

The effects of genomic inbreeding on production, reproduction, and conformation traits in US Holstein cows

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Outline

- Data Background
- Genomic Inbreeding
 - Genomic Relationship Matrix (F_{GRM})
 - Percent Homozygosity
 - Runs of Homozygosity (F_{ROH})
- Conclusions



Data Background

- 5,676 animals with genotypes
- 2,913 cows with single lactation records from 9 herds throughout the US
- 33,025 SNPs remaining after removing SNPs for call rate, MAF, and HWE
- Traits analyzed
 - Total milk yield, fat percentage, protein percentage
 - Days open
 - Stature, strength, udder depth, front teat placement
- Linear regression with effects of
 - Herd-Year-Season
 - Parity (1-4)
 - DIM for type traits

Inbreeding from Genomic Relationship Matrix

- Method utilized by USDA-AIPL to report genomic inbreeding

$$G = \frac{ZZ'}{\sum 2p(1 - p)}$$

- **Z** contains values of $0 - 2p$ for homozygotes, $1 - 2p$ for heterozygotes, and $2 - 2p$ for opposite homozygotes
- $p = 0.5$

Distribution of FGRM

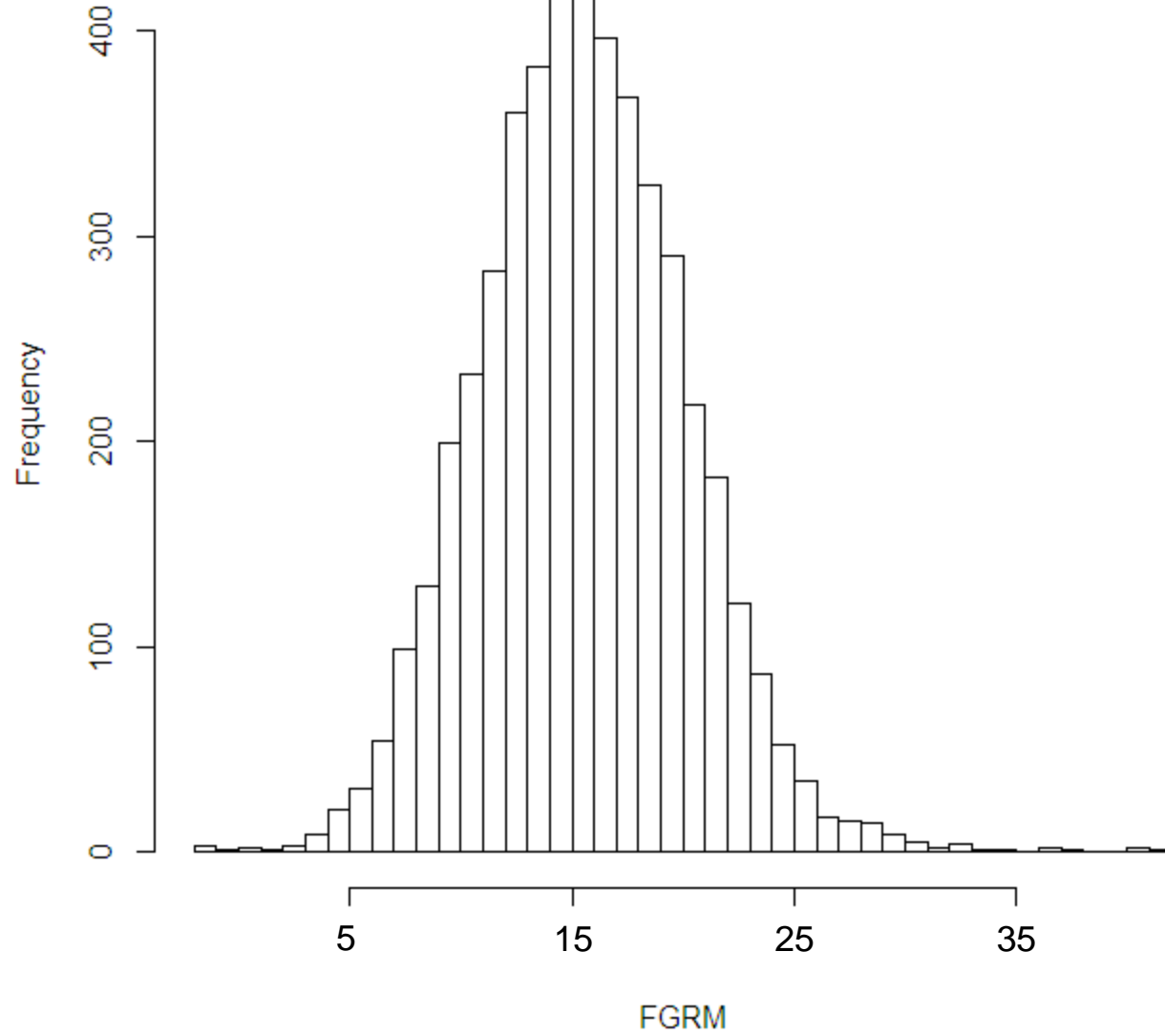


Table 1. Effect of F_{GRM} on economically important traits in dairy cows¹

Trait	Mean	SD	Δ / 1% increase in inbreeding	SE	P
205-day milk yield, kg	8,473	1,586	-23	4	0.0001
Average fat, %	3.63	0.59	0.003	0.002	0.08
Average protein, %	3.01	0.24	0.002	0.001	0.03
Days open, d	123	60	0.20	0.22	0.36
Stature	31.7	8.7	-0.09	0.02	0.0002
Strength	29.0	8.8	-0.08	0.02	0.004
Udder depth	22.4	11.1	0.03	0.03	0.29
Front teat placement	29.3	9.9	0.001	0.03	0.97

