A multivariate analysis with direct additive and hidden inbreeding depression load effects

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Introduction (I)

- Inbreeding is caused by the mating of related individuals
- Inbreeding depression is a reduction in the phenotypic yield of fitness-related traits
- Homozygosity caused by inbreeding exposes the presence of recessive alleles or losses the advantage of over-dominance
- Inbreeding depression can vary depending on the genotype of the individuals whose alleles produce identity by descent (IBD)

Introduction (II)

- Inbreeding depression load can be considered an hereditary trait whose phenotype is only expressed when inbreeding occurs in its offspring

- Purging is process of selection against recessive alleles

- "Artificial" purging can be achieved by removing individuals with bad inbreeding loads

- A prediction of the individual inbreeding load for "young" individuals is required

Inbreeding decomposition

Founder decomposition

0.2500 from founder 1
0.1250 from founder 2
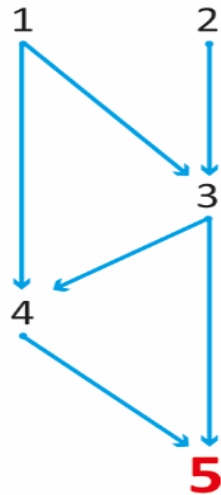
Mendelian decomposition

0.1875 from founder 1
0.0625 from founder 2
0.1250 from the mendelian sampling of 3

$F_5=0.375$

Lacy et al., 1996

Caballero and Toro, 2000
García-Cortés et al., 2010

The Model (I)

- Systematic effects (sex, age of dam, herd, year, season, etc)

- Additive genetic effects

- Residual effects

- If inbred:

       Inbreeding depression generated by:
      - Founders
      - Mendelian Sampling of non-founders

The Model (II)

- Casellas (2018)

$$y = \mu + Za + T\varepsilon_i + e$$

$$a \sim N(0, A\sigma_a^2) \qquad \varepsilon_i \sim N(0, I\sigma_i^2) \qquad e \sim N(0, I\sigma_e^2)$$

$$\varepsilon_i \sim N(0, Q\sigma_i^2) \qquad Q = \begin{pmatrix} 1 & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & \frac{1}{2}\left(\frac{F_S + F_D}{2}\right) \end{pmatrix}$$

Inbreeding loads for individuals without inbred descedants can not be predicted

The Model (III)

$$i = Pi + \varepsilon_i \qquad\qquad \varepsilon_i = (I - P)i$$

$$y = \mu + Zu + Ki + e \qquad\qquad K = T(I - P)$$

$$i \sim N\left(0, A\sigma_i^2\right) \qquad\qquad \begin{pmatrix} \mathbf{u} \\ \mathbf{i} \end{pmatrix} \sim N\left(\begin{pmatrix} 0 \\ 0 \end{pmatrix}, G \otimes A\right)$$

Example
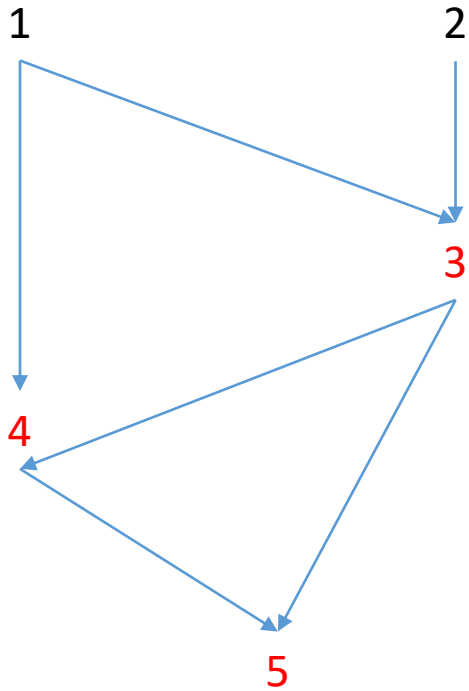
$$y = \mu + Zu + Ki + e \qquad\qquad K = T(I - P)$$

$$\mathbf{T} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ 0.25 & 0 & 0 & 0 & 0 \\ 0.1875 & 0.0625 & 0.125 & 0 & 0 \end{bmatrix}$$

