GENOMIC AND PEDIGREE METHODS TO ANALYZE INBREEDING DEPRESSION IN BASCO-BÉARNAISE RAMS

Z.G. Vitezica[1], I. Aguilar[2], J.M. Astruc[3], A. Legarra[1]

[1] INRA/INPT, UMR1388 GenPhySE, Toulouse, France,
[2] INIA, 90200, Canelones, Uruguay
[3] IDELE, 31321, Toulouse, France.

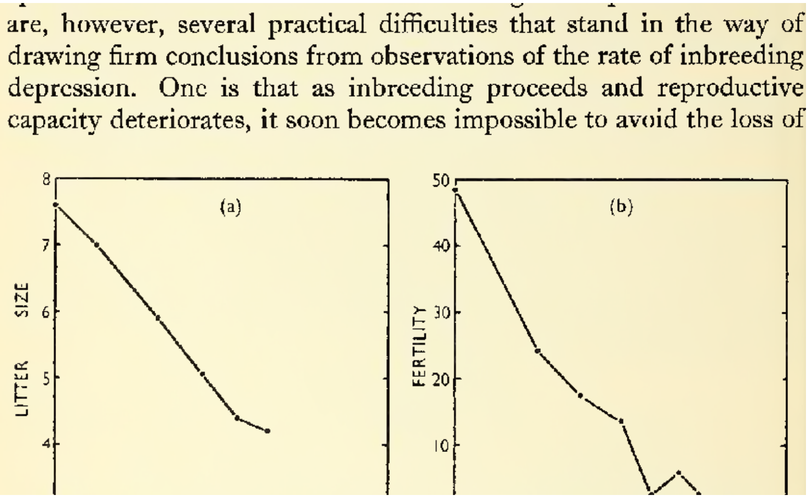
zulma.vitezica@inra.fr

Plan

- Inbreeding depression
- Dairy sheep data
- Inbreeding coefficient
- Metafounders
- Results & conclusions

What is inbreeding depression?

- Inbreeding depression is the decline in biological fitness (viability, fertility, …) as a consequence of inbreeding



are, however, several practical difficulties that stand in the way of drawing firm conclusions from observations of the rate of inbreeding depression. One is that as inbreeding proceeds and reproductive capacity deteriorates, it soon becomes impossible to avoid the loss of

(Falconer, 1981)

What we know about inbreeding depression

- It is a phenomenon that exists in animals, plants and human populations
- Inbreeding depression (ID) is caused by
  - increase of homozygosity of partially recessive alleles
  - loss of heterozygous advantage at some loci
- The genetic basis of ID are still unclear

(Charlesworth & Willis, 2009; Toro, 2016)

