CENTER FOR QUANTITATIVE GENETICS AND GENOMICS

Improvement of Genomic Prediction by Including Additive-by-Additive Epistasis

A case study in advanced wheat breeding lines

Raffo M.[1]*, Sarup P.[1,2], Guo X.[1], Liu H.[1], Jensen J.[1]

[1] Center for Quantitative Genetics and Genomics, Aarhus University, Denmark. [2] Nordic Seed A/S, Odder, Denmark. *e-mail: mraffo@qgg.au.dk

Background

Including epistasis in genomic prediction (GP) models may improve cultivar selection. Extended genomic best linear unbiased predictor (EG-BLUP, Ref.1) and natural and orthogonal interaction approach (NOIA, Ref.2) are proposed to model additive-by-additive epistasis, but their efficiency is unknown in wheat breeding.

Aims i) to evaluate the performance of EG-BLUP and NOIA for variance components (VC) estimation in a wheat breeding population, and ii) to investigate if including epistasis in GP enhances the predictive ability (PA).

Experimental data

- Grain yield // 2,060 F6 lines // 7 breeding cycles (BC)
- 21 year*locations (YL) in Denmark
- Genotyped: 15K Illumina BeadChip

Statistical models

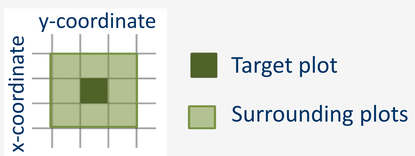
1. Baseline - without genomic information

$$y = Xb + Z_1a + Z_2f + \sum_{i=1}^{n=9} Z_is + e$$

FE *Random(R): Line* *R: GxE* *R: Sp. eff.* *R: error*

FE: fixed effect, trial nested in YL and BC; *GxE*: Genotype x Environment

Sp.eff.: spatial effect
Coordinate of target and eight surrounding plots (n=9) are used to correct by sp. variability



2. Genomic best linear unbiased predictor (G-BLUP)

Baseline + Additive genomic effect
Covariance structure (COV): G-Matrix (Ref.3)

3. EG-BLUP = *G-BLUP* + Epistatic genomic effect
COV: Hadamard product of G-Matrix

4. NOIA = *Baseline* + Additive and epistatic genomic effects COV: NOIA relationship matrices

NOTE: G-BLUP and EG-BLUP assume Linkage & Hardy-Weinberg-Equilibrium (LE & HWE) // NOIA only assumes LE.

Partition of genetic variances is shown in **Figure 1**

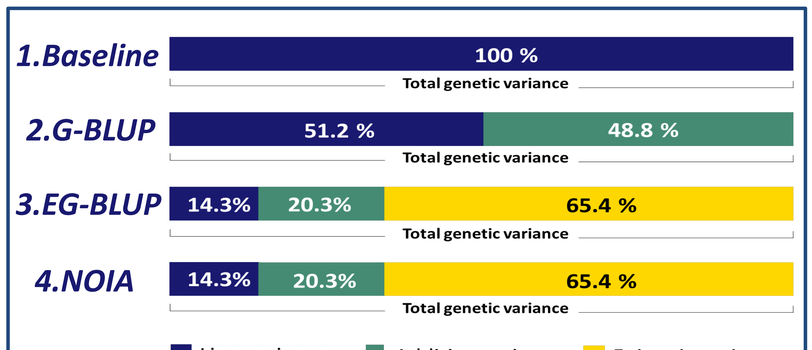


Figure 1: Proportion of genetic variances captured by model terms. VC estimated by REML using the software DMU.

Genomic prediction

- Leave One Line Out cross-validation (LOO CV)
- PA = correlation between phenotypes corrected by fixed effect and predicted values
- G-BLUP and EG-BLUP PAs are shown in **Figure 2**

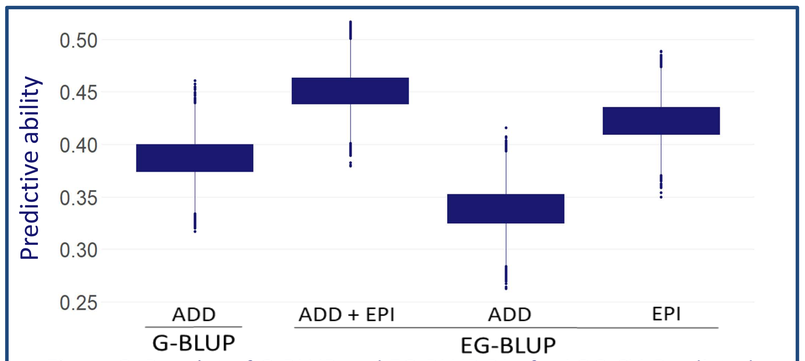


Figure 2: Boxplot of G-BLUP and EG-BLUP PAs for LOO CV. Predicted values: additive (ADD), epistatic (EPI), sum of ADD and EPI (ADD+EPI). Distribution of PAs based on bootstrap sampling, r=10,000.

Main findings

I. EG-BLUP and NOIA yielded similar estimates regardless of removing HWE requirement and did not achieve orthogonal partition of VC.

II. More research is needed to develop models that lift LE requirement and perform an orthogonal partition of VC.

III. EG-BLUP outperformed G-BLUP with a significant (p = 0.01, *t-test*) increase in PA of 16.5%.

Concluding:

Although orthogonal partitioning of genetic variances was not possible, EG-BLUP enhanced total genetic merit prediction, which can improve cultivar development.

Ref.1. Su G, Christensen O, Ostersen T, Henryon M, Lund MS (2012) Estimating additive and non-additive genetic variances and predicting genetic merits using genome-wide dense single nucleotide polymorphism markers. PLoSOne7:e45293. **Ref.2.** Alvarez-Castro and Carlborg (2007). A unified model for functional and statistical epistasis and its application in quantitative trait loci analysis. Genetics 176,1151–1167. **Ref.3.** VanRaden PM (2008) Efficient methods to compute genomic predictions. J.D.Sci91:4414-4423

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