Opportunities and obstacles of the use of genomic data in sheep breeding – large versus small populations –

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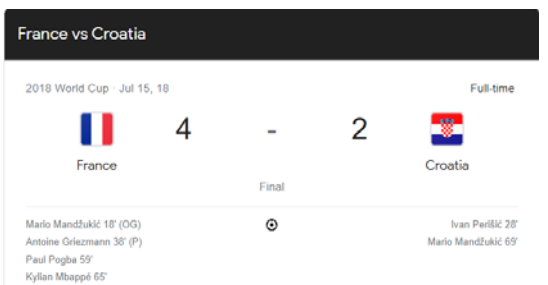
Croatia vs. France

- Inferiority complex of small country?
  - –Sport (FIFA Football World Cup)



  - –Breeding
    - No competition

Aim

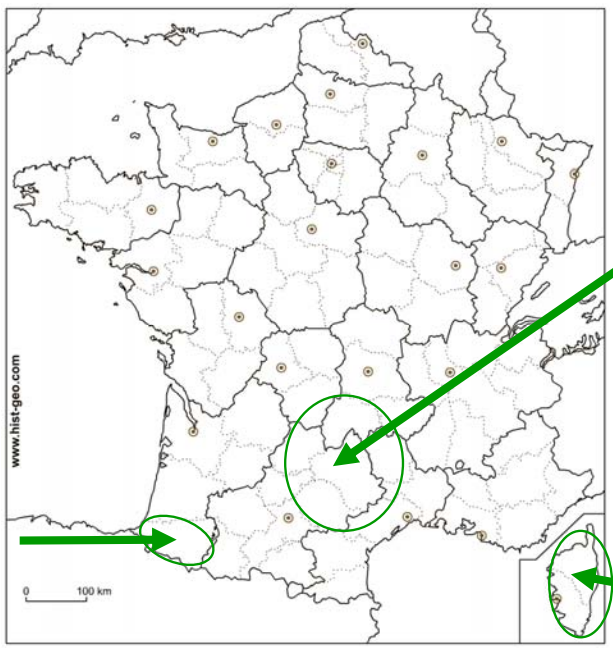
- To draw the benefit and obstacles of using genomic data in **sheep** through contrasting situations
  - Large vs. Small: France vs. Croatia

- Sheep breeds: large vs. smaller populations
  - French (Lacaune, Red-Faced Manech, Black-Faced Manech, Basco-Béarnaise, Corse)
  - Croatian (Istrian, Pag)

