



FINAL MEETING – TOLEDO MAY 2023

**WP5: Genomic/genetic modelling and methods of selection
for resilience and efficiency traits**

CD/CB INRAE & friends activities (2019-2023)
COUNCIL ON DAIRY CATTLE BREEDING

A. Legarra

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Reminder of the WP objectives

1. Develop genetic models to deal with resilience and efficiency under micro- and macro- environmental challenges
2. Infer (genomic) breeding values for R&E from longitudinal data on productive traits
3. Develop and assess methods for genomic prediction particularly suited to small ruminants
4. Develop and implement new methods for selected and under-utilised populations of sheep and goats while conserving genetic variability

Task 5.1: Novel genetic models for efficiency and resilience traits under challenge (M1-M48)

- **Objective of the task**
 - Develop genetic models to deal with resilience and efficiency under micro- and macro- environmental challenges
- **Work done so far**
 - not at INRAE
- **Main results achieved so far**
 - ...

Task 5.2: Data mining of longitudinal performance data to identify and characterise events of environmental challenges (M1-M36)

- **Objective of the task**
 - Infer (genomic) breeding values for R&E from longitudinal data on productive traits
- **Work done**
 - A method based on mixture models for datamining longitudinal performance datasets to detect unrecorded challenges -> published (Garcia-Baccino et al., GSE) and "delivered".

What did we find?



2) Detection of stress:

It is unusual that we see the stress, except when exceptional meteorological situations (but as they are uncommon, it is definitely useless).

For farms in continuous performance recording (growth in control station, milk recording with on-farm automatic meters...) we have developed a method to detect stresses / challenges (and we do hope that such equipment will be more and more affordable).

- In days with a challenge, there are more or less sensitive animals
- We detect this differential sensitivity (resilience) in performances of animals with more variations this very day.
- When looking at the daily variability, we detect, we “see” the days with stress.

What did we find?



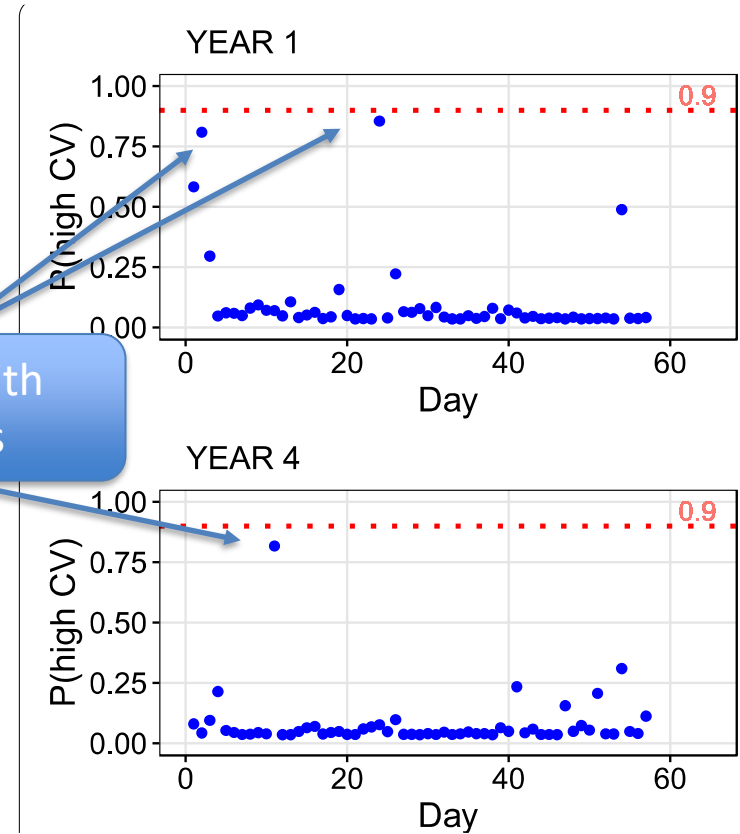
2) Detection of stress:

INRAE Unit de La Sapinière,
Daily feed intake

Our method did identify the days with stressing events (straw replacement, building repairing ...)

