Quantitative Genomics at Animal Sciences

C. Maltecca ANS
cmaltec@ncsu.edu

Bioinformatics PhD students Presentation
Research

Efficiency
Improvement of Dairy Cattle Health Through the Utilization of Producer-recorded Data and Genomic Methods

Efficiency by Input Reduction
In April 2018, CDCB launched genetic and genomic evaluations for Holstein males and females, for six of the most common and costly health events impacting dairy heifers. These new predicted transmitting abilities (PTAs) are presented as percentage points of resistance above or below the breed average. Larger, positive values are favorable.

As of August 2018, the disease resistance traits will be incorporated into Net Merit and related indexes, for Holstein, through the new sub-index, Health Trait (HTM), which will not be published separately.

These resources are available to help understand 2018 NM and the new health traits.

- **Research References**
  - Foundational research has been published in several peer-reviewed journal articles, one of which is among the top 100 most highly cited papers published in the Journal of Dairy Science since 2014 (Parvin Gaddis et al., 2014). Data editing and validation are based on peer-reviewed methods (e.g., Parvin Gaddis et al., 2012).
CDCB Health Traits

In April 2018, CDCB launched genetic and genomic evaluations for Holstein males and females, for six of the most common and costly health events impacting dairy herds. These new predicted transmitting abilities (PTAs) are presented as percentage points of resistance above or below the breed average. Larger, positive values are favorable.

As of August 2018, the disease resistance traits will be incorporated into Net merit and indexed indexes for Holsteins, through the new sub-index, Health Trait 9 (HT9), which will not be published separately. These resources are available to help understand 2019 NMB and the new health traits.

1. Research References

- Foundational research has been published in several peer-reviewed journal articles, one of which is among the top 100 most highly cited papers published in the Journal of Dairy Science since 2014 (Parker Gaddis et al., 2014). Data editing and validation are based on peer-reviewed methods (e.g., Parker Gaddis et al., 2012).
Utilizing Genomic Information to Manage the Diversity and Minimize the Unfavorable Effects of Inbreeding in Livestock Populations

Efficiency by increasing Adaptability Readiness and Response
Genomics to predict breeding values is now standard in animal breeding

- Adopted in pretty much all species
- Mature and effective machinery for the prediction of GEBV

In dairy > 2 million individuals have genotype information.

- Their genotypes not fully integrated or exploited

Opportunity to incorporate population/herd management at the genomic level.

- Purebred:
  - Management of Lethal and Sub-Lethal Mutations.
  - Functional Inbreeding Depression.
  - Genetic Diversity.
  - Breed/Population divergence.

- Crossbred:
  - Maximize heterosis.
  - Optimal Matching of Genomes.
Primary Question
Primary Question

- How can two individuals with similar breeding value be further discriminated on the basis of genomic diversity non additive effects and fitness
- Which mating pairs should we choose balancing short and long term gains as well as fitness and overall variability?
**ROH**

**Definition and advantages**

- **Pedigree Relationship**
  - Mendelian sampling probabilities
  - Underestimates the true inbreeding coefficient

- **Genomic Relationship**
  - Realized proportion of the genome that is Identical By State (IBD) or By Descent (IBD)

- **ROH Relationship**
  - Estimate autozygosity at the genomic level
  - Minimize negative effects of inbreeding
  - Assess genomic structure
ROH
Definition and advantages
ROH
Definition and advantages
A mate allocation matrix \((B; \text{Pryce et al. 2012})\) constructed:

\[ B_{ij} = \lambda_1 \times EBV_{ij} - \lambda_2 \times F_{ij} - \lambda_3 \times ILM_{ij}, \]

- Can be constructed based on lethal and unfavorable haplotypes/mutations.
- Penalize breeding value based on inbreeding metric and functional inbreeding.