Objective

- To compare different methods to estimate inbreeding depression in semen traits

Dairy sheep data

Basco-Béarnaise breed

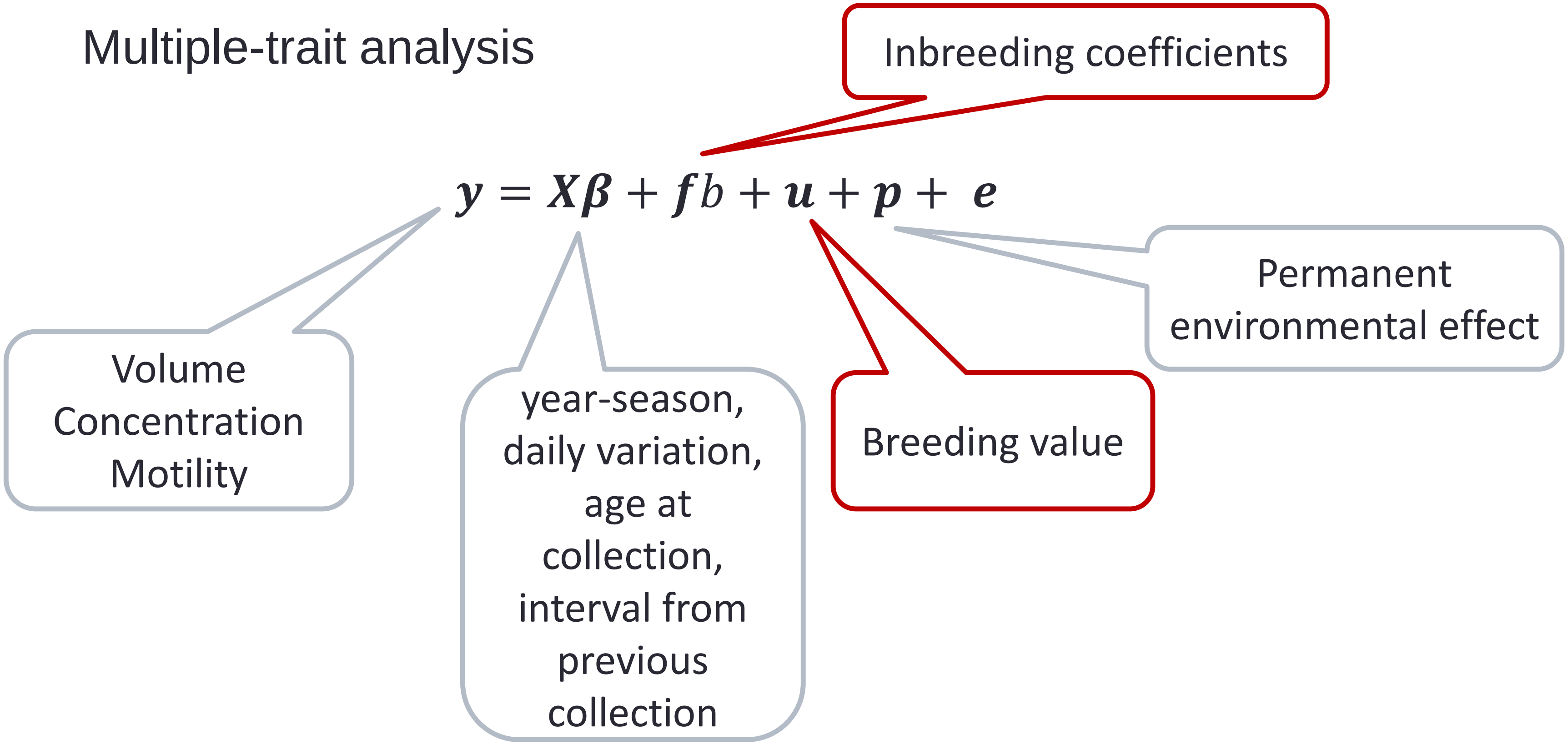
- Semen traits

Trait	Mean (SD)
Sperm volume (ml)	1.41 (0.63)
Sperm concentration (10^6/ml)	3.23 (0.64)
Motility score	4.61 (0.54)

- 620 rams in data, 16,196 records
- 8,266 animals in pedigree
- 36,464 SNPs for 1,384 rams (Illumina OvineSNP50 BeadChip).

Model and more

Multiple-trait analysis



Inbreeding coefficients

$$\boldsymbol{y} = \boldsymbol{X\beta} + \boldsymbol{f}b + \boldsymbol{u} + \boldsymbol{p} + \boldsymbol{e}$$

Volume
Concentration
Motility

year-season,
daily variation,
age at
collection,
interval from
previous
collection

Breeding value

Permanent
environmental effect

Incomplete pedigrees

- There is missing pedigree information in ancestors of the rams
- With incomplete pedigree information, inbreeding coefficients tend to be underestimated
- Pedigrees in addition to be incomplete, end up in a base population of supposedly unrelated founders.

This is false and also contradicts marker-based information that show realized relationships across founders (*i.e.* Single-Step GBLUP analysis).