$$I - P = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ -0.5 & -0.5 & 1 & 0 & 0 \\ -0.5 & 0 & -0.5 & 1 & 0 \\ 0 & 0 & -0.5 & -0.5 & 1 \end{bmatrix}$$

$$K = T(I - P) = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ 0.25 & 0 & 0 & 0 & 0 \\ 0.125 & 0 & 0.125 & 0 & 0 \end{bmatrix}$$

$$\begin{bmatrix} \mathbf{1'1} & \mathbf{1'Z} & \mathbf{1'K} \\ \mathbf{Z'1} & \mathbf{Z'Z} + A^{-1}g^{11}\sigma_e^2 & \mathbf{Z'K} + A^{-1}g^{12}\sigma_e^2 \\ \mathbf{K'1} & \mathbf{K'Z} + A^{-1}g^{21}\sigma_e^2 & \mathbf{K'K} + A^{-1}g^{22}\sigma_e^2 \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\mu}} \\ \hat{\boldsymbol{a}} \\ \hat{\boldsymbol{i}} \end{bmatrix} = \begin{bmatrix} \mathbf{1'y} \\ \mathbf{Z'y} \\ \mathbf{K'y} \end{bmatrix}$$

Beef cattle data: weaning weight

	Pirenaica	Rubia Gallega
Pedigree	308,836	384,434
Number of Data	35,126	75,194
Mean	258.37 kg (±57.97 kg)	281.36 kg (±46.70 kg)
Average Inbreeding	0.030 (±0.056)	0.020 (±0.048)

Partial inbreeding coefficients

Partial Inbreeding	Pirenaica	Rubia Gallega
$<10^{-4}$	10,996,924 (68.30 %)	1,564,740 (30.80 %)
10^{-4} -10^{-3}	3,967,842 (24.65 %)	2,559,733 (50.38 %)
10^{-3}-10^{-2}	1,028,578 (6.39 %)	823,410 (16.21 %)
10^{-1}-10^{-2}	126,238 (0.78 %)	124,155 (2.44 %)
$>10^{-1}$	9,792 (0.06 %)	8.419 (0.17 %)

PIRENAICA
8,721 ancestors

RUBIA GALLEGA
3,601 ancestors

Statistical Model

$$y = tc + Xb + Wp + Za + Ki + e$$

y   Phenotypes

c   Covariate with age of recording (170-250 days of life)

b   sex (2 levels) and age of dam (15 levels)

p   Herd-year-season effects (6,305 and 5,251 levels)

a   direct additive genetic effects

i   inbreeeding load effects

e   residuals

Gibbs Sampler: 2 chains of 550,000 iterations after discarding the first 50,000.

Results: Variance Component Estimation

	Population	
	Pirenaica	**Rubia Gallega**
σ_a^2	695.016 (25.688)	439.803 (18.121)
σ_i^2	29966.800 (5868.275)	28222.360 (5454.273)
r(a,i)	-0.429 (0.102)	-0.043 (0.087)
σ_p^2	1035.209 (27.714)	320.023 (11.273)
σ_e^2	483.060 (15.010)	1018.207 (12.612)

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F=1.00

Results: Variance Component Estimation

	Population	
	Pirenaica	**Rubia Gallega**
σ_a^2	695.016 (25.688)	439.803 (18.121)
σ_i^2	**299.66 (58.68)**	**282.224 (54.54)**
r(a,i)	-0.429 (0.102)	-0.043 (0.087)
σ_p^2	1035.209 (27.714)	320.023 (11.273)
σ_e^2	483.060 (15.010)	1018.207 (12.612)