Days with stress

Then we can calculate breeding value for resilience at these stressing days



GSE Genetics
Selection
Evolution

RESEARCH ARTICLE **Open Access**

Check for updates

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SMARTER – Deliverable D5.1



SMARTER

SMAll RuminanTs breeding for Efficiency and Resilience

Research and Innovation action: H2020 – 772787

Call: H2020-SFS-2017-2

Type of action: Research and Innovation Action (RIA)

Work programme topic: SFS-15-2016-2017

Duration of the project: 01 November 2018 – 31 October 2022

****GUIDELINES****

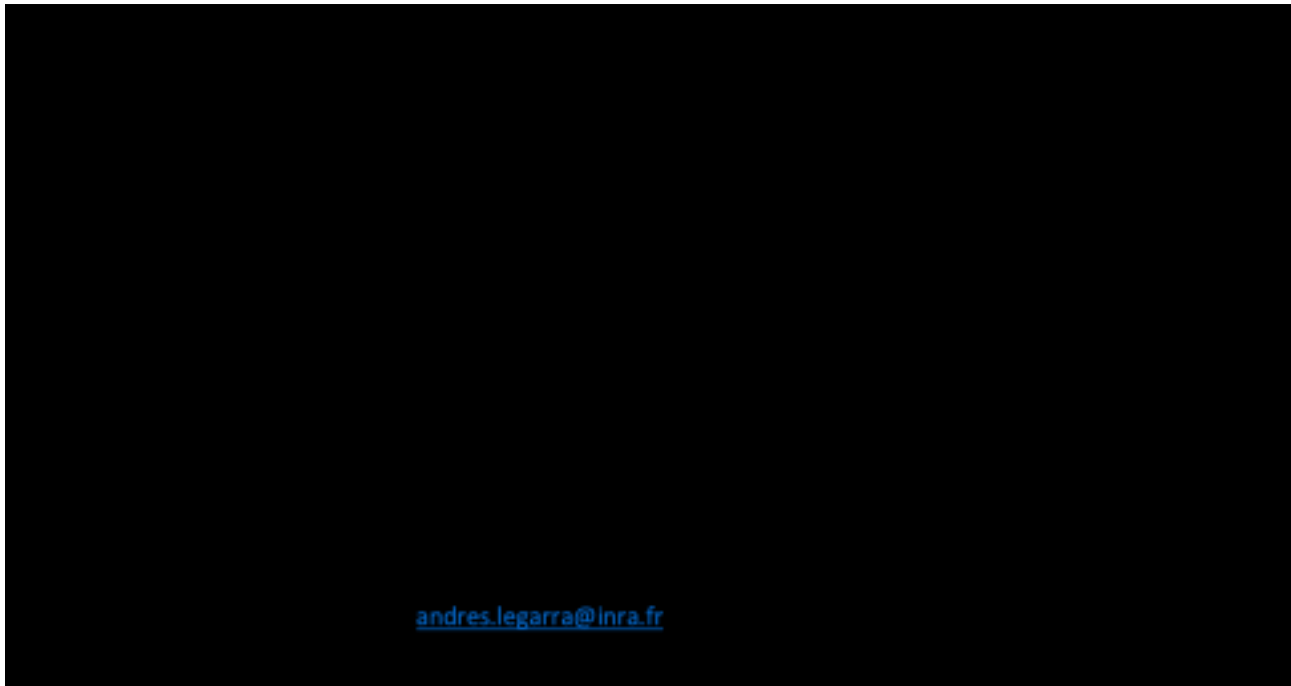
Complete parts that are highlighted in yellow

Guidelines are highlighted in green

Method for identifying environmental challenge events and
assessment of their value for selection for resilience

Carolina Garcia-Baccino

Andres Legarra



This was also part of the Smarter training School

Task 5.3: Enhancing performance of genomic prediction methodology (M1-M36)

- **Objective of the task**
 - Develop and assess methods for genomic prediction particularly suited to small ruminants
- **Work done so far**
 - Derived Linear Regression method (LR) to assess bias and accuracy of genomic prediction.
 - DONE: Application to single breed, single trait (Manech, Latxa)
 - DONE: Application to single breed, multiple trait (Lacaune)
 - Implementation in software of metafounder method for analysis of multi-population data (purebred or crossbred).
 - DONE: model-based (individual) reliability
 - DONE: existing software (blupf90)
 - DONE: change of QTL substitution effects across populations

What did we find?

