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

\[ G = \frac{Z Z'}{\sum 2p(1 - p)} \]

• \( Z \) contains values of 0 – 2p for homozygotes, 1 – 2p for heterozygotes, and 2 – 2p for opposite homozygotes

• \( p = 0.5 \)

Table 1. Effect of $F_{GRM}$ on economically important traits in dairy cows$^1$

<table>
<thead>
<tr>
<th>Trait</th>
<th>Mean</th>
<th>SD</th>
<th>Δ / 1% increase in inbreeding</th>
<th>SE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>205-day milk yield, kg</td>
<td>8,473</td>
<td>1,586</td>
<td>-23</td>
<td>4</td>
<td>0.0001</td>
</tr>
<tr>
<td>Average fat, %</td>
<td>3.63</td>
<td>0.59</td>
<td>0.003</td>
<td>0.002</td>
<td>0.08</td>
</tr>
<tr>
<td>Average protein, %</td>
<td>3.01</td>
<td>0.24</td>
<td>0.002</td>
<td>0.001</td>
<td>0.03</td>
</tr>
<tr>
<td>Days open, d</td>
<td>123</td>
<td>60</td>
<td>0.20</td>
<td>0.22</td>
<td>0.36</td>
</tr>
<tr>
<td>Stature</td>
<td>31.7</td>
<td>8.7</td>
<td>-0.09</td>
<td>0.02</td>
<td>0.0002</td>
</tr>
<tr>
<td>Strength</td>
<td>29.0</td>
<td>8.8</td>
<td>-0.08</td>
<td>0.02</td>
<td>0.0004</td>
</tr>
<tr>
<td>Udder depth</td>
<td>22.4</td>
<td>11.1</td>
<td>0.03</td>
<td>0.03</td>
<td>0.29</td>
</tr>
<tr>
<td>Front teat placement</td>
<td>29.3</td>
<td>9.9</td>
<td>0.001</td>
<td>0.03</td>
<td>0.97</td>
</tr>
</tbody>
</table>

$^1\, N = 2,913$
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

Frequency

Percent Homozygotic
Table 2. Effect of percent homozygosity on economically important traits in US Holstein dairy cows

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

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
  – Effects of inbreeding on disease risk
What is a ROH?

15 SNP ROH

21 SNP ROH

No ROH

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

Determining $F_{\text{ROH}}$

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

\[
F_{\text{ROH}} = \frac{\sum_k \text{length}(\text{ROH}_k)}{L}
\]

- $k = \text{number of ROHs for individual}$
- $L = \text{total length of genome (kb)}$
Distribution of FROH
Table 3. Effect of $F_{ROH}$ on economically important traits in US Holstein dairy cows$^1$

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>205-day milk yield, kg</td>
<td>8,473</td>
<td>1,586</td>
<td>-21</td>
<td>10</td>
<td>0.05</td>
</tr>
<tr>
<td>Average fat, %</td>
<td>3.63</td>
<td>0.59</td>
<td>-0.001</td>
<td>0.005</td>
<td>0.88</td>
</tr>
<tr>
<td>Average protein, %</td>
<td>3.01</td>
<td>0.24</td>
<td>0.0010</td>
<td>0.0020</td>
<td>0.61</td>
</tr>
<tr>
<td>Days open, d</td>
<td>123</td>
<td>60</td>
<td>1.72</td>
<td>0.54</td>
<td>0.002</td>
</tr>
<tr>
<td>Stature</td>
<td>31.7</td>
<td>8.7</td>
<td>0.07</td>
<td>0.06</td>
<td>0.27</td>
</tr>
<tr>
<td>Strength</td>
<td>29.0</td>
<td>8.8</td>
<td>-0.11</td>
<td>0.06</td>
<td>0.08</td>
</tr>
<tr>
<td>Udder depth</td>
<td>22.4</td>
<td>11.1</td>
<td>0.14</td>
<td>0.07</td>
<td>0.04</td>
</tr>
<tr>
<td>Front teat placement</td>
<td>29.3</td>
<td>9.9</td>
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</tr>
</tbody>
</table>

$^1$ N = 2,913
Conclusions

• All three measures of genomic inbreeding show effects on economically import 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