UNIVERSIDADE DE SÃO PAULO
ESCOLA SUPERIOR DE AGRICULTURA
“LUIZ DE QUEIROZ”
DEPARTAMENTO DE GENÉTICA
LGN5825 Genética e Melhoramento de Espécies Alógamas

Genomic Selection

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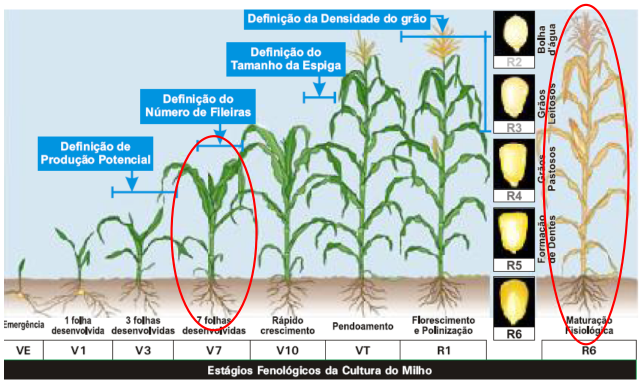
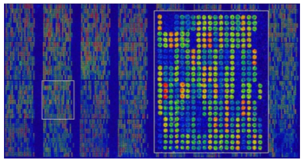
Early in(direct) selection

- Objectives:
- Reducing the interval between generations
- Using traits more accessible and cheaper evaluation
- Selecting before flowering



- Problems in the traditional selection
- Negative correlations
- Development stage – genes differentially expressed



- What about marker-selection?

$$\text{ISE}=\sqrt{\frac{h_m^2}{h_{trait}^2}}\,r_{(trait,m)}$$

$$\text{ISE}=\sqrt{\frac{1}{h_{trait}^2}}\,r_{(trait,m)}$$

$$\text{ISE}=\frac{r_{(trait,m)}}{\sqrt{h_{trait}^2}}$$

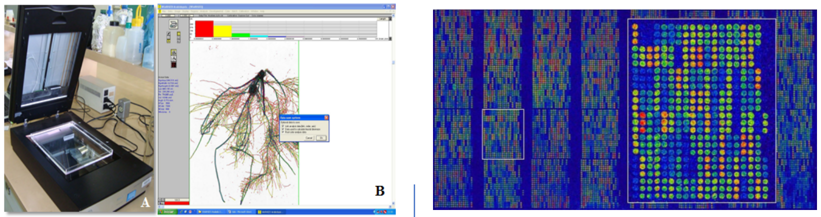
Genomic selection

- Simultaneous prediction (without tests) of the genetic effects of large numbers of markers
- Dispersed on wide genome
- Capture the effects of all loci (small and large)
- Explain much of the genetic variation of a character
- Keeps the "black box" about the genetic control
- Minor “aversion” by breeders

- Limitations
- Loss of genetic variance
- Fast inbreeding
- Initial cost

General procedures of GS

Training population
sample from population of selection
Phenotyping and genotyping
> 500 individuals



Y = Xb + Zh + e
Prediction of markers effects
Statistical equations and methods

Ex. RR-BLUP

Assumes equal variances among markers (VG / Nm)

The characters differ in the number and the markers that maximize the accuracy of prediction