3) Genomic selection:

Comparing “old” and “recent” breeding values permits to seize the quality of the breeding values estimation (whatever genomic or polygenic)

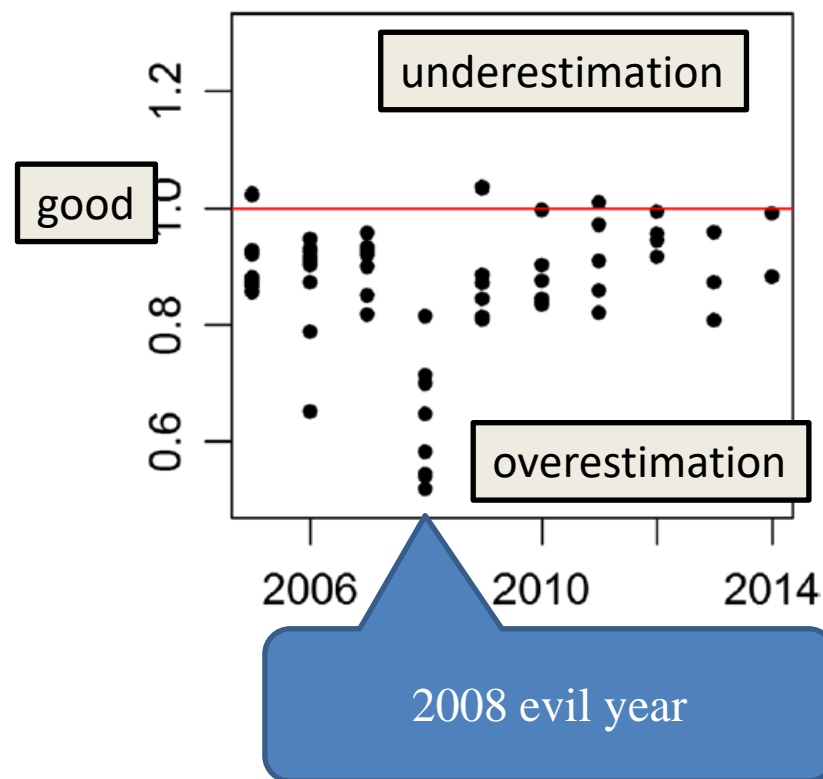
Genomic evaluation would increase the reliabilities of the breeding values between 5 and 10%

The breeding evaluations are not perfect: we underestimate or overestimate the young randomly way, according to the birth year

It does not seem to generate an important effect on selection



« bias » of EBVs



What did we find?

3) Genomic selection:

- We validated method LR using simulations
- we find more accuracy and less bias using genomic than with pedigree
- Some models are better than others



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Exploring the inclusion of genomic information and metafounders in Latxa dairy sheep genetic evaluations

I. Granada-Tajada,^{1*} A. Legarra,² and E. Ugarte¹



J. Dairy Sci. 103:529–544
<https://doi.org/10.3168/jds.2019-16603>

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Behavior of the Linear Regression method to estimate bias and accuracies with correct and incorrect genetic evaluation models

F. L. Macedo,^{1,2*} A. Reverter,² and A. Legarra¹

GSE Genetics Selection Evolution
RESEARCH ARTICLE Open Access
 Check for updates

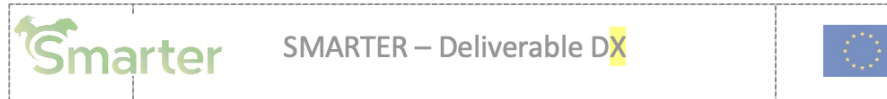


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Removing data and using metafounders alleviates biases for all traits in Lacaune dairy sheep predictions

