Estimating genomic breeding values using genomic BLUP and ridge regression BLUP

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Intro

$$\mathbf{y} = \mathbf{g} + \epsilon$$

- What is $\mathbf{g}$?

Plant ID	y	g	e
1	10	5	5
2	7	6	1
3	12	2	10

Intro

- Recall that **g** is the cumulative additive genetic effect

$$\mathbf{y} = 1\mu + \sum_k x_k \beta + e$$

W is a centered $n \times m$ marker matrix, **a** is vector of SNP effects

Ridge regression BLUP

$$\mathbf{y} = 1\mu + \sum_k x_k \beta + \epsilon$$

- Proposed before the 'big data' trend by Meuwissen et al (2001)
- $\hat{\beta} = \mathbf{X}'(\mathbf{X}\mathbf{X}' + \lambda \mathbf{I})^{-1}\mathbf{y}$
  - $\lambda = \frac{\sigma_e^2}{\sigma_\beta^2}$

Genomic BLUP

$$\mathbf{y} = 1\mu + \mathbf{Zu} + e$$

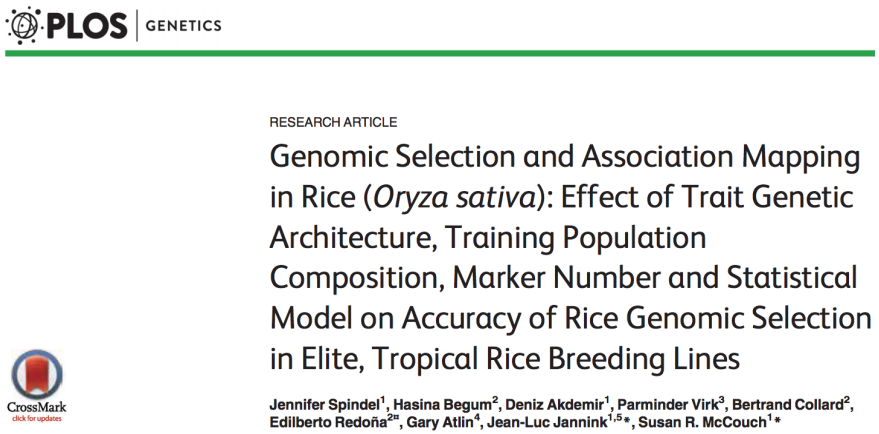
- $\hat{u} = \left[\mathbf{I} + \mathbf{G}^{-1}\frac{\sigma_e^2}{\sigma_u^2}\right]\mathbf{y}$
- How do these methods differ? How will the GEBVs differ?

Equivalence

- For gBLUP the $Var(y) = \mathbf{ZGZ}'\sigma_u^2 + \mathbf{I}\sigma_e^2$
- For rrBLUP the $Var(y) = \mathbf{XX}'\sigma_\beta^2 + \mathbf{I}\sigma_e^2$
  - What does $\mathbf{XX}'$ represent?

Demonstration with Spindel data

- 299 elite rice lines from IRRI
- genotyped with 73,147 SNPs
  - we'll use 39,560
- phenotyped for 19 traits
  - **grain yield (GY)**
  - measured in dry and wet seasons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RESEARCH ARTICLE

Genomic Selection and Association Mapping in Rice (*Oryza sativa*): Effect of Trait Genetic Architecture, Training Population Composition, Marker Number and Statistical Model on Accuracy of Rice Genomic Selection in Elite, Tropical Rice Breeding Lines

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Loading data

```
##Clear all objects
rm(list = ls())

# Load the data
pheno <- read.csv("~/Downloads/Spindel/pheno_WS.csv")
dim(pheno)
```

```
## [1] 299  20
```

```
geno <- read.table("~/Downloads/Spindel/Spindel_geno.txt",
                   sep = "\t", header = T, row.names = 1)
dim(geno)
```

```
## [1] 39560   299
```

```
geno <- t(geno)
dim(geno)
```

```
## [1]   299 39560
```

```
sum(row.names(geno) == pheno$GHID)
```

```
## [1] 299
```

Calculate a GRM

```
head(geno[,1:5])
```

```
##       S1_189590 S1_196811 S1_204765 S1_211589 S1_212693
## A1257         2         2         2         2         2
## A1258         2         2         2         2         2
## A1302         2         2         2         2         2
## B1053         2         2         2         2         2
## A1260         2         2         2         2         2
## A1304         0         0         0         0         0
```

```
Zsc <- scale(x = geno, center = T, scale = T)
GRM <- tcrossprod(Zsc)/ncol(geno)

dim(GRM)
```

```
## [1] 299 299
```

gBLUP using rrBLUP package

```
library(rrBLUP)

gBLUP <- mixed.solve(y = pheno$YLD, K = GRM)
names(gBLUP)
```

```
## [1] "Vu"   "Ve"   "beta" "u"    "LL"
```

```
length(gBLUP$u)
```

```
## [1] 299
```

rrBLUP using rrBLUP package

```
library(rrBLUP)

rrBLUP <- mixed.solve(y = pheno$YLD, Z = Zsc)
names(rrBLUP)
```

```
## [1] "Vu"   "Ve"   "beta" "u"    "LL"
```

```
length(rrBLUP$u)
```

```
## [1] 39560
```

- Why are the sizes `rrBLUP$u` and `gBLUP$u` different?
- How can we make the two comparable?

Are rrBLUP and gBLUP equivalent?