F=0.10

Results: Variance Component Estimation
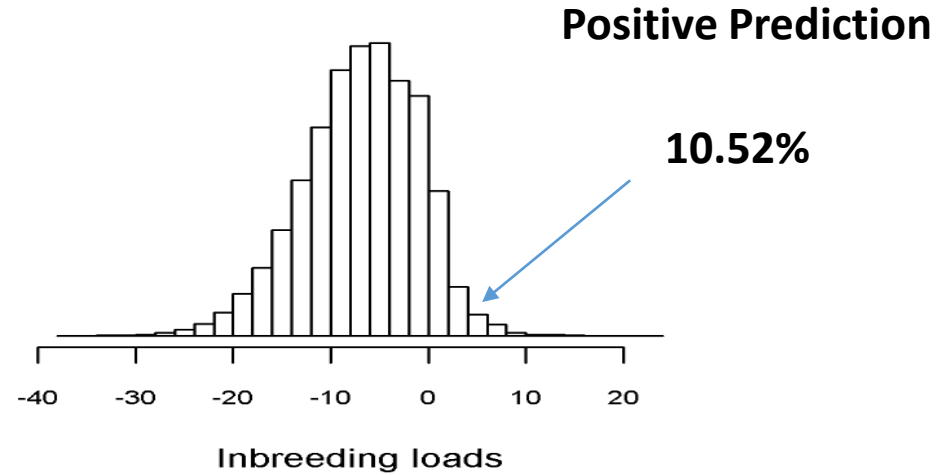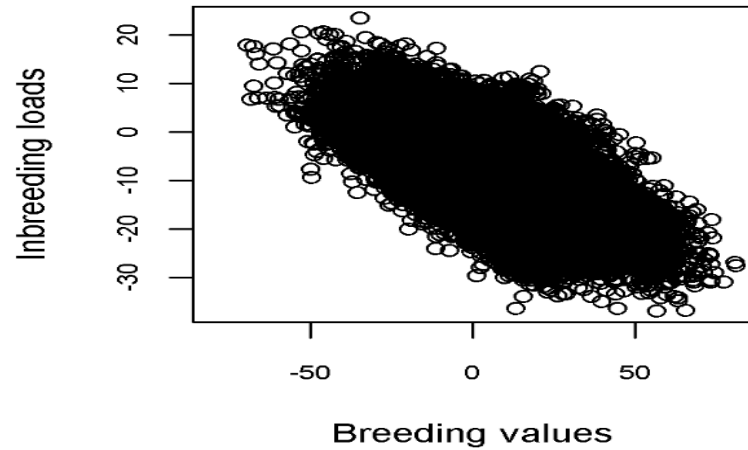

