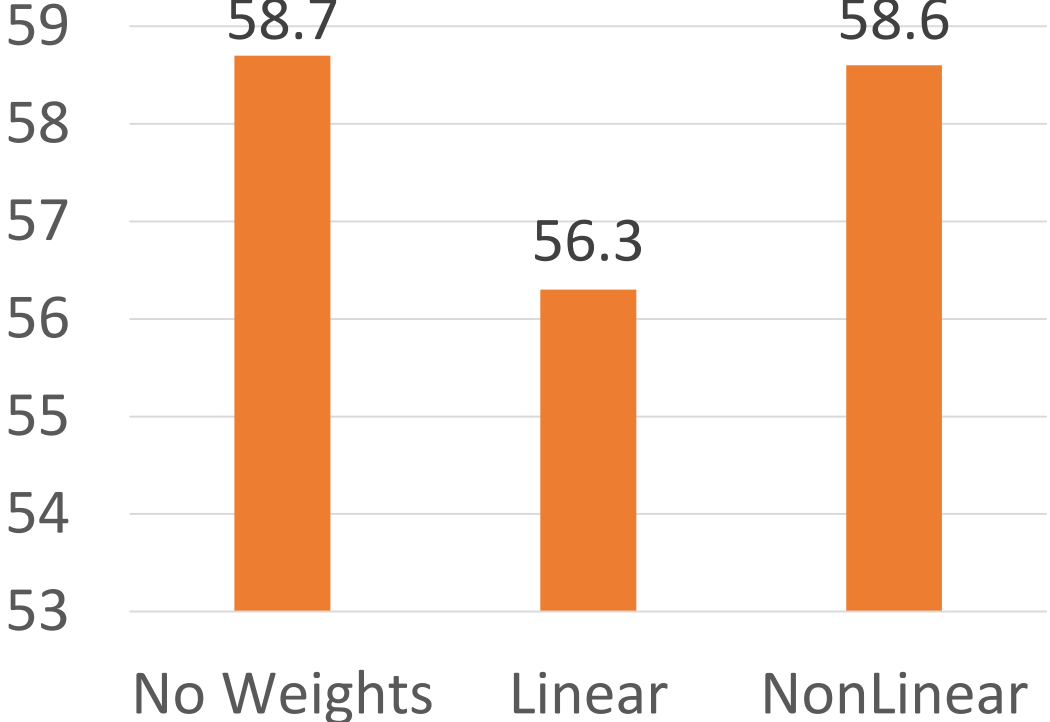


GBLUP – 54K SNP

HOMOGENEOUS RESIDUAL VARIANCE

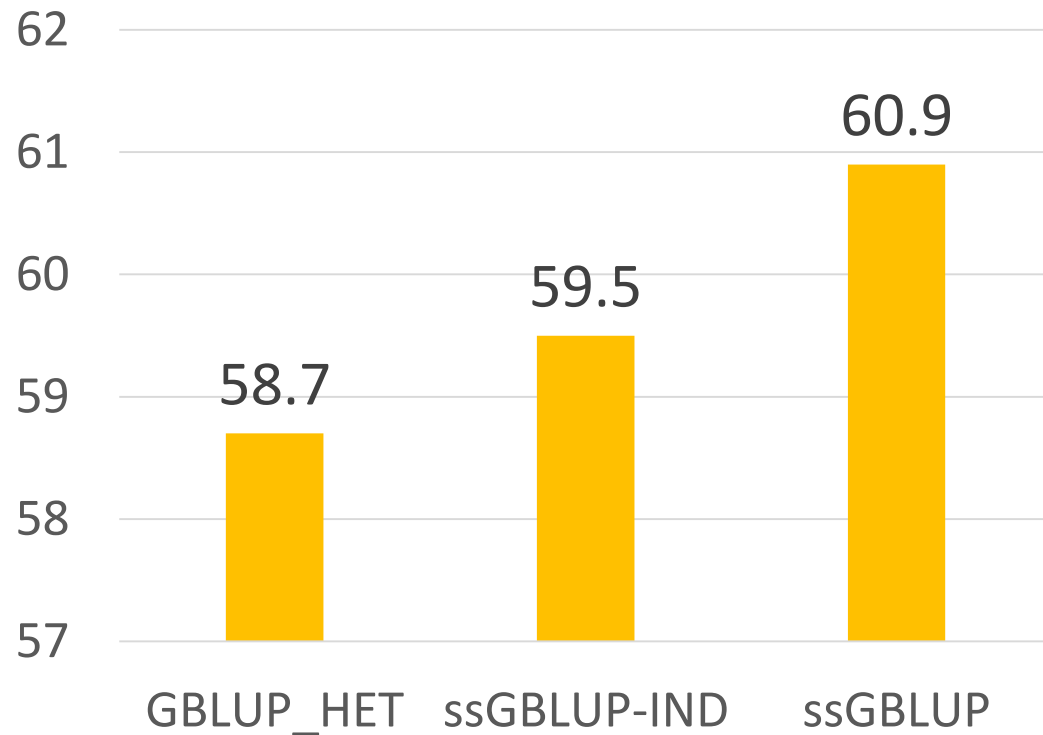


HETEROGENEOUS RESIDUAL VARIANCE

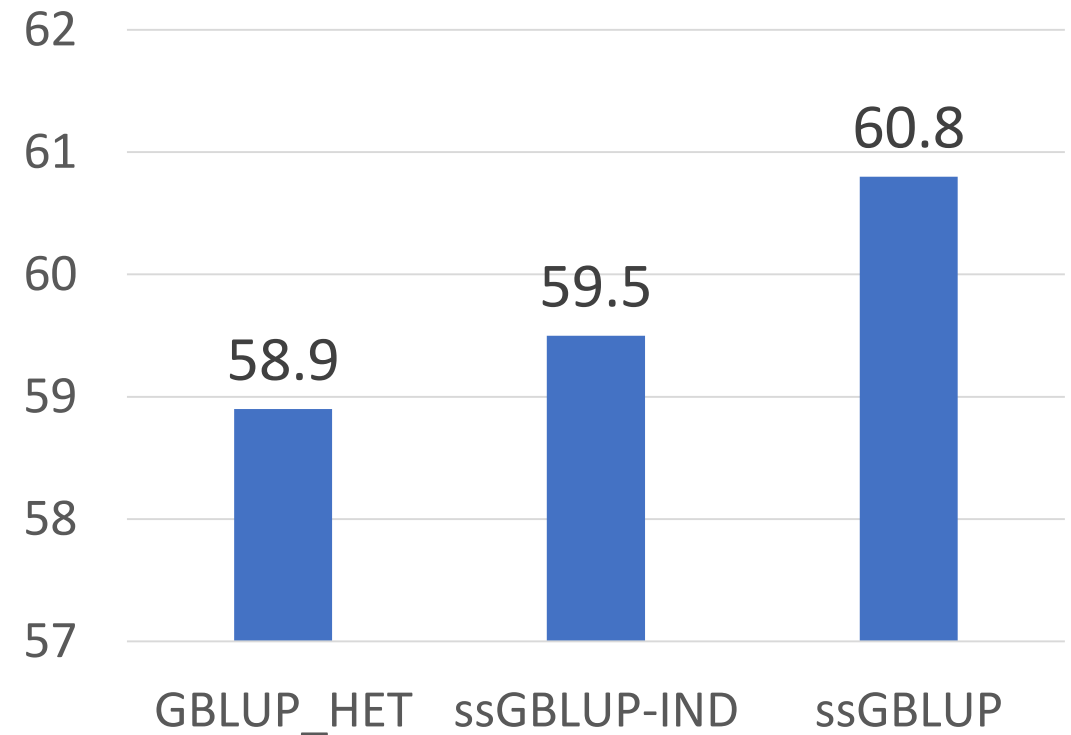


Weighted and unweighted reliabilities