Dairy sheep in France

3 traditional areas of production / 5 breeds

- Selection since 70's
- 500,000 AI per year



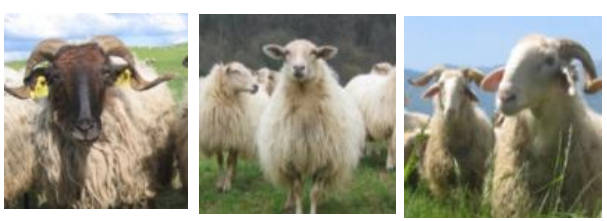
Lacaune

Roquefort area

- 800,000 ewes
- 200,000 in selection
- 300 new AI rams each year

Western Pyrenean area

- 470,000 ewes
- 120,000 in selection
- 250 new AI rams each year



3 breeds: Red-faced Manech, Black-faced Manech, Basco-Béarnaise

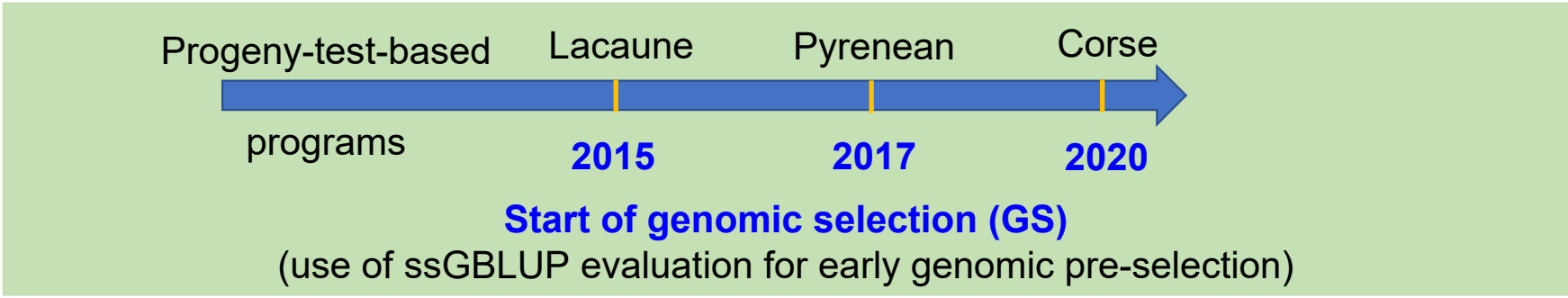
Corse

Corsica island

- 85,000 ewes
- 18,000 in selection
- 20 new AI rams each year

Breeding programs

- Dairy sheep breeding programs switched towards genomic selection
  - 2015 (Lacaune) - 2017 (Pyrenean breeds) - 2020 (Corse)

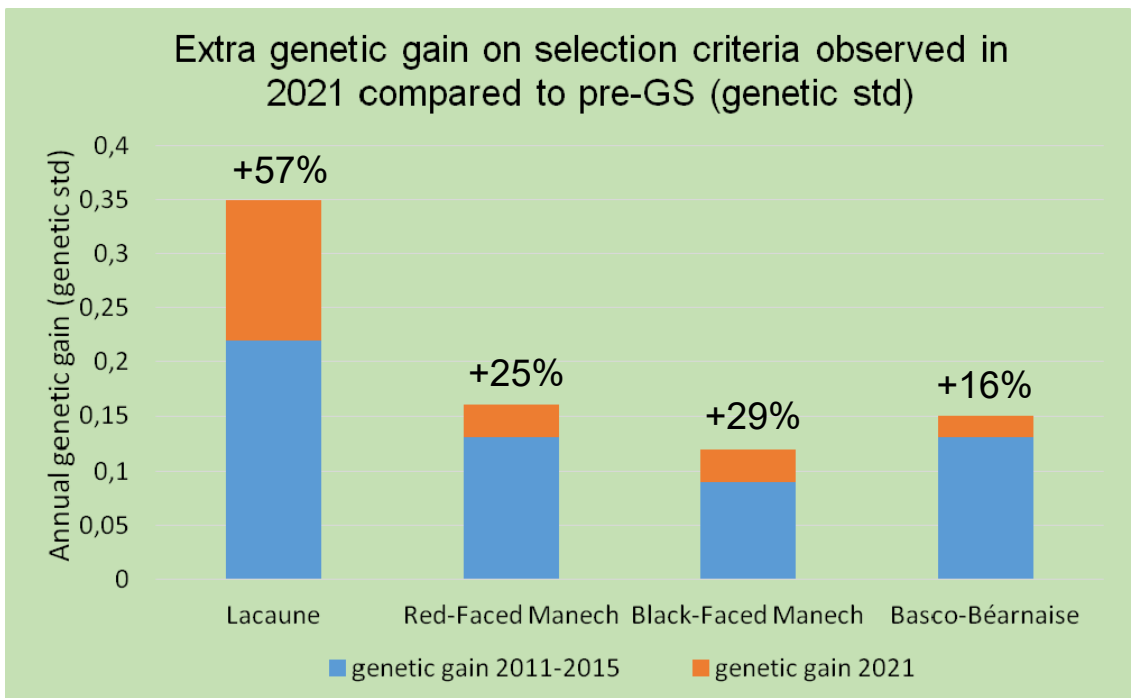


- Genomic evaluation: different reference population sizes across breed

Breed	Genotyped rams	Genotyped AI rams with daughters	Rams genotyped yearly (2023)
Lacaune	32 K	7 K (since 1996)	~3500
Red-Faced Manech	7 K	3.3 K (since 1998)	~700
Black-Faced Manech	1.3 K	0.7 K (since 1996)	~100
Basco-Béarnaise	2.4 K	1.1 K (since 1999)	~250
Corse	2.5 K	0.4 K (since 2003)	~350

