Genomic data:
Insights into breed histories, population structures and genetic background of traits

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Establishing a Linear Profile

- Define specific traits of value for breeding program
- Describe horses precisely, accurately, reproducibly
- Ultimate - full description of a horse’s phenotype
- Along with performance data from self and relatives, can derive Estimated Breeding Values (EBV) and other metrics.
Limitations of EBV

- Precision and reproducibly of measurements
- Number of traits of interest in breeding program
- Incidence of traits of interest in population

Mating two animals with high EBV will only on AVERAGE result in offspring with higher EBV

- Complex inheritance
  - Multiple genetic variants with small effects
  - Environmental effects
  - Slow genetic progress if selection for one trait is deleterious for other, harder to measure traits

Need to combine phenotype and genotype data

Genomic Profiling

- Illumina Equine SNP70 beadchip
  - 70 k SNP

- Affymetrix Axiom Equine HD chip
  - 670 k SNP

- Next generation sequencing (NGS)
  - Whole genome or exome sequencing (WGS/WES)
  - All variants, huge amount of data

Once this “profile” exists, the genetic variants can be analyzed for association with any trait that has been recorded.
Genomic Selection

- Identifying genetic variants positively associated with traits and selecting for them in a breeding program
  - (Requires: precise definition of traits of interest, consistent measurement)
  - Leverage Linear Profiling Data for the phenotyping

Genomic Selection

Two-Step Model

- Prediction Equation
  - Genomic breeding value = $f_1g_1 + f_2g_2 + f_3g_3 + \ldots$

Reference Population
- Known genotypes and phenotypes

Selection Candidates
- Marker genotypes

Selected Breeders
- Using genomic breeding values

Single-Step Models
- also being considered in livestock
  - Could include different trait groups (conformation, performance, etc.) and different breeds/populations
  - Extremely computationally intensive
  - Still in early development.
Success of Genomic Selection

- Intensity of selection
- Generation interval
- Genetic variation existing for trait
- Distance between markers and causative SNPs
- "Moving target"
  - Dependent on change in effective population size over time
  - With two-step model, reference population needs to be updated periodically, in order to measure the improvement and refine selection

Animal Selection

- Should genomic profiles and linear profiles be generated for all foals in a population?
  - Only inspected foals?
  - Only “elite” horses (successful in sport or breeding)?
  - Only “elite” stallions?
- How much of the population’s genetic variance will be captured in a sample collection strategy?
- Success is dependent on data quantity and quality.
- If a trait has not been measured / recorded / prioritized, it cannot be selected for or against.
Trait Selection

If not under selection, a trait may be negatively affected by selection for other traits.

Selection for milk production in Holstein cattle led to reduced fertility.

Figure 1. Trends in milk yield (o) and Daughter Pregnancy Rate (n) for US Holsteins. Data are from USDA-ARS Animal Improvement Programs Laboratory, February 2007 (available at http://aip.arsusda.gov/ARSWeb/eval/summary/trend.htm).

Linear Profiling Considerations

- Each horse is compared to the average for that breed
- Average of the “elite” population may be very different than the average population of all horses in the breed, or of another breed
- Even if the trait definitions are standardized, genomic selection based on linear profiling of one population may not be appropriate for a different population.

→ Genomic profiling can help evaluate differentiation between (sub)populations.
American Quarter Horse Subpopulations

Different Breeding and Performance Goals
Distinct differentiation of subpopulations


Warmblood Breeds

Hanoverians & Oldenburgers
- Low population differentiation
- “…classification of the Hanoverian and Oldenburger animals into two distinct breeds is questionable.”

Holsteiners
- Minimal overlap with the other breeds
- Distinct subpopulations within breed

Trakehners
- Separate but close to Hanoverians
- Shared use of stallions?
- Lowest prediction accuracy because smallest data set

Heuer et al.: Genomic prediction of unordered categorical traits: an application to subpopulation assignment in German Warmblood horses, Genet Sel Evol, 2016.
Which animals are being sampled?

- Genetic diversity from the whole population is not preserved in the “elite” breeding populations
- If only approved stallions are genotyped, a large amount of genetic information is lost
- Sampling mares is also essential!
  - Less preselection, varying depth of linear profiles (performance tests > studbook inspection)

Selection vs. Genetic Drift

- Effective population size (Ne)
  - Number of individuals that contribute offspring to the next generation
- Genetic drift
  - Random fixation of alleles (homozygosity) in a population due to chance, rather than selection
- Large population - greater chance that gain and loss of alleles will cancel out
- Small population – reduced heterozygosity (fewer alleles)
  - Are alleles in the “elite” population due to positive selection or random drift?
  - Loss of diversity reduces ability to select for some traits, difficult to determine what traits have already been under selection (vs. random genetic drift)
Maintaining Genetic Diversity

- Inbreeding Depression
  - Lack of diversity decreases fitness
  - Loss of alleles that would allow for selection
- Outbreeding depression
  - Offspring may not be as well adapted / competitive as either parent
- Programs to increase diversity
  - Offspring often fail licensing inspections and are not allowed to breed
    - Intended diversity is therefore lost before entering the population
- Avoid the problem
  - Use genomic profiling to identify animals with high genetic diversity
    AND favourable genetic variants for traits of interest

Final Thoughts

- It is easier to preserve genetic diversity than to regain it
- Avoid extreme use of a small number of stallions
- Cryopreservation
  - Save sperm/embryos of many horses (not just “elite” stallions) for future use if genetic diversity is high or they have rare alleles
- Design your selection strategy and breeding goals to optimize the full potential of your breed.
- Consider genetic variants associated with traits of interest and overall genetic diversity to allow for sustainable genetic progress.
Thank you!