F. L. Macedo,^{1,2,*} J. M. Astruc,³ T. H. E. Meuwissen,² and A. Legarra¹



SMARTER

SMALL Ruminants breeding for Efficiency and Resilience

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****GUIDELINES****

Complete parts that are highlighted in yellow

Guidelines are highlighted in green

Use of method LR to assess potential bias due to design of cross-validation analysis

Andres Legarra

INRAE

* Deliverable leader – Contact: andres.legarra@inrae.fr

DELIVERABLE D5.3

MILESTONE MS19

A computer software or method for assessing and avoiding potential bias due to design of cross-validation analysis

Andres Legarra*

Fernando Macedo

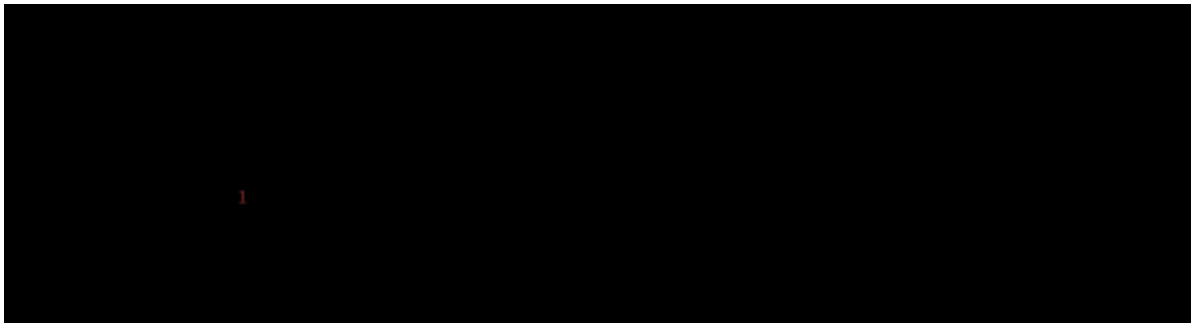
INRAE, GenPhySE, Toulouse

* Milestone leader – Contact: andres.legarra@inrae.fr

Task 5.3: Enhancing performance of genomic prediction methodology (M1-M36)

- **Objective of the task**
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 - DONE: model-based (individual) reliability
 - DONE: existing software (blupf90)
 - DONE: change of QTL substitution effects across populations

- Metafounders allow easier treatment of missing relationships within breeds (Unknown Parent Groups) and across breeds (crossbreds) and better compatibility of **G** and **A** for Single Step
- They have been programmed in blupf90 and their use explained in a Tutorial



MILESTONE MS20

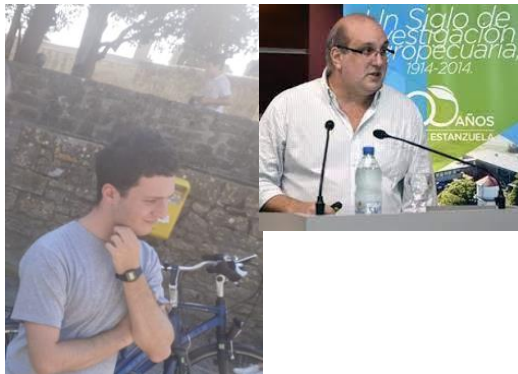
A computer software to improve calculation of genomic relationship between purebred and crossbred populations

Andres Legarra

INRA, GenPhySE, Toulouse

* Milestone leader – Contact: andres.legarra@inrae.fr

- DONE: reliability with genetic groups/metafounders
 - the reliability with fixed genetic groups is undefined , which means that (a) there is no theory and (b) the approximations can be very bad
 - metafounder are random effects so we can have a definition
 - We have now a good definition and methods for estimation
 - Work with Matias Bermann (UGA – “not Smarter”) and Ignacio Aguilar (INIA Uy – “Smarter”)



RESEARCH ARTICLE

Open Access



- Reliability

- A reliability refers to a base population
- With metafounders, we use one (e.g. the oldest) base population (metafounder) as a reference,
- we use reliability of the contrast $(u_i^{mf} - u_{mf}^{mf})$:

$$rel^{mf} = 1 - \frac{PEV(u_i^{mf} - u_{mf}^{mf})}{Var(u_i^{mf} - u_{mf}^{mf})} = \frac{PEV(u_i) + PEV(u_{mf}) - 2PEC(u_i, u_{mf})}{(A_{ii}^{(\gamma)} + A_{mf,mf}^{(\gamma)} - 2A_{i,mf}^{(\gamma)}) \sigma_{u-related}^2}$$

- this is equal to the “classical” reliability if there is 1 metafounder
- Programmed in blupf90+ using a few matrix algebra tricks

What did we find?