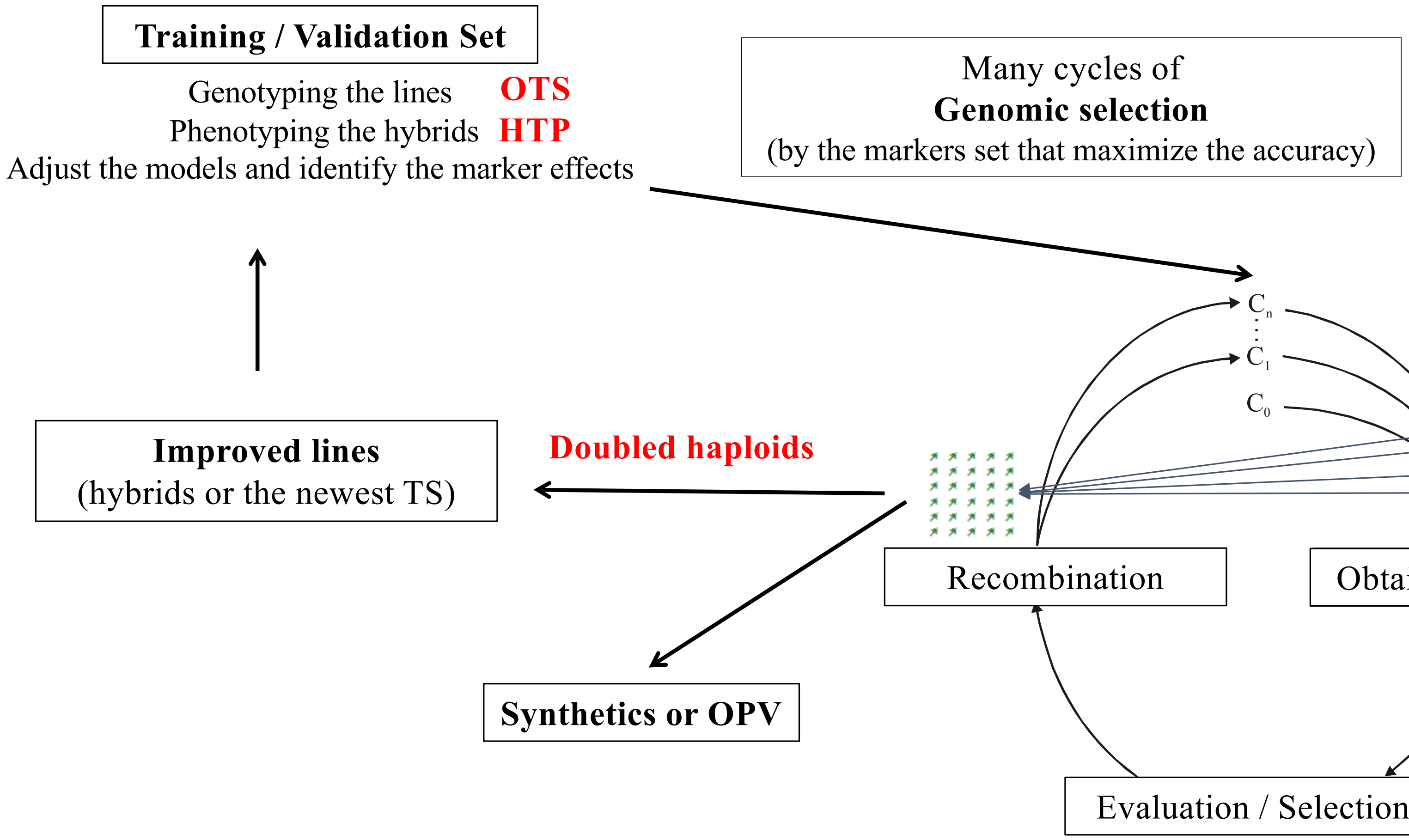
Validation of markers
New and independent population or
Statistical methods of cross-validation

Cross-validation methods

Application in Selection Schemes
Only genotyping
Breeding populations

GEBV = Zh

Genomic Recurrent Selection



Training / Validation Set

Genotyping the lines **OTS**
Phenotyping the hybrids **HTP**
Adjust the models and identify the marker effects

Many cycles of
Genomic selection
(by the markers set that maximize the accuracy)

Improved lines
(hybrids or the newest TS)

