How to Consider Genetic Characteristics in Dairy Cattle Breeding?

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Background

VanRaden et al. (2011) showed that some Holstein Haplotypes (HH1, HH2, HH3) may cause embryonic loss in the homozygote state

- HH1 BTA 5: 62 Mb - 64 Mb, APAF1
- HH2 BTA 1: 93 Mb – 98 Mb
- HH3 BTA 8: 95 Mb – 96 Mb, SMC2

Fritz et al. (2013) and Cooper et al. (2013) identified additional haplotypes

- HH4 BTA 1: 2.1 Mb – 2.9 Mb, GART
- HH5 BTA 9: 92 Mb – 94 Mb

Carriers of these haplotypes have a reduced non return rate, because bb embryos die

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\[ \rightarrow 50\% \text{ carrier (Bb)} \]

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\[ \rightarrow 50\% \text{ carrier (Bb)} \]
\[ \rightarrow 25\% \text{ death (bb)} \]
Background
Economics of fertility defect HH1

- Pawnee Farm Arlinda Chief (born 1962) (VanRaden, 2014)
  - Carrier HH1
  - Contributed 14% of genes to the current Holstein population
  - $25 billion value of increased milk yield
  - $0.4 billion cost of HH1 mid-term abortions

- How many more fertility defects are there?
  - Average 0.2 / animal based on inbreeding depression
  (VanRaden and Miller, 2006 JDS)
**Background**

**Identification of genetic disorders**

- Each animal of every breed carries genetic disorders

- Number of known genetic disorders will drastically increase
  - Large scale genotyping of the population
  - Next generation sequencing

- E.g.: VSD – vertebral and spinal dysplasia (Kromik et al., Genetics 2015)
  - Variable number of vertebrae & neurological deficits
  - T gene
  - Easy to eliminate
  - Young dominate mutation
  - Very low allele frequency
Background

Publication & handling of genetic disorders

- It’s not intended to „destroy“ the Holstein breed, or single bulls

- Important to find the right handling of genetic disorders
  - How to use bulls with good and bad genetic characteristics?
  - →Find the appropriate mating partner

- Comprehensive investigations are needed before publication of genetic defects/disorders
  - Allele frequency
  - Inheritance
  - Economic value
  - Causal mutation
  - …
Background
Positive genetic traits

- Other genetic characteristics are desirable (Polled, Casein), and should be spread into the population.

- Question: How to combine positive and negative characteristics for publications and mating decisions?

- **Aim:**
  - Index of genetic properties which summarize the genetic characteristics and their economic values.
Materials and Methods
Risk matings

- Maternal grandsire
- Maternal granddam
- Maternal grandsire
- Maternal granddam

- Sire
- Dam
- Sire
- Dam

- Carrier
- Unknown
- Non-carrier
- Unknown

12.5% of all embryos die
0% of all embryos die
Materials and Methods
Survival of embryos (HH1)

![Graph showing survival of embryos over time. The graph includes lines representing different mating combinations: carrier x carrier, carrier x non-carrier, non-carrier x carrier, and non-carrier x non-carrier.](image)
Materials and Methods
Survival of embryos (HH5)

![Graph showing survival of embryos over time for different mating types: carrier x carrier, carrier x non-carrier, non-carrier x carrier, non-carrier x non-carrier. The graph indicates a decrease in survival over time, with distinct curves for each mating type.]

### Materials and Methods

#### Genetic effects

<table>
<thead>
<tr>
<th></th>
<th>NRR56 decrease heifer (%)</th>
<th>NRR90 decrease heifer (%)</th>
<th>NRR56 decrease cow (%)</th>
<th>NRR90 decrease cow (%)</th>
<th>Stillbirth increase (%)</th>
<th>Economic loss per embryo (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BY</td>
<td>-0.2 ± 0.3</td>
<td>-1.6 ± 0.3 ***</td>
<td>0.5 ± 0.5</td>
<td>-0.7 ± 0.6</td>
<td>1.8 ± 0.3***</td>
<td>95</td>
</tr>
<tr>
<td>HH1</td>
<td>-0.5 ± 0.3</td>
<td>-2.1 ± 0.3 ***</td>
<td>1.5 ± 0.8</td>
<td>0.8 ± 0.8</td>
<td>1.3 ± 0.2***</td>
<td>95</td>
</tr>
<tr>
<td>HH2</td>
<td>-0.6 ± 0.1</td>
<td>-2.8 ± 0.1</td>
<td>-0.3 ± 0.3</td>
<td>-0.2 ± 2.8</td>
<td>2.7 ± 0.9 **</td>
<td>95</td>
</tr>
<tr>
<td>HH3</td>
<td>-3.5 ± 0.7***</td>
<td>-4.4 ± 0.7 ***</td>
<td>-2.8 ± 1.5</td>
<td>-3.2 ± 1.5 *</td>
<td>-0.3 ± 0.5</td>
<td>52</td>
</tr>
<tr>
<td>HH4</td>
<td>-4.0 ± 0.4***</td>
<td>-4.2 ± 0.4 ***</td>
<td>-2.3 ± 0.9 *</td>
<td>-3.1 ± 0.9 **</td>
<td>-0.7 ± 0.2**</td>
<td>52</td>
</tr>
<tr>
<td>HH5</td>
<td>-3.0 ± 0.3 **</td>
<td>-1.0 ± 1.2</td>
<td>2.3 ± 0.2</td>
<td>-1.1 ± 0.3</td>
<td>2.1 ± 0.8*</td>
<td>52</td>
</tr>
</tbody>
</table>
Materials and Methods
Carrier frequency & economic weights