3) Combining breeds for a better prediction:

When we combine two (close) populations, do we have a boost of the genomic reliabilities?

That would mean that the same genes have the same effects across breeds. Yet, it is not true:

- the Myostatin gene produces “culards” animals in some bovine breeds, but not in other breeds
- the DGAT1 gene increases milk yield by +350 kg/yr in Holstein but +140 kg/yr in Normande

It looks like clear that the breeds must be “close” for gene effects to be the same, but how much close?

We have proposed a way to calculate it ...



+



+



+



=

?

What did we find?

3) Combining breeds for a better prediction:

Genes effects are similar if:

$$r(\alpha_i^b, \alpha_i^{b'}) \approx \frac{\sqrt{\sigma_A^2}}{\sqrt{\sigma_A^2 + \frac{8F_{ST}}{1 - F_{ST}} \sigma_{AA}^2}}$$

Breeds are close

And the action of the genes is not too much "epistatic"



Similarity between the genes effects (rough estimation!!)

- Manech Tête Rousse – Latxa Cara Rubia: 0.98 😊
- Manech Tête Rousse – Manech Tête Noire: 0.92 😞
- Manech Tête Rousse – Lacaune: 0.80 😞

...and moreover, we assume that the environment and the breeding system are alike



OXFORD

GENETICS

DOI: 10.1093/genetics/lyab138

The correlation of substitution effects across populations and generations in the presence of nonadditive functional gene action



Task 5.4: Incorporating genomic information to improve management of genetic diversity and to promote expression of heterosis (M1-M36)

- **Objective of the task**
 - Develop and implement new methods for selected and under-utilised populations of sheep and goats while conserving genetic variability
- **Work done**
 - Method to calculate inbreeding combining genotyped and ungenotyped individuals.
 - Inbreeding depression analysis of reproductive traits
 - Reduction of genetic variance due to Bulmer / due to inbreeding
 - selection footprint in Manech Tete Rousse
 - characterization of long-term contributions



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Short communication: Methods to compute genomic inbreeding for ungenotyped individuals

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³UMR GABI, INRA, AgroParisTech, Université Paris-Saclay, 78350 Jouy-en-Josas, France

Programmed in the blupf90 suite (preGSf90)