¹ N = 2,913

Percent Homozygosity

- Calculated as the percentage of SNPs which were homozygous

$$PH = \frac{N_{AA} + N_{BB}}{N_{AA} + N_{AB} + N_{BB}}$$

Distribution of Percent Homozygosity

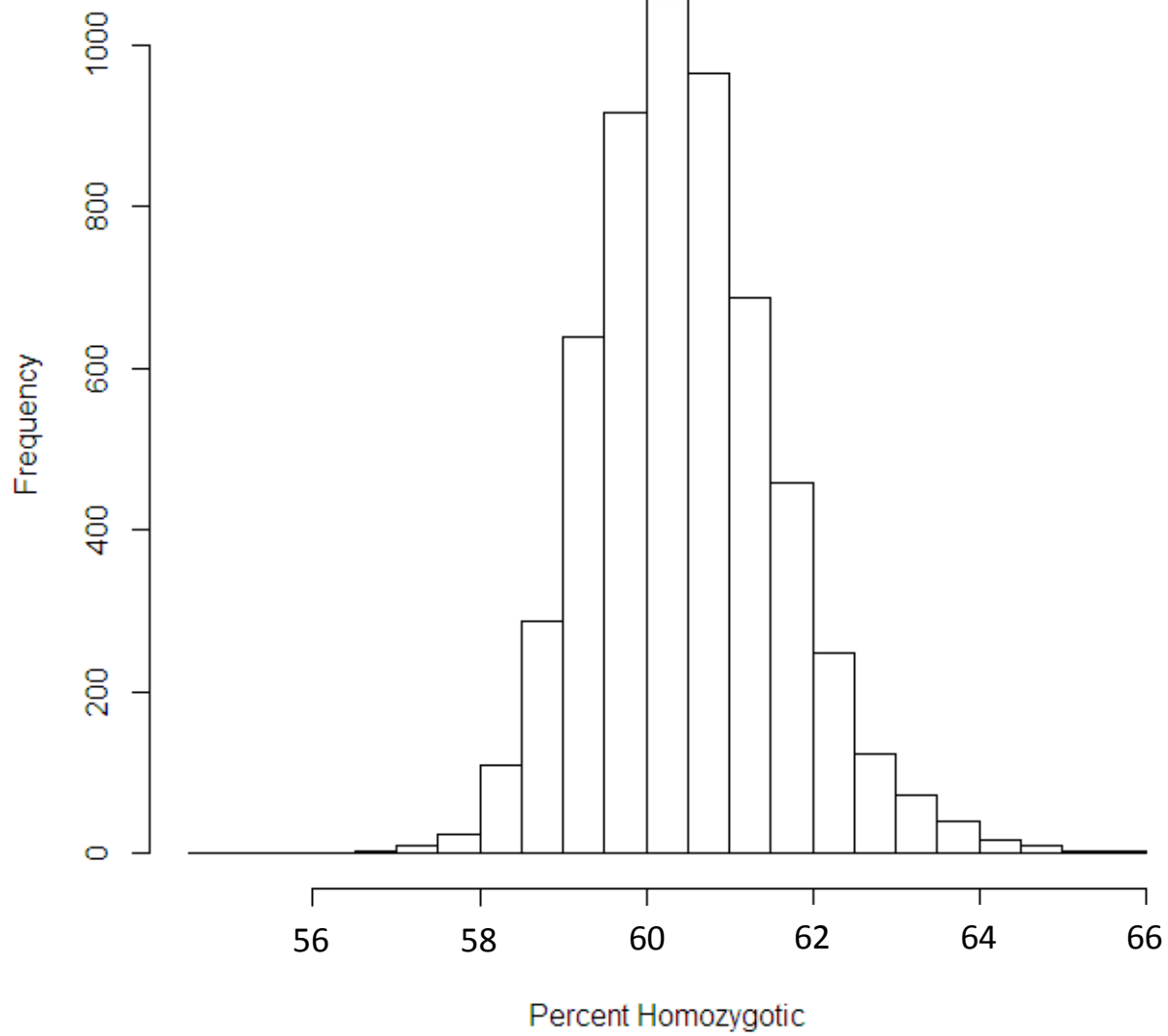


Table 2. Effect of percent homozygosity on economically important traits in US Holstein dairy cows¹

Trait	Mean	SD	Δ / 1% increase in inbreeding	SE	P
205-day milk yield, kg	8,473	1,586	-53	19	0.005
Average fat, %	3.63	0.59	-0.003	0.008	0.73
Average protein, %	3.01	0.24	-0.0024	0.0036	0.51
Days open, d	123	60	1.76	1.00	0.08
Stature	31.7	8.7	-0.06	0.12	0.60
Strength	29.0	8.8	-0.40	0.11	0.0005
Udder depth	22.4	11.1	0.11	0.13	0.37
Front teat placement	29.3	9.9	0.35	0.15	0.02

¹ N = 2,913

Runs of Homozygosity

- Inbred animals should have stretches homozygous DNA
- Length of runs depends on how recent inbreeding occurs
- Percentage of genome in a ROH
- Studied in humans for past decade
 - Record population history
 - Kirin, M, et al. 2010. **Genomic runs of homozygosity record population history and consanguinity.** PloS ONE 5:e13996.
 - Effects of inbreeding on disease risk
 - Simon-Sanchez, J, et al. 2012. **Cooperative genome-wide analysis shows increased homozygosity in early onset Parkinson's Disease.** Plos ONE. 7(3):e28787.

What is a ROH?

