

# Longitudinal effects of muscular hypertrophy allele on milk production traits during the lactation using a novel equivalent model when molecular information is limited

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# Context

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- In 1973, Mid and High Belgian breed was divided officially into 2 types
- 1<sup>st</sup> type: Meat Belgian Blue



Young bull



Cow

# Context

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- Meat Belgian Blue (BBB)
  - Double muscling phenotype
  - Muscle Hypertrophy (*mh*) syndrome
  - Caused by 11 bp deletion in *Myostatin* gene
    - ✓ *mh* allele: deletion
    - ✓ + allele: allele without deletion
    - ✓ *mh* allele frequency close to 100 %

# Context

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- 2<sup>nd</sup> type: Dual Purpose Belgian Blue (DP-BBB)
  - Local breed in Belgium
  - Vulnerable status (FAO criteria)
  - Related to the *Bleue du Nord* (in France)
  - Supported by an INTERREG IVa project



# Context

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- Dual Purpose Belgian Blue (DP-BBB)
  - Average milk yield: 4,000 kg (up to 7,000 kg)
  - Strong muscling (much less caesareans)
  - *mh* allele
    - ✓ less frequent than BBB (allele frequency: 60 %)

# Context

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- DP-BBB: *mh/mh*



Bull



Cow

# Context

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- DP-BBB: +/+



Bull



Cow

# General objective

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*mh* allele could influence milk production

**But molecular information is limited**

**→ We need a practical method to integrate molecular information**



# Methodology

## ■ Mixed Inheritance Model

- Combining fixed gene effects  $\mathbf{g}$  and random polygenic  $\mathbf{u}$  effects

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{ZQg} + \mathbf{Zu} + \mathbf{e}$$

- Usual assumptions concerning distribution of random effects

$$E \begin{bmatrix} \mathbf{u} \\ \mathbf{e} \end{bmatrix} = \begin{bmatrix} \mathbf{0} \\ \mathbf{0} \end{bmatrix} \text{ and } \text{Var} \begin{bmatrix} \mathbf{u} \\ \mathbf{e} \end{bmatrix} = \begin{bmatrix} \mathbf{G} & \mathbf{0} \\ \mathbf{0} & \mathbf{R} \end{bmatrix}$$

# Methodology

- Equivalent Mixed Inheritance Model
  - Fixed gene effects and random polygenic effects replaced by a combined genetic effect  $\mathbf{u}^*$

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{u}^* + \mathbf{e} \text{ where } \mathbf{u}^* = \mathbf{Q}\mathbf{g} + \mathbf{u}$$

- Modification of assumptions

$$E \begin{bmatrix} \mathbf{u}^* \\ \mathbf{e} \end{bmatrix} = \begin{bmatrix} \mathbf{Q}\mathbf{g} \\ \mathbf{0} \end{bmatrix} \text{ and } \text{Var} \begin{bmatrix} \mathbf{u}^* \\ \mathbf{e} \end{bmatrix} = \begin{bmatrix} \mathbf{G} & \mathbf{0} \\ \mathbf{0} & \mathbf{R} \end{bmatrix}$$

# Methodology

- Associated Mixed Model Equations
  - Following Quaas (*J. Dairy Sci.* 1988, 71, 1338-1345)
  - Same strategy to integrate genetic groups
  - Joint estimation of  $\beta$ ,  $u^*$  and  $g$

$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z & 0 \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} & -G^{-1}Q \\ 0 & -Q'G^{-1} & Q'G^{-1}Q \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u}^* \\ \hat{g} \end{bmatrix} = \begin{bmatrix} X'Ry \\ Z'Ry \\ 0 \end{bmatrix}$$

# Methodology

- Associated Mixed Model Equations

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} & \mathbf{0} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \mathbf{G}^{-1} & -\mathbf{G}^{-1}\mathbf{Q} \\ \mathbf{0} & -\mathbf{Q}'\mathbf{G}^{-1} & \mathbf{Q}'\mathbf{G}^{-1}\mathbf{Q} \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \\ \hat{\mathbf{g}} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}\mathbf{y} \\ \mathbf{0} \end{bmatrix}$$