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OPTION saveDiagHOrig

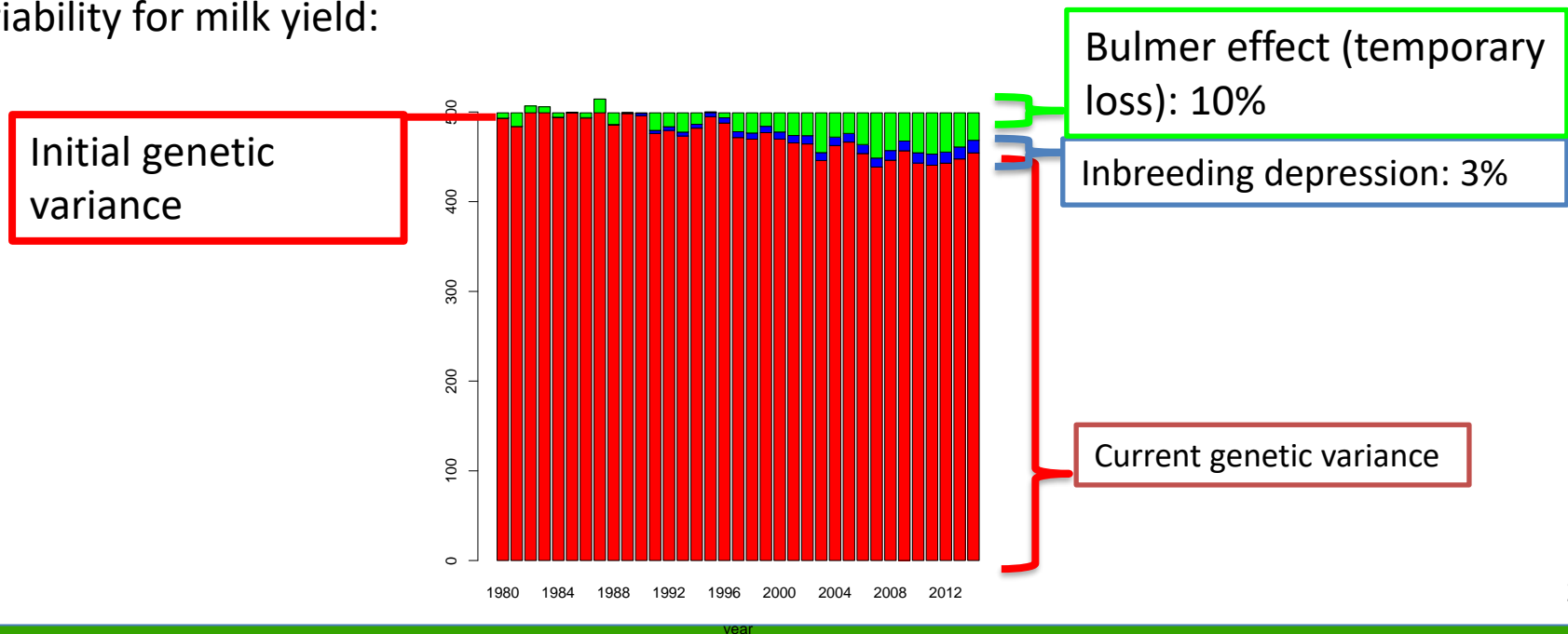
What did we find?



4) A better way to manage inbreeding:

We have better estimated the evolution of genetic variability, which is indeed well managed.

In particular, we have verified the effect of 30 yrs of selection on the genetic variability for milk yield:

