Combining approaches for the analysis of the genetic structure of the Avileña-Negra Ibérica beef cattle breed

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63rd Annual EAAP Meeting Session 42. Genetics free communications Bratislava, Slovakia. 27-31 August, 2012.





Introduction. Study motivation

- Avileña-Negra Ibérica (ANI) is under a selection program since 1990.
- Genomic selection could be a potential tool to be used in a context of a multibreed Spanish evaluation.
- ANI breed is involved in GWAS.
- Population stratification has raised concerns in genomic selection (Deckers 2007) and GWAS (Price et al. 2006, 2011).
- Sample of herds for deep phenotyping. Random?



Determine if there is a hidden structure in the Avileña-Negra Ibérica breed.

Data

- ANI production system is fully extensive.
- Since 2005 ANI association has made a great effort to assess pedigree using a panel of 17 microsatellites.
- As a result we have a database of 13343 individuals from 59 herds.

| Microsatellites | n of alleles | H Obs | Н Ехр | |
|-----------------|--------------|-------|-------|--|
| BM1818 | 9 | 0.626 | 0.654 | |
| BM1824 | 6 | 0.680 | 0.717 | |
| BM2113 | 11 | 0.817 | 0.852 | |
| CSRM60 | 10 0.643 | | 0.689 | |
| ETH3 | 10 | 0.717 | 0.747 | |
| ETH10 | 9 | 0.690 | 0.721 | |
| ETH185 | 13 | 0.706 | 0.727 | |
| ETH225 | 8 | 0.731 | 0.762 | |
| ILSTS006 | 12 | 0.790 | 0.836 | |
| INRA005 | 5 | 0.643 | 0.661 | |
| INRA023 | 11 | 0.741 | 0.765 | |
| INRA063 | 6 | 0.557 | 0.577 | |
| SPS115 | 8 | 0.374 | 0.387 | |
| TGLA53 | 18 | 0.781 | 0.811 | |
| TGLA122 | 22 | 0.831 | 0.858 | |
| TGLA126 | 8 | 0.684 | 0.726 | |
| TGLA227 | 13 | 0.803 | 0.830 | |

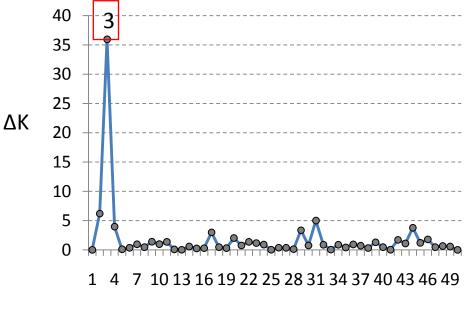
- None in H-W equilibrium
- Population stratification?

Methods. Tools to infer population structure

- We used three tools to infer the population structure: There are two main approaches to infer population structure:
- 1. Model based: STRUCTURE software (Pritchard et al. 2000).
- 2. Distance based.
 - Based on maximazing Nei's distance (Rodriguez-Ramilo et al. 2009).
 - Based on graphical clustering algorithm (K.J. Abraham and Rohan Fernando 2012)

STRUCTURE (Pritchard et al. 2000)

 We used Evanno et al. (2005) criterion to determine the number of clusters (subpopulations).





 $\Delta K = m(|L(K+1) - 2L(K) + L(K-1)|)/std[L(K)]$

- We found H-W equilibrium in:
- 1. Cluster 1 (n=3077): 12 microsatellites
- 2. Cluster 2 (n=6055): 4 microsatellites
- 3. Cluster 3 (n=4211): 7 microsatellites

Nei's distance maximizing method (Rodriguez-Ramilo et al. 2009)

- We tried from 2 to 5 clusters
- It divided the population in clusters of similar sizes

| | 2 clusters | | | | |
|-----|------------|-------------------|--|--|--|
| | Cluster 1 | uster 1 Cluster 2 | | | |
| N | 6670 | 6673 | | | |
| H-W | 1 micro | 1 micro | | | |

| | 3 clusters | | |
|-----|------------|-----------|-----------|
| | Cluster 1 | Cluster 2 | Cluster 3 |
| Ν | 4569 | 4375 | 4399 |
| H-W | 1 micro | 2 micros | 2 micros |

This approach does not identify any structure

Graphical clustering: molecular coancestry (K.J. Abraham and Rohan Fernando 2012)

It was developed by J.K.Abraham to identify gene networks and it is being

adapted to study the population structure.