- Solving of whole system is equivalent of solving iteratively two systems of equations
  - ✓ 1<sup>st</sup>, solving for the third row

$$\mathbf{Q}'\mathbf{G}^{-1}\mathbf{Q}\hat{\mathbf{g}} = \mathbf{Q}'\mathbf{G}^{-1}\hat{\mathbf{u}}^*$$

# Methodology

- Associated Mixed Model Equations

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} & \mathbf{0} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \mathbf{G}^{-1} & -\mathbf{G}^{-1}\mathbf{Q} \\ \mathbf{0} & -\mathbf{Q}'\mathbf{G}^{-1} & \mathbf{Q}'\mathbf{G}^{-1}\mathbf{Q} \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \\ \hat{\mathbf{g}} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}\mathbf{y} \\ \mathbf{0} \end{bmatrix}$$

- Solving of whole system is equivalent of solving iteratively two systems of equations

✓ 2<sup>nd</sup>, solving the system

$$\begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{X}'\mathbf{R}^{-1}\mathbf{Z} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{X} & \mathbf{Z}'\mathbf{R}^{-1}\mathbf{Z} + \mathbf{G}^{-1} \end{bmatrix} \begin{bmatrix} \hat{\boldsymbol{\beta}} \\ \hat{\mathbf{u}}^* \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{R}^{-1}\mathbf{y} \\ \mathbf{Z}'\mathbf{R}^{-1}\mathbf{y} + \mathbf{G}^{-1}\mathbf{Q}\hat{\mathbf{g}} \end{bmatrix}$$

# Methodology

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- Associated Mixed Model Equations
  - Solving iteratively until relative differences in estimation of  $\mathbf{g} < 10^{-5}$
- Advantages
  - Could allow solving when only limited number of genotyped animals
  - Gene effect could be estimated from limited known genotypes

# Material

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- Data used for official genetic evaluations in the Walloon Region of Belgium
  - Pedigree: 1,606,024 animals
  - Data: 11,117,505 Test-day records
  - 689,057 cows with production records

# Material

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- Molecular information
  - *mh* genotypes available
    - ✓ 108 DP-BBB bulls
    - ✓ 1,891 DP-BBB cows with production records
  - Offspring of genotyped animals
    - ✓ 11,768 cows with production records