Benefits of genomic selection

- Generating an annual genetic gain for economical index ranging from 0.12 to 0.35 genetic standard deviation
- Increase in genetic gain from 16 to 57%



Multiple purpose of genotyping

- Cost of genotypings in sheep: higher than in cattle when compared to the animal value

- => Multi-purpose valorisation of the genotypings

– Genomic selection (through genomic evaluation)
– Major genes
    - PRP – scrapie resistance
    - SOCS2 – susceptibility to Somatic Cells
    - Horn – management of horn in Red-faced Manech
    - New genes in the next years – lethal mutations, cryptorchidism
– Parentage verification and discovery

Parentage verification and discovery

- Parentage verification followed by parentage discovery applied on males chosen for genomic selection (before genomic pre-selection)

Breed	Percentage of wrong sire	Percentage of sire discovery when wrong sire
Lacaune	4.6	92
Pyrenean breeds	4.4	87

- Sire discovery on ewes in flocks that does not do AI (including organic farms where synchronisation by hormone is forbidden)

Breed	Number of females submitted to sire discovery in 2023	Percentage of sire assignation
Lacaune	1,483	95
Pyrenean breeds	2,091	95

Dairy sheep in Croatia:
traditional production area - Mediterranean area (islands, coasts of the Adriatic Sea and Dalmatian hinterland)
2 breeds under selection

Istria

- ~ 13,800 ewes
- Breeding and selection
  - 1,026 ewes and 35 rams, 12 flocks
  - Dual purpose (dairy & meat)
  - Native mating

Istrian sheep

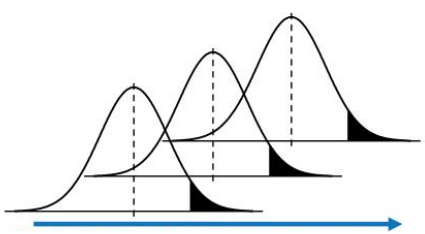
Pag island

- ~ 30,000 ewes
- Breeding and selection
  - 4,086 ewes and 78 rams, 34 flocks
  - Dairy orientated
  - Native mating, harsh environment, (“BURA” > 200 km/h), exotic aromatic plants, forage enriched with sea salt

Pag sheep

Breeding program

- Milk recording (ICAR)
- Dairy traits (milk, fat, protein, SCC)
- Aim → to increase milk yield



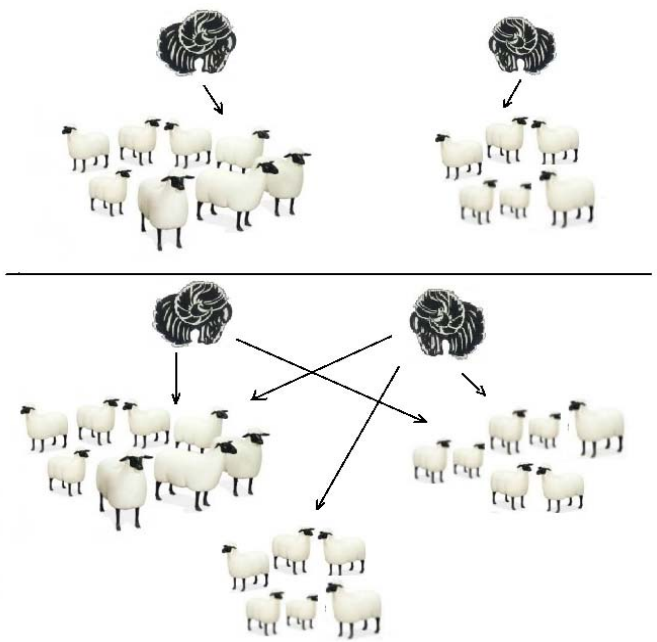
- Pedigree and dairy records
- Pedigree BLUP →