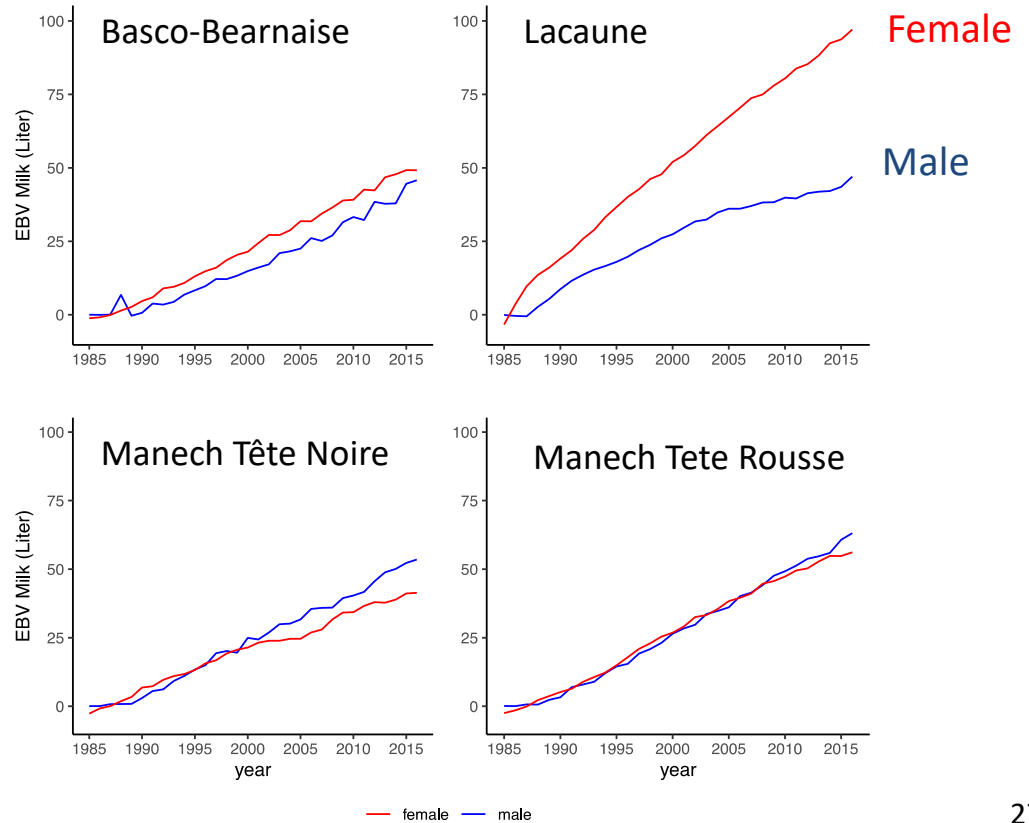


Task 5.4: Incorporating genomic information to improve management of genetic diversity and to promote expression of heterosis (M1-M36)



- Characterization of long-term contributions
 - Tracing back all Mendelian Sampling that constitute the genetic progress (Woolliams et al. 1999, Garcia-Cortes et al. 2008)
 - R package AlphaPart (Obsteter et al)
 - It allows finding where genetic variation is drawn from
 - French dairy breeds: Basco-Bearnaise, Lacaune, Manech Tete Rouse, Manech Tete Noire

- Tracing back, by sex, Mendelian Sampling that constitute the long-term genetic progress





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Genomic and pedigree estimation of inbreeding depression for semen traits in the Basco-Béarnaise dairy sheep breed

S. Antonios,¹ S. T. Rodríguez-Ramilo,² I. Aguilar,³ J. M. Astruc,⁴ A. Legarra,¹ and Z. G. Vitezica^{1,*}
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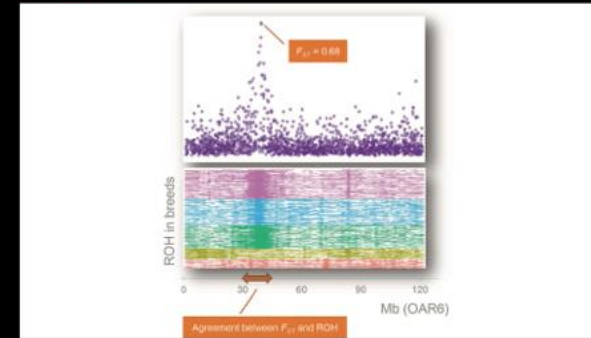
JDS
 Communications
 2021, 2:132–136

<https://doi.org/10.3168/jds.2020-0011>
 Short Communication
 Genetics

Islands of runs of homozygosity indicate selection signatures in *Ovis aries* 6 (OAR6) of French dairy sheep

S. T. Rodríguez-Ramilo,^{1,*} A. Reverter,² and A. Legarra,¹

Graphical Abstract



Contents lists available at ScienceDirect

Animal
 The international journal of animal biosciences



The levels of artificial insemination and missing sire information make genomic selection not always beneficial in meat sheep

J. Raoul^{a,b,*}, J.M. Elsen^b

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Inbreeding, effective population size, and coancestry in the Latxa dairy sheep breed

J. González-Talavera,^{1,*} S. T. Rodríguez-Ramilo,² A. Legarra,¹ and E. Ugarriza,³



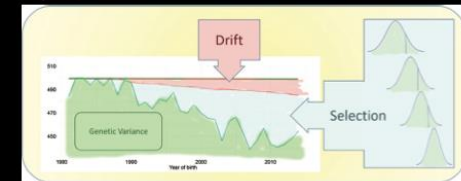
JDS
 Communications
 2021, 2:31–34

<https://doi.org/10.3168/jds.2020-0010>
 Short Communication
 Genetics

Selection and drift reduce genetic variation for milk yield in Manech Tête Rousse dairy sheep

Fernando L. Macedo,^{1,*} Ole F. Christensen,² and Andrés Legarra,¹

Graphical Abstract



Milestones and Deliverables status

Milestones: All done

Deliverables: all done for INRAE