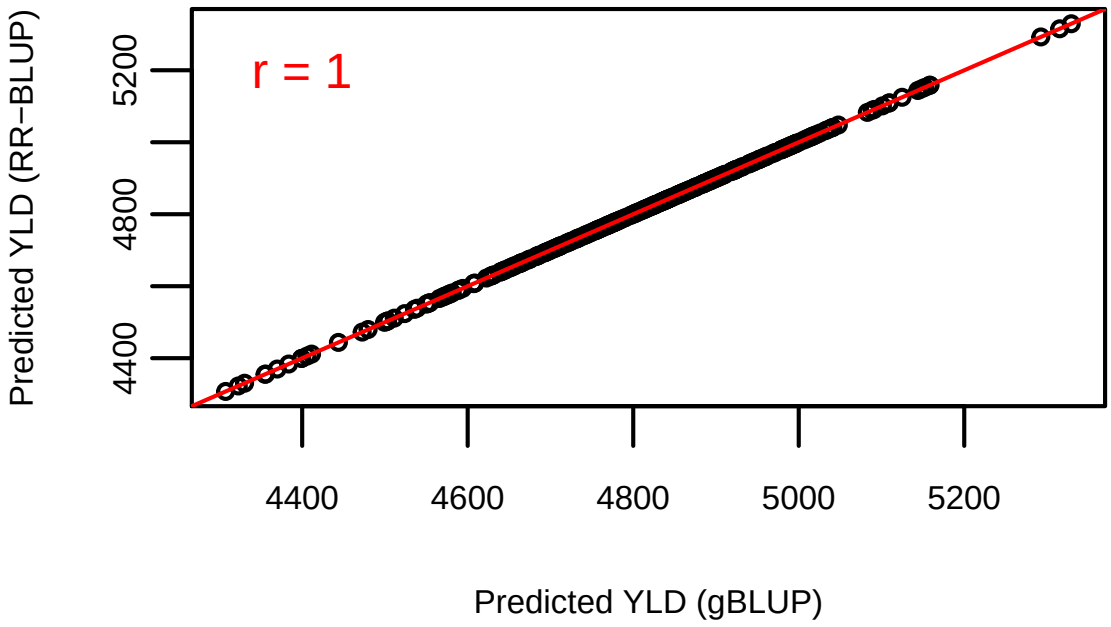
- Recall

$$\hat{g} = W\hat{a}$$

```
#calculate GEBVs from predicted marker effects
gBLUP_rr <- Zsc %*% rrBLUP$u

gBLUP_YLD <- gBLUP$u + as.numeric(gBLUP$beta)
gBLUP_rr_YLD <- gBLUP_rr + as.numeric(rrBLUP$beta)
```

Are rrBLUP and gBLUP equivalent?

```
par(mar=c(3,4,0.5,0.5), mgp=c(1.8,0.5,0), xpd = F, cex.lab = 0.5,
    cex.axis = 0.5)
plot(gBLUP_YLD, gBLUP_rr_YLD, ylab = "Predicted YLD (RR-BLUP)",
     xlab = "Predicted YLD (gBLUP)", pch = 21, cex = 0.5)

abline(lm(gBLUP_rr_YLD ~ gBLUP_YLD), col = "red")

text(x = 4400, y = 5200, paste0("r = ",
  round(cor(gBLUP_YLD, gBLUP_rr_YLD),2)), col = "red", cex = 0.75)
```



How accurate are our predictions?

- How can we estimate how accurate our predicted genomic breeding values are?

How accurate are our predictions?

- How can we estimate how accurate our predicted genomic breeding values are?
  - Compare predicted and observed breeding values for a new population
  - Partition dataset and use one for training and one for prediction

Two fold cross validation

- For some dataset
  (1) randomly split the the individuals into two equal sized (or close to) sets
  (2) mask the observations in one set (testing set), keep observations for other set (training set)
  (3) fit the model using training set and predict the values for the missing individuals
  (4) take the correlation between predicted GEBVs for test set and observed phenotypes for test set
  (5) repeat 1 - 4

Two fold cross validation

```
pheno_train <- pheno
#define the testing and training sets
set.seed(123)
train_set <- sample (1:length(pheno$GHID), size = length(ph
test_set <- setdiff(1:length(pheno$GHID), train_set)
length(train_set)
```

```
## [1] 149
```

```
length(test_set)
```

```
## [1] 150
```

```
#Mask the phenotypes for the testing set
pheno_train[test_set ,]$YLD <- NA
```

Run RRBLUP with training set

```
library(rrBLUP)
##rrBLUP
rrBLUP_train <- mixed.solve(y = pheno_train$YLD, Z = Zsc)
rrBLUP_train <- Zsc %*% rrBLUP_train$u
length(rrBLUP_train)
```

```
## [1] 299
```

Assess predictive ability from rrBLUP approaches

```
rrBLUP_test <- rrBLUP_train[test_set]
pheno_test <- pheno[test_set ,]

cor(pheno_test$YLD, rrBLUP_test)
```

```
## [1] 0.1618154
```

References

- Endelman, J. B. Ridge regression and other kernels for genomic selection with R package rrBLUP. Plant Genome 4, 250–255 (2011).
- Habier, D., Fernando, R. L. & Dekkers, J. C. M. The impact of genetic relationship information on genome-assisted breeding values. Genetics 177, 2389–2397 (2007).
- Meuwissen, T. H. E., Hayes, B. J. & Goddard, M. E. Prediction of total genetic value using genome-wide dense marker maps. Genetics 157, 1819–1829 (2001).
- Spindel, J. et al. Genomic selection and association mapping in rice (Oryza sativa): effect of trait genetic architecture, training population composition, marker number and statistical model on accuracy of rice genomic selection in elite, tropical rice breeding lines. PLoS Genet. 11, e1004982 (2015).