$$\begin{bmatrix} \mathbf{b} \\ \mathbf{a} \end{bmatrix} = \begin{bmatrix} \mathbf{X'X} & \mathbf{X'Z} \\ \mathbf{Z'X} & \mathbf{Z'Z+A^{-1}\lambda} \end{bmatrix}^{-} \begin{bmatrix} \mathbf{X'y} \\ \mathbf{Z'y} \end{bmatrix}$$

Numerator relationship matrix

BLUP issues

Disconnected flocks !!!!



Connected

BLUP

BLUP

The issue of disconnectedness:

- Neglected in some breeding programs. BLUP is not MAGIC!!!
- Impossible to disentangle genetic from environmental effects
- Small ruminants and beef cattle NO/limited use of AI

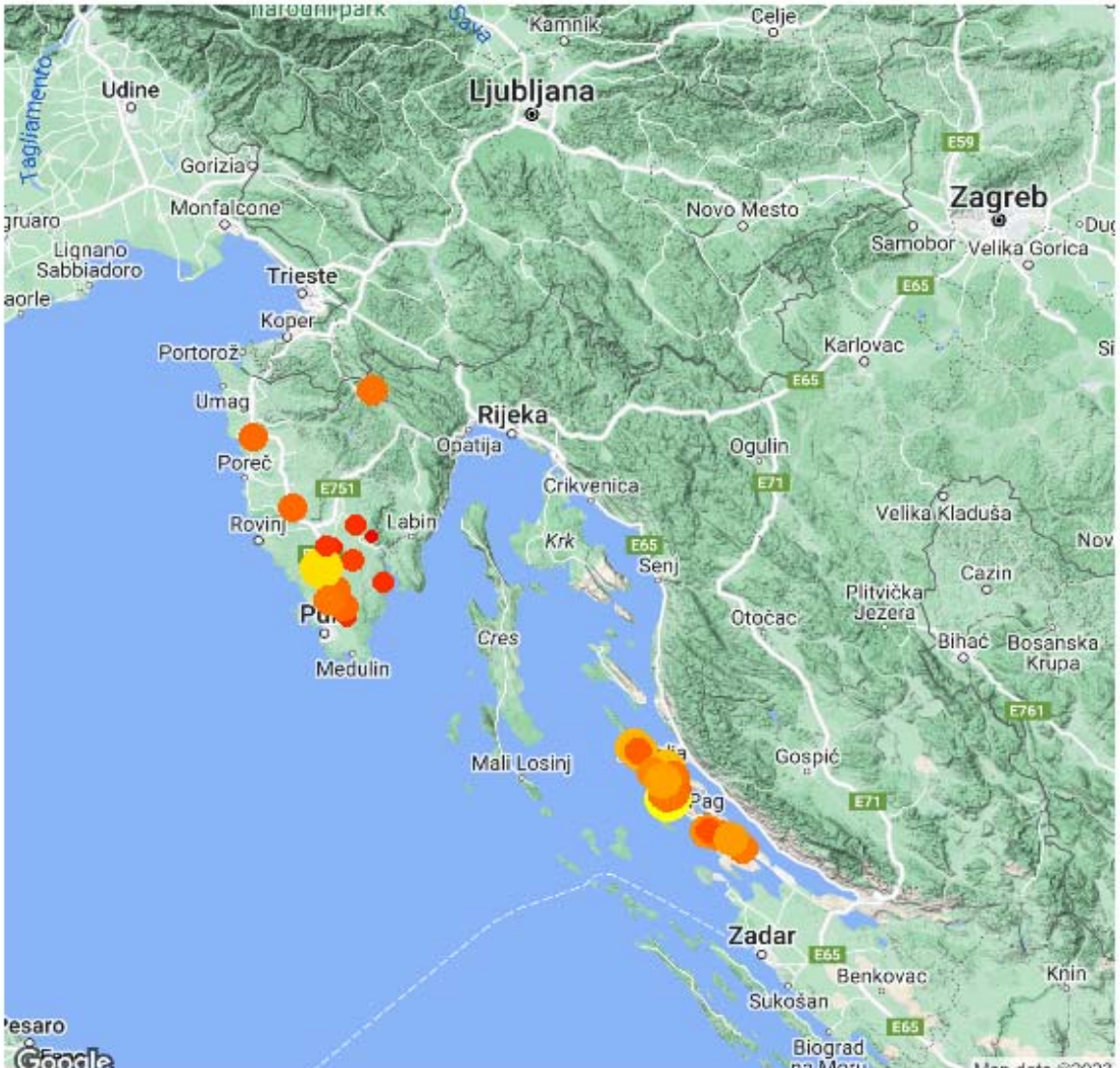
Future genetic improvement

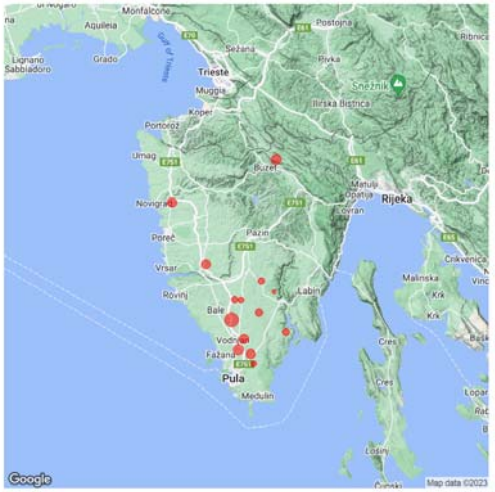
- Goal
  - Dairy performance improvement via selection
    - Important for long term productive and economic viability
  - Maintenance of the existing genetic variability