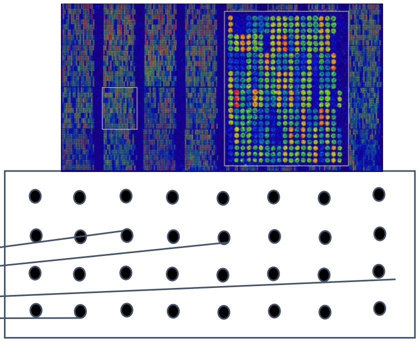
Doubled haploids

Synthetics or OPV

Recombination

Obtaining progenies

Evaluation / Selection



RR-BLUP/GS

- It’s a multiple regression
- Each marker is a factor/parameter

5 individuals
7 markers

MM	2
Mm	1
mm	0

Individuo	Diâmetro	Marca 1	Marca 2	Marca 3	Marca 4	Marca 5	Marca 6	Marca 7
1	9.87	2	0	0	0	2	0	0
2	14.48	1	1	0	0	1	1	0
3	8.91	0	2	0	0	0	0	2
4	14.64	1	0	1	0	1	0	0
5	9.55	1	0	0	1	1	1	0

$$X = \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 1 \end{bmatrix}$$

$$\boxed{\mathbf{Y = Xb + Zh + e}}$$

$$\begin{bmatrix} \hat{b} \\ \hat{h} \end{bmatrix}$$

$$\begin{bmatrix} \mathbf{X'X} & \mathbf{X'Z} \\ \mathbf{Z'X} & \mathbf{Z'Z} + \dfrac{\sigma_e^2}{\sigma_{Am}^2 / n} \end{bmatrix} \begin{bmatrix} \overset{\frown}{\mathbf{b}} \\ \overset{\frown}{\mathbf{h}} \end{bmatrix} = \begin{bmatrix} \mathbf{X'y} \\ \mathbf{Z'y} \end{bmatrix}$$

RR-BLUP/GS

$$\begin{bmatrix} \mathbf{X'X} & \mathbf{X'Z} \\ \mathbf{Z'X} & \mathbf{Z'Z} + \dfrac{\sigma_e^2}{\sigma_{Am}^2 / n} \end{bmatrix} \begin{bmatrix} \widehat{\mathbf{b}} \\ \widehat{\mathbf{h}} \end{bmatrix} = \begin{bmatrix} \mathbf{X'y} \\ \mathbf{Z'y} \end{bmatrix} \longrightarrow \begin{bmatrix} \hat{b} \\ \hat{h} \end{bmatrix} = \begin{bmatrix} 12.4519 \\ -0.3526 \\ 0.2761 \\ 1.4467 \\ -1.3701 \\ -0.3526 \\ 0.5436 \\ -1.63765 \end{bmatrix}$$

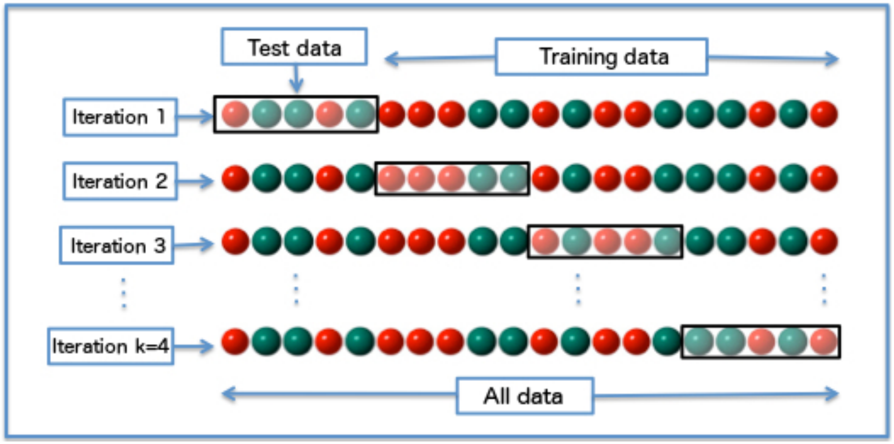
- Genomic estimated breeding values
- h = marker effects