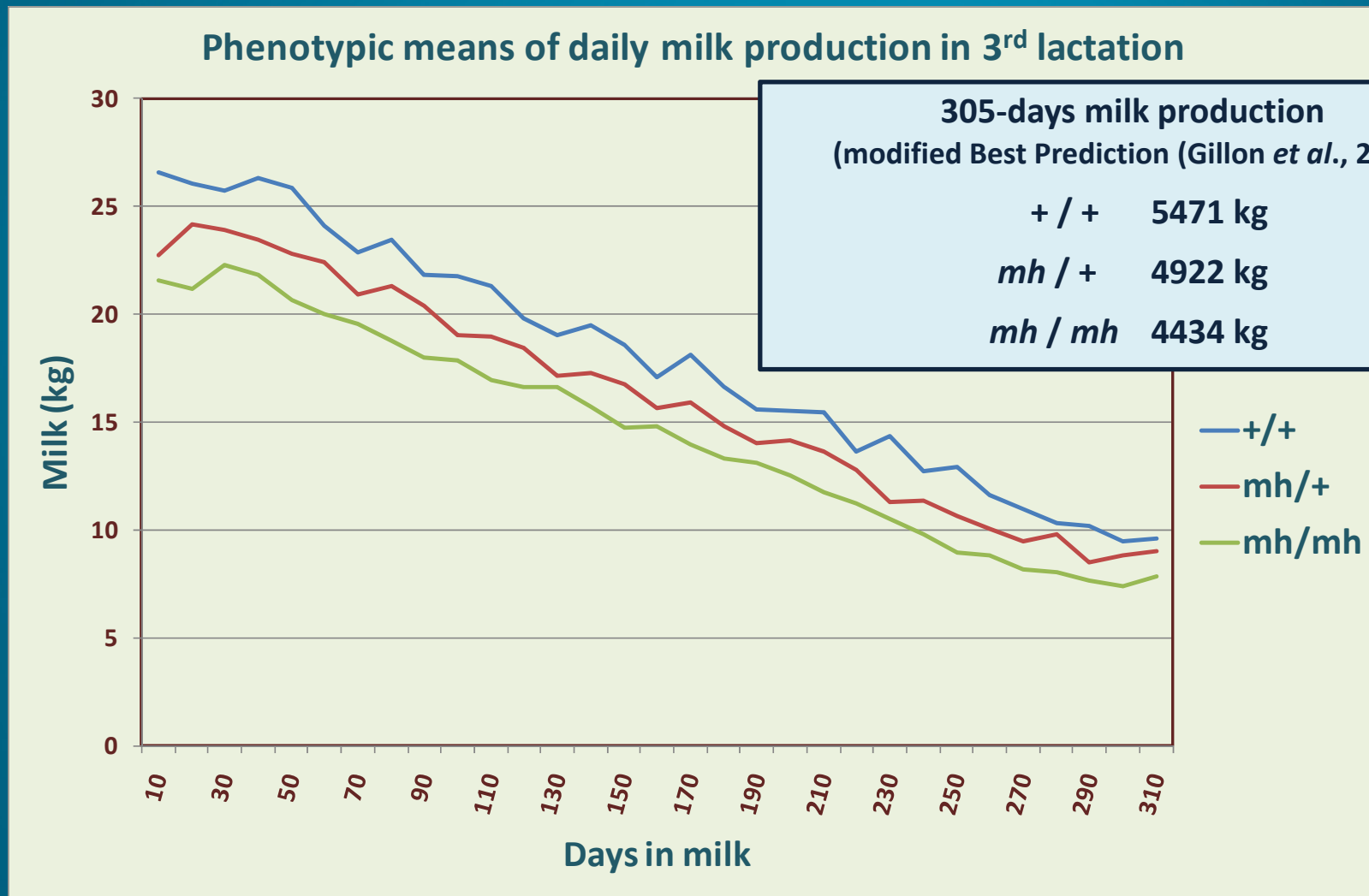


# Statistical Model

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- Random regression test-day model
  - Official Walloon Model used for routine run
  - Multi-trait multi-lactation model
    - ✓ 3 traits x 3 lactations

# Results



# Results

- Allelic substitution effect of the *mh* allele on 305-days production yields (kg)

	Milk	Fat	Protein
1 <sup>st</sup> lactation	- 155.8	- 8.73	- 5.27
2 <sup>nd</sup> lactation	- 142.0	- 8.40	- 5.43
3 <sup>rd</sup> lactation	- 178.2	- 9.67	- 6.23
Means - 3 lact.	- 158.7	- 8.93	- 5.64

305-days production yields (kg, modified Best Prediction, Gillon *et al.*, 2010)

	Milk	Fat	Protein
Means - 3 lact.	4420	157	145

# Results

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- Allelic substitution effect of the *mh* allele on 305-days production yields (kg)
  - Buske *et al.* (2010) *J. Anim. Breed. Genet.* 127: 272-279
    - ✓ Based on a Bayesian approach using additional prior information on the distribution of external EBV
    - ✓ Additive effect
      - 120.3 kg Milk    - 5.5 kg Fat    - 4.0 kg Protein

# Results

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- Allelic substitution effect of the *mh* allele on 305-days production yields (kg)
  - Buske *et al.* (2010) *Animal* (accepted)
    - ✓ By regression on observed or estimated gene content
    - ✓ Estimated gene content using method of Gengler *et al.* (2007, *Animal* 1:21-28)
    - ✓ Additive effect
      - 76.1 kg Milk    - 3.6 kg Fat    - 2.8 kg Protein