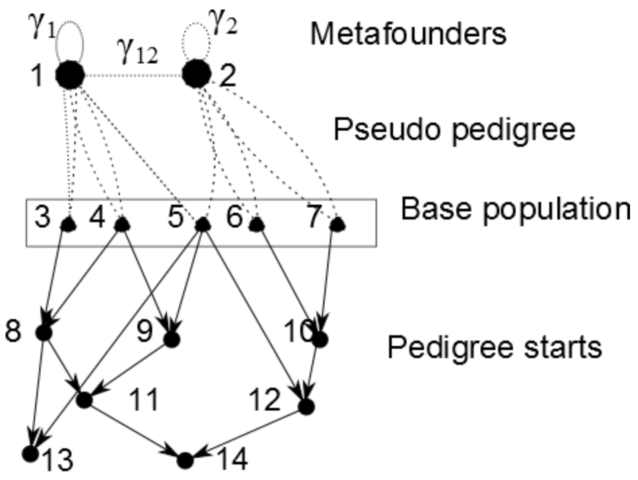
Inbreeding coefficients

$\boldsymbol{f}$, were estimated using four methods:

- traditional pedigree-based inbreeding ($\boldsymbol{f}_{PED}$)
- pedigree-based inbreeding but accounting for non-zero relationships for unknown parents (VanRaden, 1992; Aguilar and Misztal, 2008) ($\boldsymbol{f}_{PED_{non-zero}}$)
- pedigree-based inbreeding with metafounder relationships ($\boldsymbol{f}_{PED_{MF}}$)
- combined inbreeding (from a relationship matrix $\boldsymbol{H}$ using pedigree and genotypes) with metafounder relationships ($\boldsymbol{f}_{H_{MF}}$)

What is a metafounder?

- Pseudo-individuals that can be seen as a pool of ancestral gametes
- Metafounders condensate the relationship information of ancestral population



$$\boldsymbol{\Gamma} = \begin{pmatrix} \gamma_{11} & \gamma_{12} & \\ & \gamma_{22} & \\ & & \dots \end{pmatrix}$$

Ancestral relationships in matrix $\boldsymbol{\Gamma}$

Legarra et al., 2015

Why use metafounders?

- Probably more accurate estimates of inbreeding depression could be obtained
- Inclusion of metafounder relationships account for missing pedigrees
- All animals (ungenotyped and genotyped) are accounted for computing inbreeding coefficients

Metafounders in our data

Ancestral relationships in matrix $\mathbf{\Gamma}$

$$\mathbf{\Gamma} = \begin{pmatrix} 0.568 & 0.116 & 0.328 & 0.391 & 0.414 \\ & 0.949 & 0.323 & 0.332 & 0.335 \\ & & 0.733 & 0.344 & 0.356 \\ & & & 0.712 & 0.376 \\ & & & & 0.456 \end{pmatrix}$$

- 5 metafounders:
  - 1974-1980, 1980-1988, 1988-1994, 1994-2000, > 2000

Ancestral relationships (matrix $\boldsymbol{\Gamma}$), were estimated from pedigree and marker data using GLS (Garcia-Baccino et al., 2017)

Inbreeding depression analysis

$$\boldsymbol{y} = \boldsymbol{X\beta} + \boldsymbol{f}b + \boldsymbol{u} + \boldsymbol{p} + \boldsymbol{e}$$

Inbreeding coefficients:

$$\boldsymbol{f}_{PED}$$

$$\boldsymbol{f}_{PED_{non-zero}}$$

$$\boldsymbol{f}_{PED_{MF}}$$

$$\boldsymbol{f}_{H_{MF}}$$

$$Var(\boldsymbol{u}) = \boldsymbol{A}\sigma_u^2$$

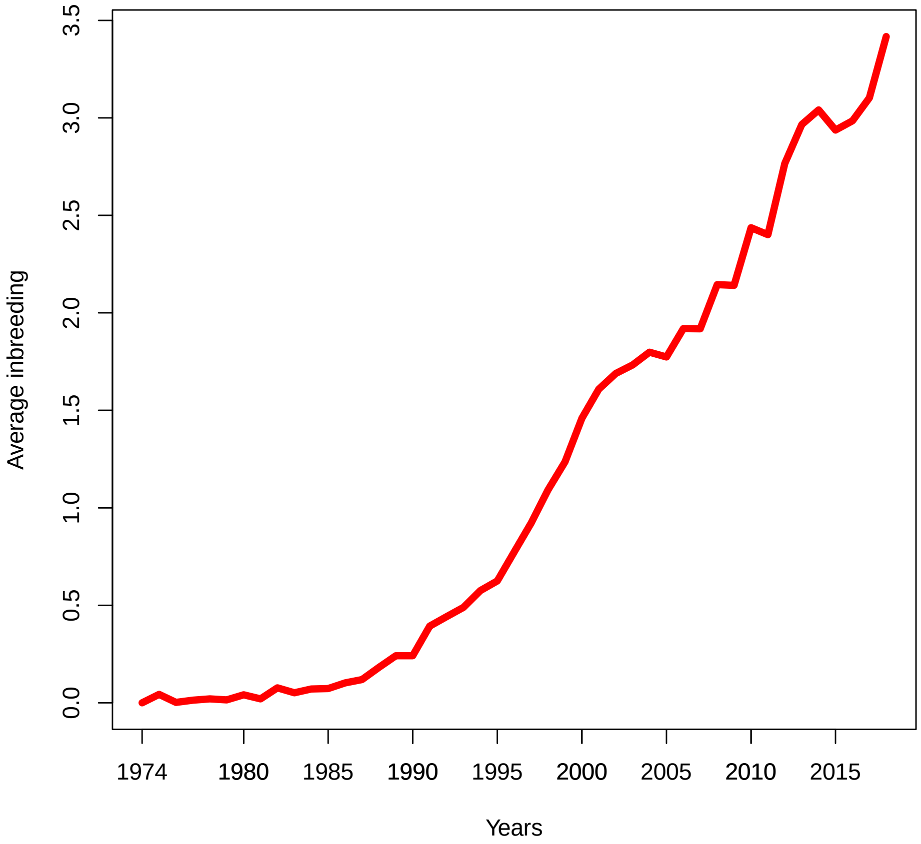
$$Var(\boldsymbol{u}) = \boldsymbol{A}\sigma_u^2$$

$$Var(\boldsymbol{u}) = \boldsymbol{A}^{\Gamma}\sigma_u^2$$

$$Var(\boldsymbol{u}) = \boldsymbol{H}^{\Gamma}\sigma_u^2$$

$$\boldsymbol{H}^{(\Gamma)-1} = \boldsymbol{A}^{(\Gamma)-1} + \begin{pmatrix} 0 & 0 \\ 0 & \boldsymbol{G}^{-1} - \boldsymbol{A}_{22}^{(\Gamma)-1} \end{pmatrix}$$

