Estimating Myostatin gene effect on milk performance traits using estimated gene content for a large number of non-genotyped cows

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Context

• **Situations**
  – where estimation of single gene effects for quantitative traits is important

• **Different scenarios**
  – ↗ genetic gain:
    • By selecting animals with desirable gene variants
  – To avoid overemphasis on single gene variants
• Difficult to obtain reliable estimates
  – Not all (few) genotyped animals
  – Genotyping more ➔ Expensive
  – Genotyping all ➔ Impossible
• Other solution: estimating missing genotypes
  – Different methods (e.g., Van Arendonk et al., 1981)
  – Estimating gene content (number of alleles) (Gengler et al., 2007)
Context

• Deletion in Myostatin gene: ‘mh’ allele
  – Responsible for double-muscling in all cattle breeds (Bellinge et al., 2005)
  – Present in Dual-Purpose Belgian Blue (DP-BBB)
  – Influence on milk performance traits?
    • But, not well known → few genotyped animals
    • However, important in DP-BBB & used as selection tool

▶ Estimation of ‘mh’ allele effect on milk production traits
Materials & Methods

- **Data structure & genotypes**
  - Data used for the official routine genetic evaluation for Walloon Region of Belgium
  - 13,992,889 test-day records for 1\textsuperscript{st}, 2\textsuperscript{nd} & 3\textsuperscript{rd} lactation
    - 799,778 cows
    - Breeds:
      - Holstein, Belgian Blue Breed (BBB), Others Red-White breeds
      - Mixed herds and crossbreds
  - Heterogeneous breed composition

➤ Additional issue for genotype estimation
Materials & Methods

• Data structure & genotypes
  – Pedigree file: 1,429,939 animals
  – 1,416 genotyped DP-BBB animals (⇒ 1,183 cows)
    • Few genotyped animals

Can other genotypes be assumed?
Materials & Methods

• Addition «assumed» known genotypes
  – BBB animals (sires) from the meat type
    • Used for AI
    • Born after 1985
      ➤ Assumed to be mh/mh (n=830)
  – Purebred non-BBB animals
    ➤ Assumed to be +/+ (n=659,971)
Materials & Methods

• Gene content estimation
  – For other animals (n=767,722)
    • Estimation of gene content (Gengler et al., 2007)
  – For the founders
    • 10 genetic groups
      ✓ According to breed
      ✓ By distinguishing:
        – BBB & non-BBB animals
        – Herd-book type of animal (meat & DP)
        – Year of birth
# Results & Discussion

- **Estimated gene content of non-genotyped animals**
  - Development of Myostatin gene content over time

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<th>Group of animals</th>
<th>Estimated average gene content</th>
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BBB = Belgian Blue Breed; M = meat type; DP = dual-purpose type.

1Values between 0 (+/+ ) and 2 (mh/mh) represent the gene content for 'mh' allele.

62nd EAAP Annual Meeting, Stavanger, Norway, August 29th - September 1st 2011
Results & Discussion

- Estimated gene content of non-genotyped animals
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Results & Discussion

• **Estimated gene content of non-genotyped animals**
  
  – Hypothesis
    * Necessity to use genetic groups and to include animals with assumed genotypes to obtain valid estimations of gene content
  
  – To test this hypothesis
    * Estimation without these genetic groups & assumptions
      – Estimated mean gene content of 1.349
    * Unrealistic results because:
      – Extreme founder allele frequency obtained only from genotyped BBB animals
      – Weak or non-existing (different breeds) links between genotyped and non-genotyped animals
Results & Discussion

• **Estimated gene content of non-genotyped animals**
  – More realistic results
  – Show potential for gene content estimation with:
    – Use of genetic groups
    – Use of assumptions
      » when few genotyped animals in a large heterogeneous population under selection
  – However, its accuracy depends mainly on:
    ✗ with increasing number of genotyped relatives
    ✗ when closer relationships between genotyped and non-genotyped animals
Materials & Methods

- **Statistical model to estimate ‘mh’ effect**
  - Based on routine genetic evaluation model for milk production traits (Auvray & Gengler, 2002; Croquet et al., 2006)
    - Multi-lactation, multi-trait random regression model
    - (Co)variance components
    - Fixed regression on observed or estimated gene content

- **Standard errors for regression coefficients**
  - Mixed model conjugate gradient normal equations
    (Harville, 1979; Croquet et al., 2006)
Results & Discussion

• Allele substitution effects of the ‘mh’ allele
  ✓ On milk, fat and protein yield (kg/305 days) through all lactations & for each lactation (n= 13,992,889)

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<th>Mean</th>
<th>1</th>
<th>2</th>
<th>3</th>
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<tbody>
<tr>
<td>Trait</td>
<td>Effect</td>
<td>Effect</td>
<td>s.e.</td>
<td>t-value</td>
</tr>
<tr>
<td>Milk</td>
<td>-76.06</td>
<td>-70.80</td>
<td>8.30</td>
<td>8.53***</td>
</tr>
<tr>
<td>Fat</td>
<td>-3.62</td>
<td>-3.02</td>
<td>0.35</td>
<td>8.62***</td>
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<tr>
<td>Protein</td>
<td>-2.84</td>
<td>-2.57</td>
<td>0.25</td>
<td>10.28***</td>
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✓ 1 copy of the ‘mh’ allele
  ▪ Very high significant decrease in milk, fat and protein yields
Results & Discussion

• Additive effects
  – The power to detect a candidate gene effect depends
    • on the magnitude of the effect that was estimated
    • on the standard error of this estimation
  – In this study, estimated ‘mh’ allele effects were large enough to be significant
    • Although standard errors ↗ with increasing lactation number
      – Because less records in higher lactation number
  – However,
    • Potentially biased allele effect estimation as effects lower than in other studies (Buske et al., 2010)
      – Selection of animals for genotyping randomly?
      – Inclusion of a large number of animals with estimated genotypes?
Conclusion

• To estimate more accurately gene content of large heterogeneous population
  – Inclusion of additional assumptions
    • As information about genetic groups
      (here based on breeds, phenotypic selection and year of birth)
  – Groups expressing differences in expected founders allele frequencies

• Estimation of the ‘mh’ allele effect possible
Thank you for your attention

• Acknowledgments

➢ National Fund for Scientific Research
  • Support for N. Gengler (Research Associate)

➢ Walloon Regional Ministry, SPW – DGO3
  • Project D31-1224/S1

➢ Walloon Breeders Association