Ratios of phenotypic variance (Pirenaica)
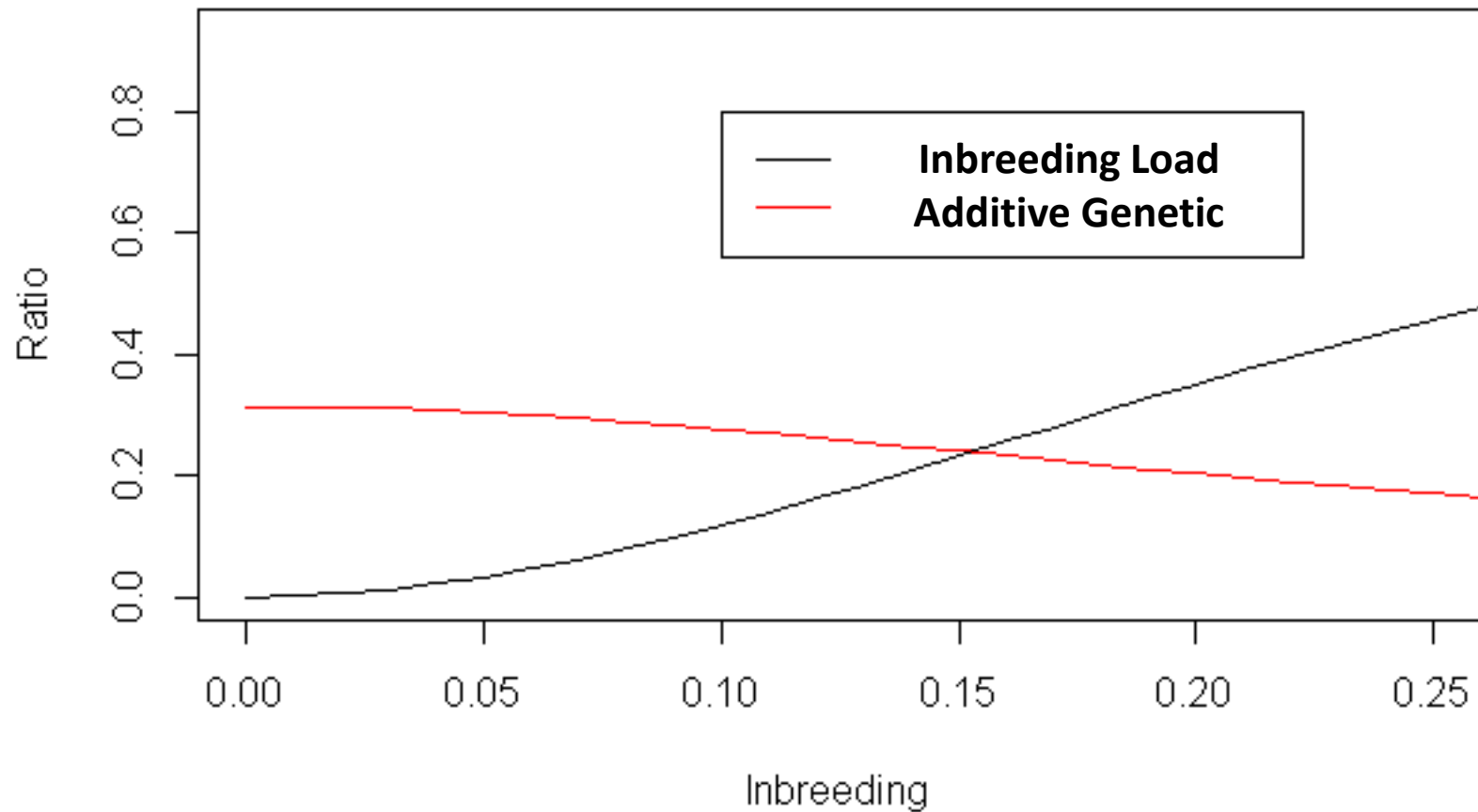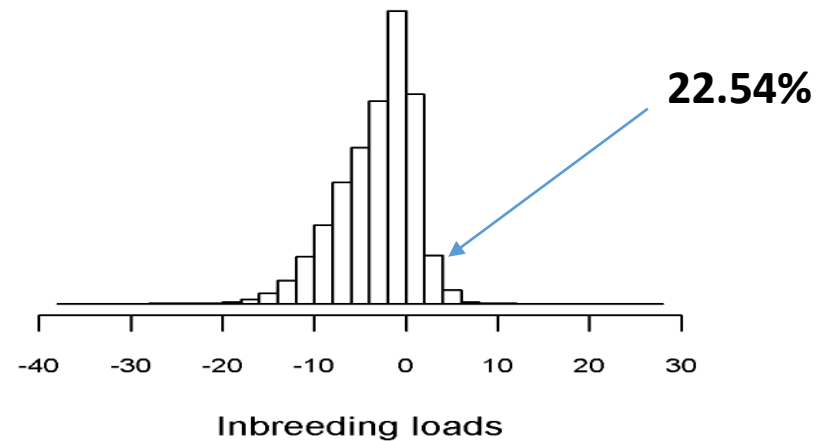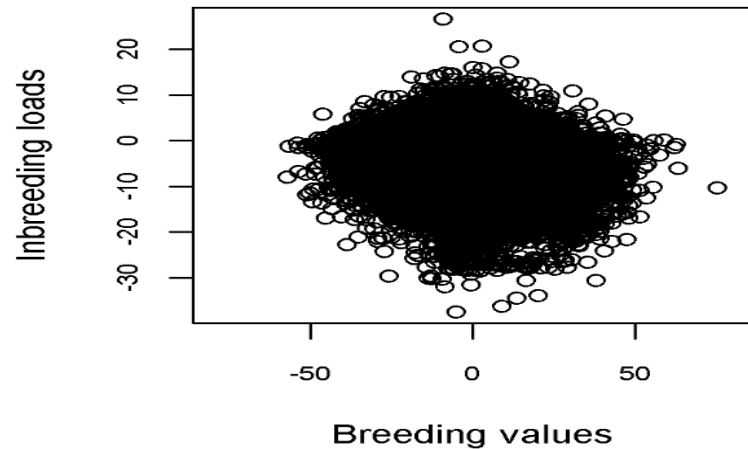
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Results: Breeding values and Inbreeding Loads

Conclusions

- Predictive ability of inbreeding load of "young" individuals
- Useful for "artificial" purging

- Inbreeding load explains a relevant percentage of variance
- Negative correlation between direct additive effects and inbreeding loads

Thank you!!!