A A A A B A B B A A B A B A B A A A A A A A A A B
A A A B B B B B A A B A B A B A B A A A A B B B B B

15 SNP ROH

B A A B A A A A B B B B A B B A B A B A A A B B B A
B B B B B A A A B B B B A B B A B A B A A A B B B A

21 SNP ROH

B B B A A A A A B A B A A B A A B B A A A A A B B A
B A B A B A A B B A B B A B A B A B B A A B A B A A

No ROH

A B B A A A B B A A B A B A A B B B B A A A B A B B
A B B A A A B B A A A B B A A B B B B A A A A B B B

2 10 SNP ROH

ROH Discovery

- ROHs were discovered using PLINK
- Methods were based on Howrigan et al.
 - LD pruning was performed on the data set with 7,993 SNPs remaining
 - Minimum length of ROHs 30 SNPs, corresponding to inbreeding in about the last 10 generations
 - No heterozygote and 1 missing SNP were allowed in each 30 SNP section

•Purcell et al. 2007. **PLINK: a tool set for whole-genome association and population-based linkage analysis.** Am J Hum Genet. 81(3):559-575.

•Howrigan et al. 2011. **Detecting autozygosity through runs of homozygosity: A comparison of three autozygosity detection algorithms.** BMC Genomics. 12:460.

Determining F_{ROH}

- F_{ROH} = Percent of the genome contained within ROHs (Percent Identical by Decent)

$$F_{ROH} = \frac{\sum_k length(ROH_k)}{L}$$

- k = number of ROHs for individual
- L = total length of genome (kb)