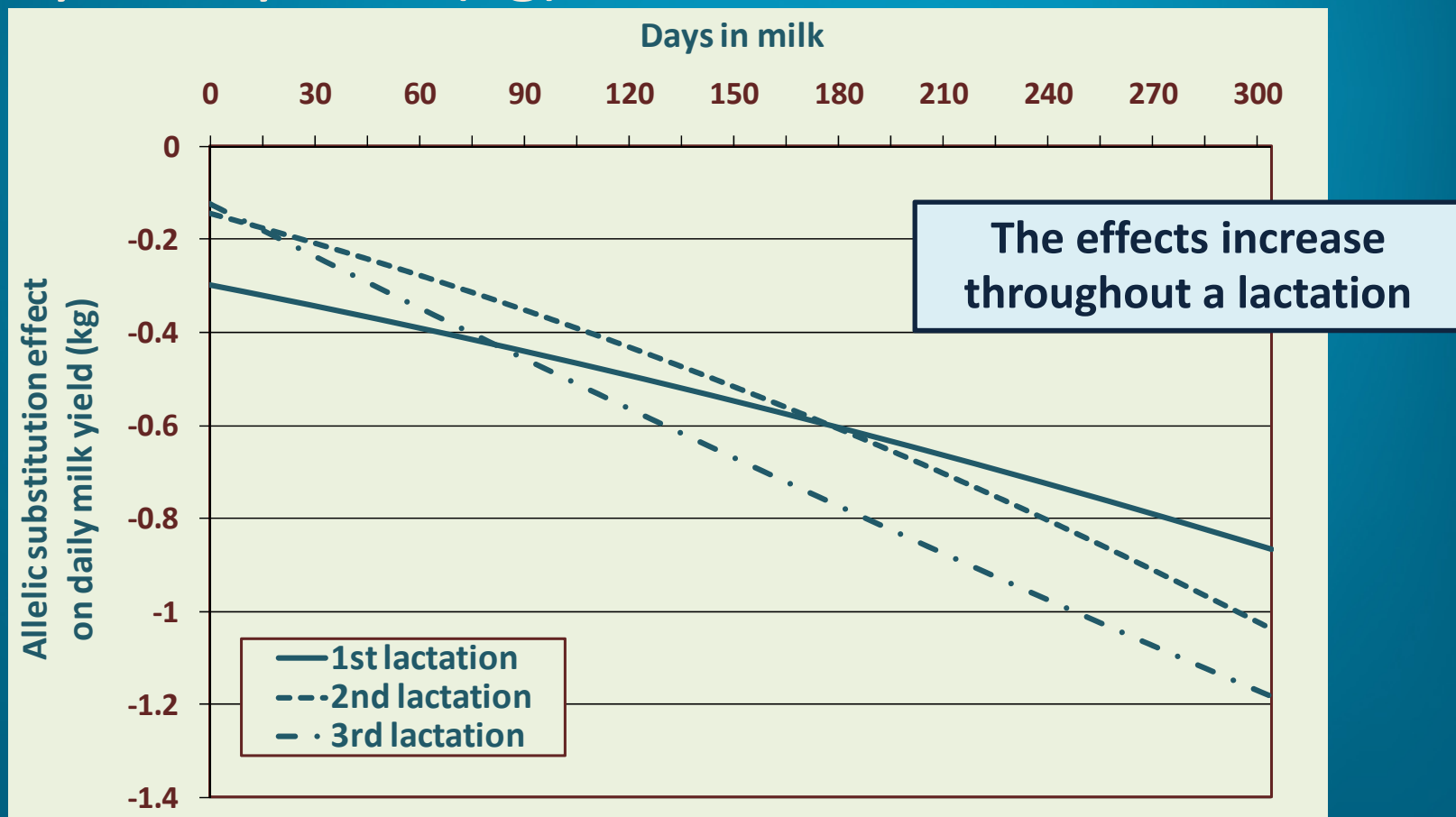
# Results

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- When applied on a random regression model
  - ➔ Possibility to model the gene effect
  - ➔ Within the first 3 lactations
  - ➔ For Milk, Fat and Protein yields

# Results

- Estimated substitution effect of the *mh* allele on daily milk yields (kg)



# Conclusion

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- Equivalent mixed inheritance model
  - We can use incomplete genotyped population
  - When applied on a random regression model, possibility to model the gene effect within lactations
- Estimation of *mh* allele substitution effects
  - Negative effect on milk production as expected
  - Effect variable during the first 3 lactations
  - Presence of *mh* allele reduces persistency of lactations



# Thank you for your attention

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