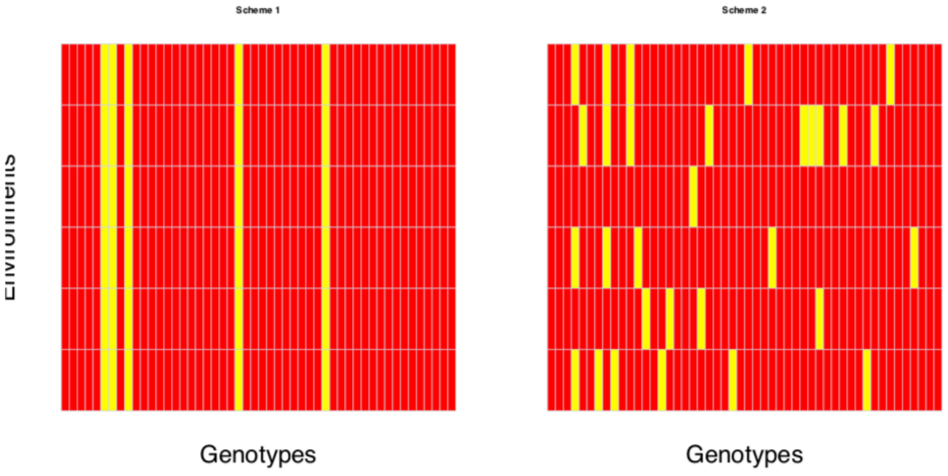
$$\boxed{\mathbf{GEBV = Zh}}$$

$$\boxed{\begin{bmatrix} -1.4104 \\ \boxed{0.1145} \\ -2.7230 \\ \boxed{0.7415} \\ -1.5317 \end{bmatrix}} = \begin{matrix} 2 & 0 & 0 & 0 & 2 & 0 & 0 \\ 1 & 1 & 0 & 0 & 1 & 1 & 0 \\ 0 & 2 & 0 & 0 & 0 & 0 & 2 \\ 1 & 0 & 1 & 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 1 & 1 & 1 & 0 \end{matrix} \;\mathbf{x}\; \begin{bmatrix} -0.3526 \\ 0.2761 \\ 1.4467 \\ -1.3701 \\ -0.3526 \\ 0.5436 \\ -1.63765 \end{bmatrix}$$

Cross-validation

- Estimate how accurately a predictive model will perform in practice
- Avoid overfitting
- Partitioning the original sample into a training set to train the model, and a test set to evaluate it
- E.g., partitioning the data set into two sets of 80% for training and 20% for test
- In k-fold cross-validation, the original sample is randomly partitioned into k equal size subsamples
- Multi-environment models - Two main schemes (CV1 and CV2)
- ***k*-fold cross-validation vs. Repeated random sub-sampling validation**





G-BLUP method

- Equivalent to the RR-BLUP but less computing consuming
- Easy to extend it to other factors or kind of kernels

$$\mathbf{Y = Xb + Za + e}$$

$$\begin{bmatrix} X'X & X'Z \\ Z'X & Z'Z + G_a^{-1}\frac{\sigma_e^2}{\sigma_a^2} \end{bmatrix} \begin{bmatrix} \hat{u} \\ \tilde{a} \end{bmatrix} = \begin{bmatrix} X'y \\ Z'y \end{bmatrix}$$

$$Ga = \frac{WW'}{\sum_{i=1}^{n}(2piqi)}$$

Efeitos aditivos: W

$$W = \begin{cases} Se\ MM; & 2 \quad \rightarrow 2 - 2p = 2q \\ Se\ Mm; & 1 \quad \rightarrow 1 - 2p = q - p \\ Se\ mm; & 0 \quad \rightarrow 0 - 2p = -2p \end{cases}$$

$$\mathbf{GEBV = Za}$$

$$\mathbf{Y = Xb + Za + Zd + e}$$

$$\begin{bmatrix} X'X & X'Z & X'Z \\ Z'X & Z'Z + G_a^{-1}\frac{\sigma_e^2}{\sigma_a^2} & Z'Z \\ Z'X & Z'Z & Z'Z + G_d^{-1}\frac{\sigma_e^2}{\sigma_d^2} \end{bmatrix} \begin{bmatrix} \hat{u} \\ \tilde{a} \\ \tilde{d} \end{bmatrix} = \begin{bmatrix} X'y \\ Z'y \\ Z'y \end{bmatrix}$$