    - Vital for their resilience in unpredictable future environment

- Implementation of the basic principles of genomic optimum contribution selection (OCS) in existing breeding program
  - To provide **selection progress** on targeted trait/s with **minimal loss** of genetic variability (ultimate goal of project OPTI SHEEP, CSF, IP: 2019-04-3559)

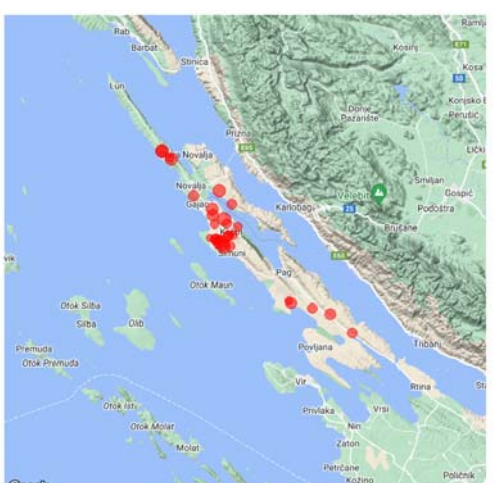
Genotyping – as a first step

- Genotyping with the OvineSNP50 chip - Weatherbys Ireland
  - Funds for genotyping: Project OPTI-SHEEP (CSF - IP-2019-04-3559), Submeasure 10.2., Breeding Association of Sheep and Goats
- Genotypes (N=**3,976**)
  - Istrian – 1,293 (1,207 ewes, 86 rams)
  - Pag – 2,683 (2,543 ewes, 140 rams)
  - Almost the whole breeding population of Istrian and Pag was genotyped