- Birth years 2011 - 2013 were used to determine the allele frequency in the German population

- Polled:
  - Economic value: 7 €/calf (5 € salary, 2 € drugs)
  - Social policy value not considered

- No other positive traits, because no economic benefit for an average farmer
Materials and Methods
Carrier frequency of the analyzed traits
Materials and Methods
Index for genetic characteristics (Falconer, 1980)

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Average effect (AV)</th>
</tr>
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<tbody>
<tr>
<td>AA</td>
<td>2q ( \alpha )</td>
</tr>
<tr>
<td>AB</td>
<td>(q-p) ( \alpha )</td>
</tr>
<tr>
<td>BB</td>
<td>-2p ( \alpha )</td>
</tr>
</tbody>
</table>

\( \alpha \): economic value
p & q: allele frequency of the population
AV: Average economic effect in a given population

\[ GI = \sum_{k=1}^{n} AV_k \]

\( \rightarrow \) Genetic index: \( GI = \sum_{k=1}^{n} AV_k \)
Materials and Methods
Simulation of a genomic breeding program

250,000 cows with milk recording

2,500 sire dams  
= best 1%
500 genotyped bull calves

29 genomic

1 99%-proven

Bull-sires

95%
5%

Cow-sires

94%
6%

Täubert et al., 2012
Materials and Methods
Simulation of a genomic breeding program

- EBV = true breeding value + mendelian sampling + residual

- Breeding values for the base cow population:
  - Mean: 100
  - Standard deviation: 20
  - Reliability: 50%

- Breeding values for the AI bulls:
  - 500 bulls with mean 130
  - Selection of the top 30
  - Reliability 67% genomic bulls 99 % proven bulls

- No mating of close related animals

- 100 repeats of the simulation
Materials and Methods
Breeding scenarios

- **A**: Selection of all animals due to breeding values – assortative mating
  - No consideration of genetic index

- **I**: Selection dam-dam due to the genetic index

- Selection of the AI bulls always due to EBVs
Results
Development of the breeding values over 20 generations
Results
Development of the genetic index over 20 generations

![Graph showing the development of the genetic index over 20 generations for bulls and dams. The x-axis represents generations, ranging from 5 to 20, and the y-axis represents the mean genetic index of bulls, ranging from -40 to -20. Two scenarios, A and I, are depicted with distinct line colors for bulls and dams.]
Results
Development of the allele frequencies over 20 generations

Scenario A

Scenario I

Mean allele frequency

Generation

Trait: Brachyspina, HH1, HH2, HH3, HH4, HH5USA, Polled
Conclusion

- Genetic index method to combine different genetic characteristic with different economic values

- Further investigation is needed to determine the correct phenotype (time of embryo loss) and the economic value

- Breeding programs: The index should be used for the female path, bulls should be selected due to breeding values
gBAP+ considers all genomic information:
- Genomic breeding values
- Inbreeding
- Genetic characteristics
- Prediction of genetic variation in potential offspring
### Prospective Genomic mating software gBAP+

<table>
<thead>
<tr>
<th>Sperm ($\sigma_a$)</th>
<th>Ovar ($\sigma_a$)</th>
<th>Offspring ($\sigma_a$)</th>
<th>&gt;1$\sigma_a$</th>
<th>&gt;2$\sigma_a$</th>
<th>&gt;3$\sigma_a$</th>
<th>&gt;4$\sigma_a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>MGBV</td>
<td>VGBV</td>
<td>MGBV</td>
<td>VGBV</td>
<td>E(mBV)</td>
<td>E(vBV)</td>
<td>p(%)</td>
</tr>
<tr>
<td>1.81</td>
<td>0.29</td>
<td>0.55</td>
<td>0.39</td>
<td>2.36</td>
<td>0.68</td>
<td>98</td>
</tr>
<tr>
<td>1.68</td>
<td>0.52</td>
<td>2.23</td>
<td>0.91</td>
<td>91</td>
<td>3</td>
<td>60</td>
</tr>
</tbody>
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*Segelke et al., GSE 2014*
Acknowledgements

German national organization FBF is thanked for financial support

Thank you for attendance!