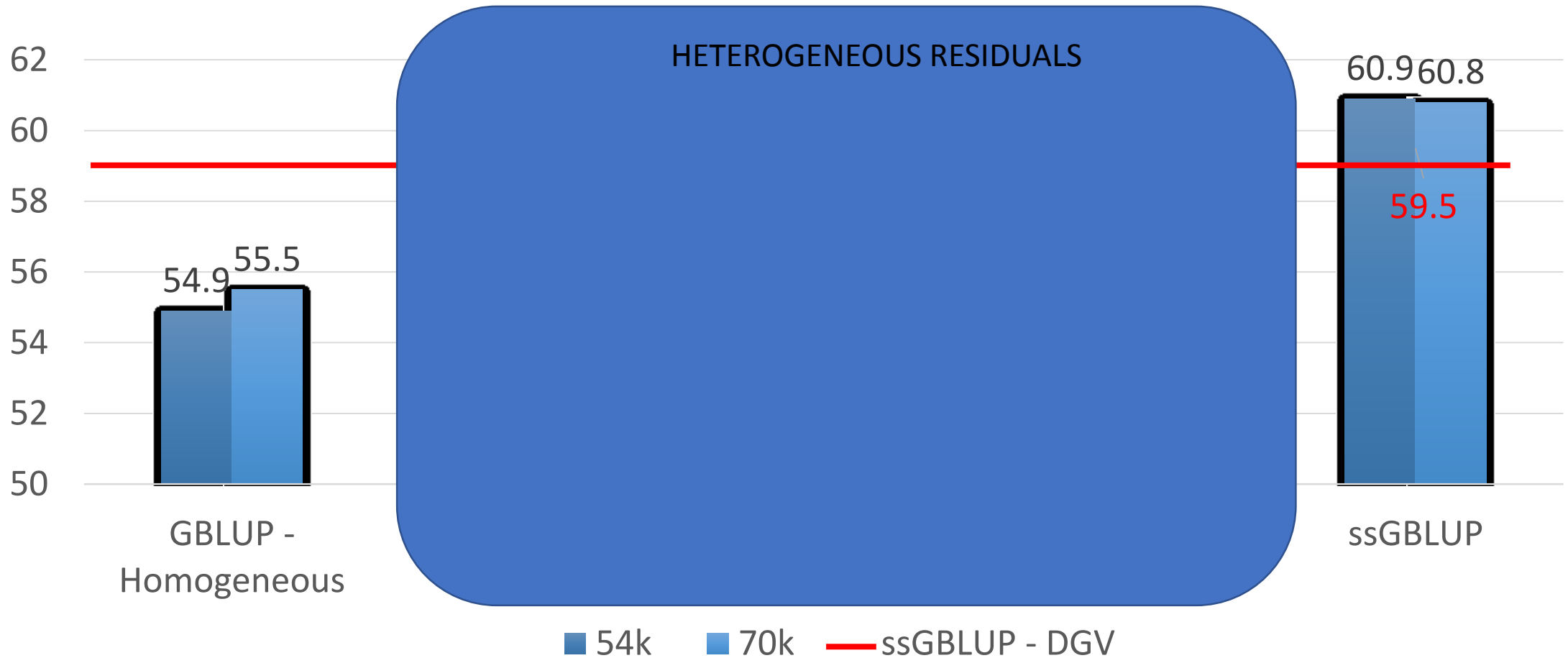
Unweighted GRM



Weighted GRM



Including causative variants



Conclusion

- Gains with inclusion of causative variants is limited when trait is polygenic
- Gains with causative variants has more impact in GBLUP than in ssGBLUP
 - More data is used in single-step methodology, therefore impact of prior is less important
- Non-linear methodology is better for weighting marker effects than linear weights