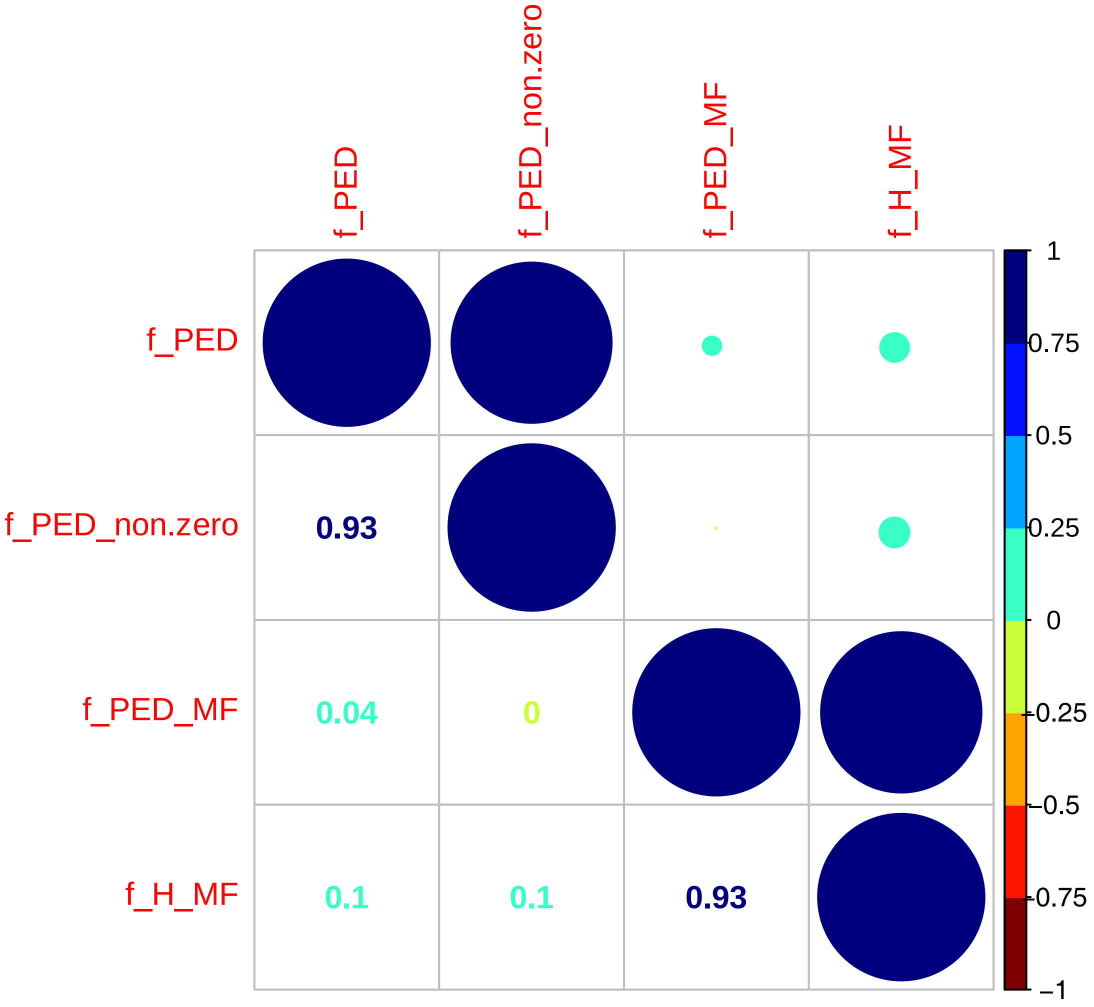
Results



- The rate of inbreeding, calculated as the regression of pedigree inbreeding on birth year (1974 to 2018), was 0.08% / year

Inbreeding coefficient correlation

- The measures of inbreeding when considering metafounders are weakly correlated with pedigree-based metrics



Estimated inbreeding depression

Method	Semen traits		
	Volume	Concentration	Motility
f_{PED}	-0.096 (0.880)	1.104 (0.978)	-1.241 (0.681)
$f_{PED_{non-zero}}$	-0.290 (0.996)	1.056 (1.108)	-1.259 (0.771)
$f_{PED_{MF}}$	-0.979 (1.006)	1.617 (1.103)	**-1.676 (0.768)**
$f_{H_{MF}}$	-0.248 (0.703)	0.545 (0.807)	**-1.115 (0.557)**

A 10% increase in inbreeding resulted in a reduction in motility of around 0.1 points in the scale (from 1 to 5) and a deterioration in male fertility

Values are expressed as the change in phenotypic mean per 100% increase in inbreeding (SE are in parenthesis).

Conclusions

- Metafounders help with missing pedigree information
- Inbreeding depression estimation seems more accurate using metafounders
- We are doing analyses with ROH that confirm these results
- Motility was unfavorably impacted by increasing of inbreeding in Basco-Béarnaise breed

Acknowledgements

Smarter

SMAll RuminanTs breeding for Efficiency and Resilience

H2020 project: Smarter

Poctefa (Feder Funds): Ardi

INRA project: GDivSelGen

EFA 208/16

ardi

Research, Development and Innovation in sheep

Interreg

POCTEFA

UNIÓN EUROPEA
UNION EUROPÉENNE

FEDER

Fondo Europeo de Desarrollo Regional

Fonds Européen de Développement Régional

Project partially supported by the Genotoul bioinformatics platform Toulouse Midi-Pyrenees.

Thanks for your attention!

Inbreeding coefficient distribution