Efeitos de dominância: S

$$S = \begin{cases} Se\ MM; & 0 \quad \rightarrow -2q^2 \\ Se\ Mm; & 1 \quad \rightarrow 2pq \\ Se\ mm; & 0 \quad \rightarrow -2p^2 \end{cases}$$

$$G_d = \frac{SS'}{\sum_{i=1}^{n}(2\mathrm{p}_i q_i)^2}$$

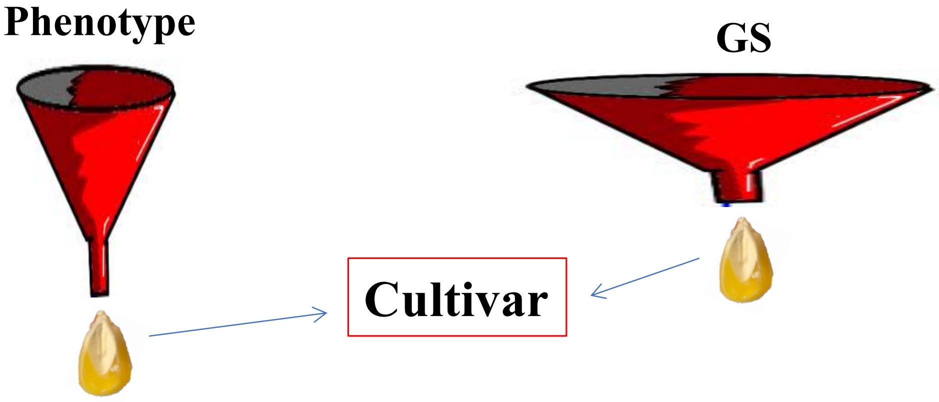
$$\mathbf{GV = Za + Zd}$$

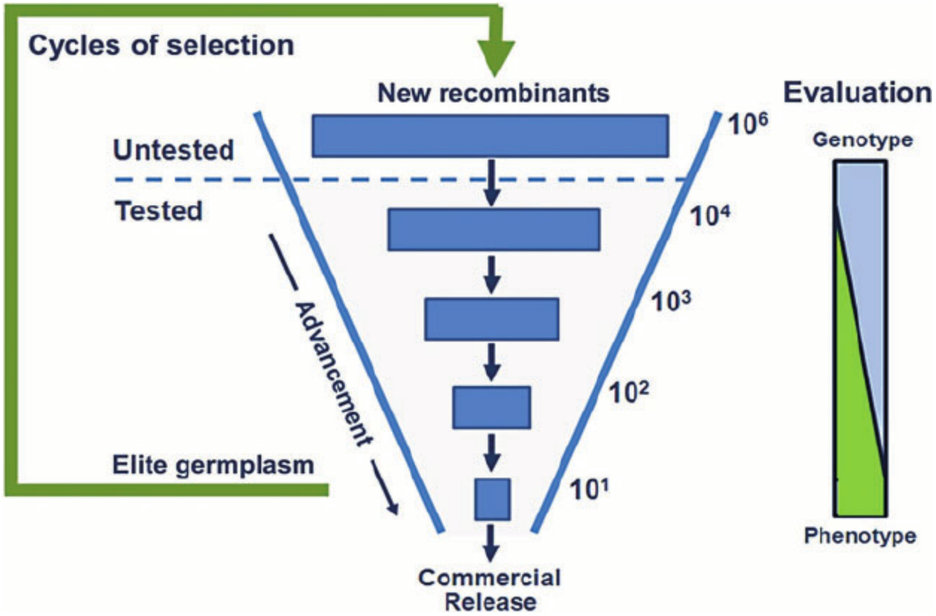
Factors Affecting Prediction Accuracy

- Marker density and LD decay
- Effective population size – diversity
- Training set – populations structure, who phenotyping, stage, update the data, …
- Genetic relationship between training population and selection candidates
- Rare alleles (MAF < 5%)
- Missing data and imputation method (*call rate* < 95%)
- Statistical model
- Correlated traits (multi-trait models)
- Progeny size and ploidy
- Crossover GE
- Number of cycles of GS

GS applied to breeding programs

- GS modifies significantly the way to select





- Reducing the time to develop cultivars
- Increasing the effective size and selection intensity
- Increasing the genetic gain per unit time