- It has two steps:
 - 1. To identify the individuals that will be nodes of the clusters.
 - 2. Clusters construction: Aggregating individuals to each of the nodes.
- Key points:
 - 1. Determine the threshold to find the nodes.
 - 2. Determine the threshold to aggregate individuals.

Graphical clustering. Identification of cluster nodes

- Nodes are individuals that have:
 - A minimum coancestry (provided a threshold) among them.
 - A maximum average coancestry with the rest of the population.

• We used 150 sweeps per

threshold.

We used several thresholds.

| Nº of | Molecular coancestry treshold for identifying clusters nodes | | | | | | |
|-------|--|-------|-------|-------|-------|-------|-------|
| nodes | 0,147 | 0,162 | 0,177 | 0,191 | 0,201 | 0,221 | 0,235 |
| 2 | 18% | 1% | 4% | | | | |
| 3 | 68% | 43% | 42% | | | | |
| 4 | 14% | 55% | 47% | 3% | | | |
| 5 | | 1% | 7% | 25% | | | |
| 6 | | | 1% | 45% | 4% | | |
| 7 | | | | 24% | 26% | | |
| 8 | | | | 5% | 34% | 2% | |
| 9 | | | | | 26% | 7% | |
| 10 | | | | | 5% | 11% | |
| 11 | | | | | 4% | 25% | 1% |
| 12 | | | | | 1% | 28% | 2% |
| 13 | | | | | | 18% | 5% |
| 14 | | | | | | 8% | 11% |
| 15 | | | | | | 1% | 21% |
| 16 | | | | | | 1% | 21% |
| 17 | | | | | | | 20% |
| 18 | | | | | | | 9% |
| 19 | | | | | | | 7% |
| 20 | | | | | | | 2% |

Graphical clustering. Aggregating individuals

- The key point is to define the threshold that determines the minimum coancestry value to aggregate individuals to a cluster.
- An individual will be aggregated iff his coancestry with all individuals previously allocated into the cluster is above the threshold. ⁽³⁾
- We tried for the case of 3 clusters (similar to STRUCTURE) and we used:
 - an aggregation threshold of 0.184.
 - 150 sweeps.
- Animals were assigned to a cluster in two steps:
 - When they appear at least in 10% of the sweeps associated to a node.
 - The posterior probability of being associated to a node was the highest.

Graphical clustering. Aggregating individuals

- The clusters built were:
- 1. Cluster 1 (n=2807): H-W in 5 microsatellites
- 2. Cluster 2 (n=2324): H-W in 5 microsatellites
- 3. Cluster 3 (n=921): H-W in 11 microsatellites
- Independent individuals according to the aggregating threshold (n=7363): no H-W.

| f _{ij} | Cluster 1 | Cluster 2 | Cluster 3 | Group of indep. |
|--------------------|-----------|-----------|-----------|-----------------|
| Cluster 1 | 0,3301 | | | |
| Cluster 2 | 0,3157 | 0,3337 | | |
| Cluster 3 | 0,3156 | 0,3175 | 0,3366 | |
| Group of indep. | 0,2746 | 0,2741 | 0,2723 | 0,246 |

Conclusions

- Very preliminary results.
- It seems that the proposed method is a good way to infer population structure in a population of related individuals.
- This method determines the population structure in a fast way.
- Up to now results suggest that ANI breed population may be stratified in three subpopulations, leaving a set of individuals that cannot be assigned to any of the subpopulations.

Acknowledgements

- J.K.Abraham wish to acknowledge CAPE-Brazil for its funding.
- D. Martín-Collado is funded by MAGRAMA-FEAGAS.
- Avileña-Negra Ibérica Association has provided the genotype information.
- J. Fernández for his useful comments









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