Veličina populacije 10 50 100



Veličina populacije 30 60 100 150

OCS implementation

- Transition from pedigree based BLUP to single-step GBLUP
- Development of pipelines for routine genomic OCS - in progress
- **BLUPF90** a family of programs
  - RENUMF90, AIREMLF90, BLUPF90
- Pedigree additive relationship combined with genomic information (following the theory of ssGBLUP)
  - Numerator relationship matrix A^{-1} was replaced by matrix H^{-1}

However

- Many practical and scientific questions
- Estimation of specific genetic parameters
  - Linkage disequilibrium
  - Genomic inbreeding
  - Genetic connectedness between flocks
  - How to optimize selection with maintenance of genetic diversity, the results could also be beneficial to other sheep and livestock breeding programs

ESTIMATION OF GENETIC CONNECTEDNESS BETWEEN FLOCKS IN POPULATION OF ISTRIAN SHEEP

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Introduction

- Istrian sheep breed is Croatian indigenous breed under selection for dairy traits (milk, protein and fat).
- ISSUE → potential bias in ranking of BLUP estimated EBVs from different flocks due to low connectedness.
- **AIM:** To determine level of connectedness as an indirect measure of bias of comparison of e

Material & methods

- **Information:** 1895 performance tested animals belonging to 14 flocks (7208 animals in the pedigree)
- **Software:** R package "GCA"
- **Statistics:** ***PEVD*** → prediction error variance of differences in EBVs between animals belonging to different flocks

The PEV of the EBVs obtained from diagonal of the inverse of the coefficient matrix. Pairwise PEVDs were first computed at the individual level as follows: $PEVD(\hat{u}_i\text{-}\hat{u}_j) = [PEV(\hat{u}_i) + PEV(\hat{u}_j) - 2PEC(\hat{u}_i,\hat{u}_j)] = (C_{ii}^{22} - C_{ij}^{22} - C_{ji}^{22} - C_{jj}^{22}) * \sigma_e^2$ and thereafter summarized at management unit level as follows: $PEVD_{ij} = \frac{1}{n_i * n_j} \sum PEVD_{ij}$

Picture 1. Ewes of Istrian sheep breed

Results

- $PEVD_{ij}$ from 0.752 to 0.824 (Figure 1.)
- The average $PEVD_{ij}$ ~ 0.78

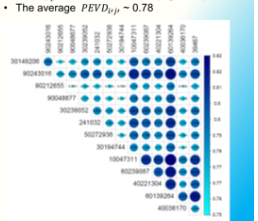

Figure 1. Estimates of connectedness between flocks

Conclusions

- Connectedness differed between the flocks, but results are inconclusive in term of bias in ranking EBVs from different flocks (no benchmark defined for PEVD statistics).
- Our previous work on this population suggests low level of connectedness between the flocks (insufficient for unbiased ranking of EBVs).
- Specially designed long-term breeding schemes should be established in order to strengthen connectedness between the flocks and make this population suitable for fair joint (between flock) genetic evaluation system.

Acknowledgement: Study supported by the Croatian Science Foundation. Genomic characterization, preservation and optimum contribution selection of Croatian dairy sheep, OPTI-SHEEP, grant number IP-2019-04-3559.

Genomic PCA – a proxy for monitoring genetic connectedness between flocks (case study on sheep)

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Aim & conclusion

- Disconnectedness leads to biased ranking of animals (EBVs) in joint between-flock genetic evaluation system
- Genomic selection could alleviate this issue, but only if flocks share the same genes (alleles)
- **AIM:** Can genomic PCA be used as an easy-to implement method to monitor connectedness????
- **CONCLUSION:** More research on this issue is needed for firm conclusion, but results obtained so far implicate that genomic PCA can be used as proxy for monitoring connectedness between flocks in any population

Picture 1. Tissue sampling for DNA testing

Material and methods

- Istrian sheep breed, 719 individuals from 14 flocks included in routine performance recording scheme (dairy traits).
- Single-squeeze tissue sampling = minimal distress to the animal
- Genomic markers: OvineSNP50 BeadChip array (Illumina)
- Quality control and genomic PCA : BLUPf90 program family
- Connectedness ("GCA", R programing environment)