<table>
<thead>
<tr>
<th>Sire</th>
<th>Dam1</th>
<th>Dam2</th>
<th>Dam3</th>
<th>Dam4</th>
<th>Dam5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>B_{Sire 1, Dam 1}</td>
<td>B_{Sire 1, Dam 2}</td>
<td>B_{Sire 1, Dam 3}</td>
<td>B_{Sire 1, Dam 4}</td>
<td>B_{Sire 1, Dam 5}</td>
</tr>
<tr>
<td>2</td>
<td>B_{Sire 2, Dam 1}</td>
<td>B_{Sire 2, Dam 2}</td>
<td>B_{Sire 2, Dam 3}</td>
<td>B_{Sire 2, Dam 4}</td>
<td>B_{Sire 2, Dam 5}</td>
</tr>
<tr>
<td>3</td>
<td>B_{Sire 3, Dam 1}</td>
<td>B_{Sire 3, Dam 2}</td>
<td>B_{Sire 3, Dam 3}</td>
<td>B_{Sire 3, Dam 4}</td>
<td>B_{Sire 3, Dam 5}</td>
</tr>
<tr>
<td>4</td>
<td>B_{Sire 4, Dam 1}</td>
<td>B_{Sire 4, Dam 2}</td>
<td>B_{Sire 4, Dam 3}</td>
<td>B_{Sire 4, Dam 4}</td>
<td>B_{Sire 4, Dam 5}</td>
</tr>
<tr>
<td>5</td>
<td>B_{Sire 5, Dam 1}</td>
<td>B_{Sire 5, Dam 2}</td>
<td>B_{Sire 5, Dam 3}</td>
<td>B_{Sire 5, Dam 4}</td>
<td>B_{Sire 5, Dam 5}</td>
</tr>
</tbody>
</table>
Mating Design

Inbreeding Load

Design: 100_0_0

Design: 80_20_0

Design: 80_10_10

Design: 80_0_20
Scan the genome using heuristics to 'tag' unfavorable ROH and formally test impact of each ROH genotype.

Developed standalone software that is available on github:

- https://github.com/jeremyhoward/Unfavorable-Haplotype-Finder

A heuristic method to identify runs of homozygosity associated with reduced performance in livestock

J. T. Howard,*§ F. Tiezzi,* Y. Huang,+ K. A. Gray,+ and C. Maltecca*‡

*Department of Animal Science, North Carolina State University, Raleigh 27695-7627; ‡Sandhill Pommer Genetics, Rose Hill, NC 28458, and §Genetics Program, North Carolina State University, Raleigh 27695-7627
From Host to Guest and Back: Selection at the Intersection between the Gut Microbiome and the Host Genome in Breeding for Efficient Growth in Swine

Efficiency by exploiting the variability generated by host microbiome interaction
Efficiency of producing meat determined:

- Feed Costs
- Quality of lean meat produced

Using feed resources more efficiently

- Through diet
- Exploiting genomic variability for feed efficiency

Concentrating only on the pig variability

- Diminished marginal gains
- Losses of overall fitness

Introduction
Producing meat efficiently
The intestinal microbiome:
- Affects degradation of carbohydrates
- Provides short chain fatty acid
- Produces essential vitamins

Different Composition of gut microbiome:
- Alter ability of degrading enzymes
- Maintain population balance
- Influence overall health status
- Controls fatness and growth
Microbial diversity in pigs has been described to some extent. Composition and function of a healthy microbial population not yet employed as a tool to maximize animal health and performance.

We focused on two main objectives:

- Characterizing temporal changes in the microbiome community of pig feces with respect to both composition and diversity.
- Investigating the potential influence of host genetics on this diversity.
Statement

Efficiency

Genetics

Management

Diet

Microbiome
Trials

Duroc

Large White

Landrace

1200 Individuals

Feed Intake

Feeding Behavior

Genotypes

Microbiome

wean 15wk 22wk
Genetics of Microbial Temporal Variation
Predicting Growth With Microbial Composition

Christian Maltecca | Bioinformatics PhD students
The Genomic Architecture of Microbial Composition

BF14
BF18
BF22

WT14
WT18
WT22

LD14
LD18
LD22

gVar
mVar
pVar
rVar
The Genomic Architecture of Microbial Composition
The Genomic Architecture of Microbial Composition

Figure 3: Manhattan plots of chromosome segments that harbored single nucleotide polymorphisms (SNPs) significantly associated with taxon-operational taxonomic units (OTUs), with false discovery rate (FDR) at least 5%. The OTUs presented in this Figure are those sampled at week 15 in the finding trial, and they were found significantly associated (FDR at least 5%) on the phylogenetic record. Each Manhattan plot is accompanied with boxplots that show distributions of transformed OTU abundance within each group of genotypes (homozygote 1, homozygote 2, heterozygote). Red dot in each boxplot represents the mean of transformed OTU abundance.
Few things that help being be an happy student in my group:

- Be willing to learn old QG and breeding :)
- Some stats helps (freq. bayesian...)
- Know scripting (bash perl awk ...)
- Know R and or Python Julia
- Know one ancient language (Fortran C++)
- Like to toy around with messy data