Distribution of FROH

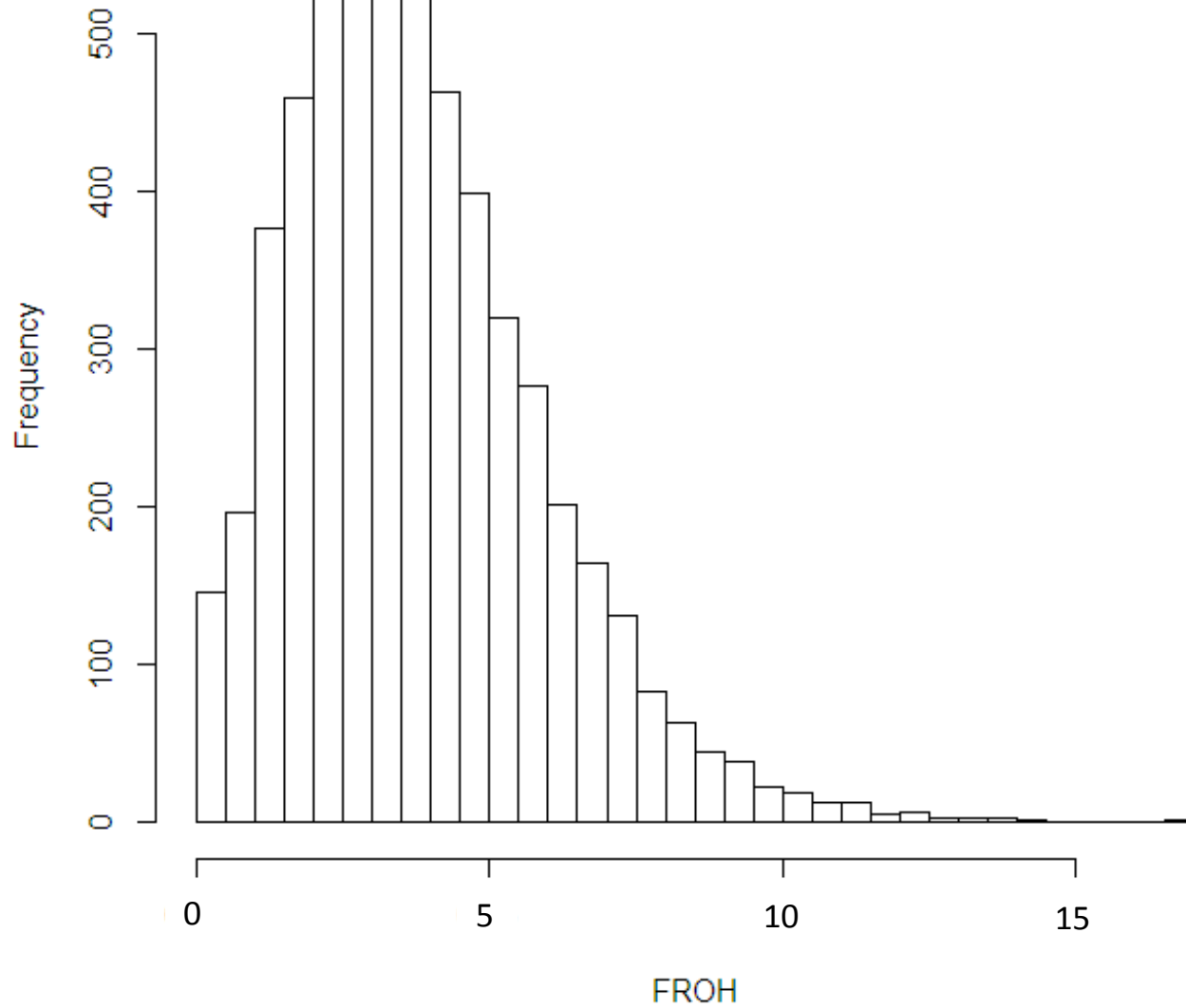


Table 3. Effect of F_{ROH} on economically important traits in US Holstein dairy cows¹

Trait	Mean	SD	Δ / 1% increase in inbreeding	SE	P
205-day milk yield, kg	8,473	1,586	-21	10	0.05
Average fat, %	3.63	0.59	-0.001	0.005	0.88
Average protein, %	3.01	0.24	0.0010	0.0020	0.61
Days open, d	123	60	1.72	0.54	0.002
Stature	31.7	8.7	0.07	0.06	0.27
Strength	29.0	8.8	-0.11	0.06	0.08
Udder depth	22.4	11.1	0.14	0.07	0.04
Front teat placement	29.3	9.9	0.25	0.08	0.003

¹ N = 2,913

Conclusions

- All three measures of genomic inbreeding show effects on economically important dairy traits
- Effects on several traits are index specific
 - Days open significant for percent homozygosity and F_{ROH}
 - Fat and protein percentage significant for F_{GRM}
- Results consistent with pedigree inbreeding