Results

- Genetic variance explained by PC1 and PC2 was 5.8 and 3.5%, respectively
- PCA results revealed flocks of dissimilar genetic profile implicating poor genetic connectedness between them
- Comparison of PCA results with connectedness statistics (*gene flow, genetic drift variance*, pedigree and genomic based *PEV*, *CD*, and *r*) revealed substantial matching. However, some discrepancies made impossible to claim that genomic PCA is accurate enough on this purpose.
- More research is needed to generalize success of the method, but based on our theoretical knowledge in genomics and statistics, we believe that PCA can well serve the purpose.

Figure 1. Stratification of flocks based on first two principal components (PCA analysis)

Figure 2. Estimates of connectedness based on SNP marker information (PEVD statistics)

Acknowledgement: Study supported by the Croatian Science Foundation. Genomic characterization, preservation and optimum contribution selection of Croatian dairy sheep, OPTI-SHEEP, grant number IP-2019-04-3559.

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Partitioning of genetic trends by flock in Istrian sheep breed

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AIM & CONCLUSION

Genetic trends play an important role in monitoring success of selection
Partition of breeding values is an effective tool for detecting main providers of selection gain
The aims of this study were:
1) estimate genetic trends for fat content (FC) and protein content (PC) from 2000 to 2019
2) partition genetic trends (BV) by flock

The obtained results implicate **absence of systematic selection** for PC and FC, regardless of regular provision of breeders with BVs for these traits

MATERIAL

- Istrian breed
- 38,293 test-day records
- 6,477 animals
- Traits
  - Fat content (FC)
  - Protein content (PC)

METHODS

- Estimation of BVs
  A single-trait repeatability fixed regression test-day model
- Decomposition of the overall genetic trend
  R package 'AlphaPart'

Picture 1. Flock of Istrian sheep

RESULTS

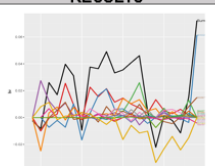


Figure 1. Decomposition of the overall genetic trend for FC by flock

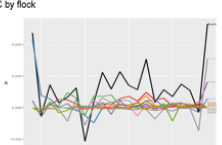
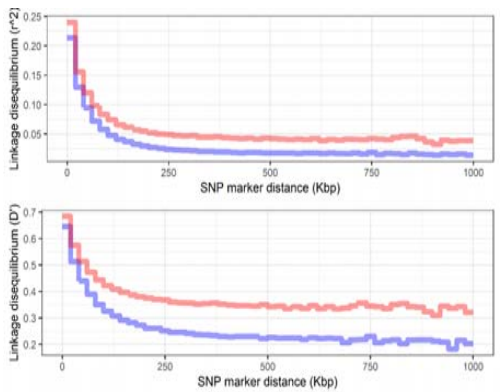
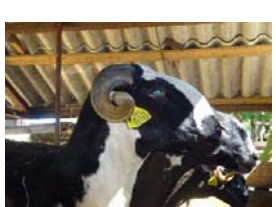


Figure 2. Decomposition of the overall genetic trend for PC by flock

Supported by the Croatian Science Foundation
Genomic characterization, preservation and optimum contribution selection of Croatian dairy sheep, OPTI-SHEEP, grant number IP-2019-04-3559.



LD decay in Istrian (red) and Pag (blue) sheep



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International initiative

- Across country evaluation in some multi-country breeds
  - Case of ARDI project between French Manech et Spanish Latxa (dairy sheep)
  - Interest in goats for Saanen or Alpine
  - Lacaune in Croatia – increasing population – inclusion either in French or international evaluation
- Share of genotypings / panel of SNPs
  - For parentage verification or genomic selection
- Share expertise across breeds of sheep and goat

European Reference Centre could serve this idea to better exchange in small ruminant (not only on phenotyping as it is the case in the SGC WG, but also on genetic evaluation, valorisation of genotypings)

Thank you for the attention!