Modelling QTL on BTA06 in dairy cattle using random regression test day model

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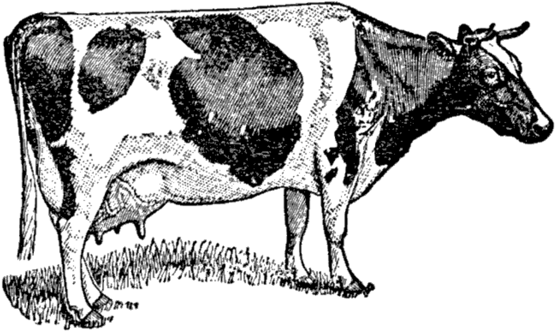
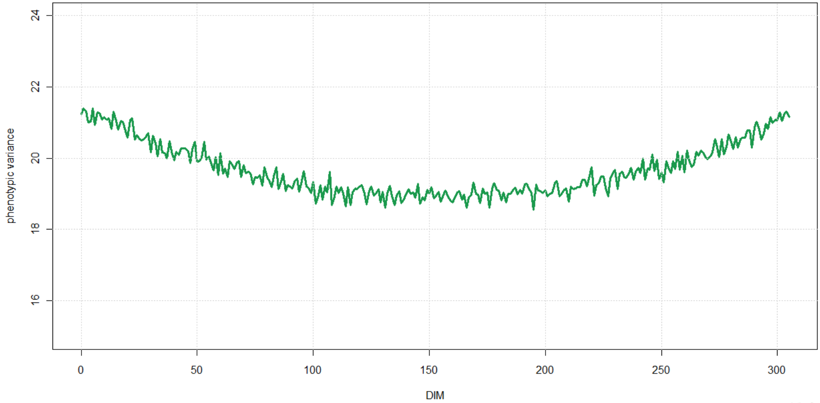
Outline

1. Motivation
2. Data Set
3. Methods
4. Results

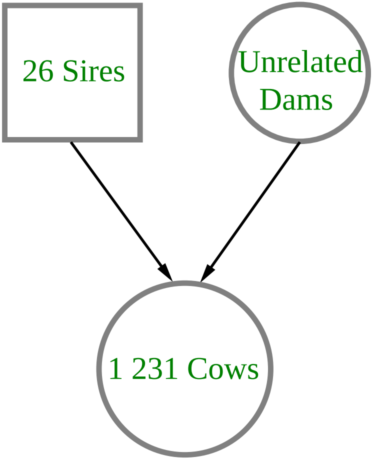


Main Aim

Checking if gene effects are vary or constant in time



Material – animals



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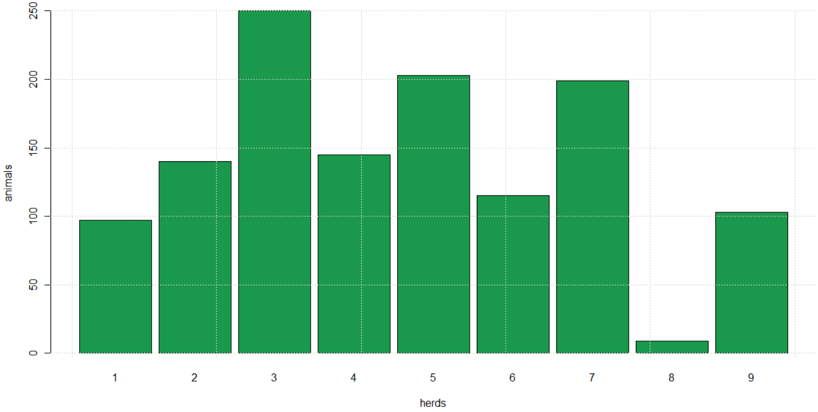

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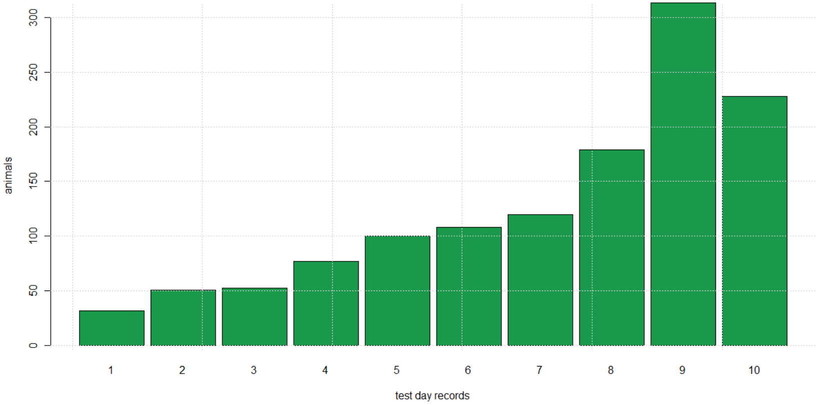

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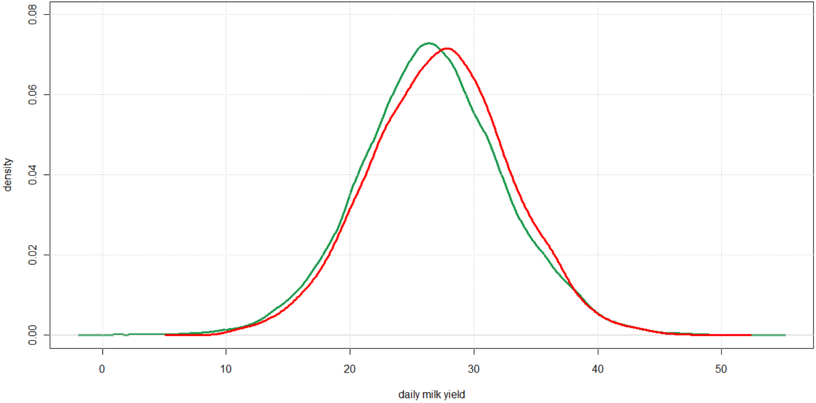

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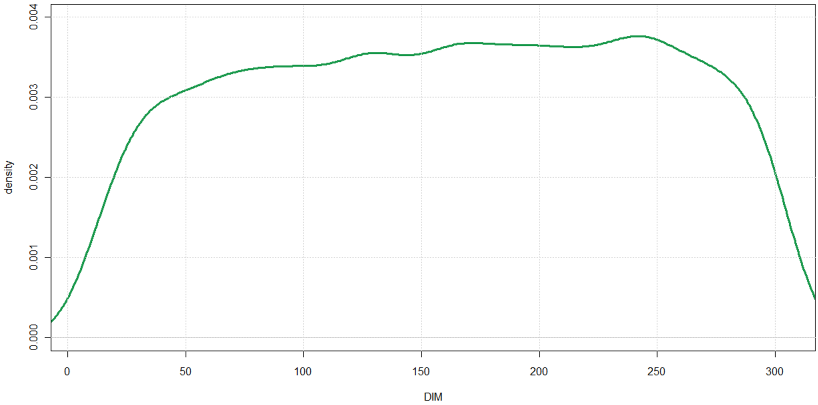
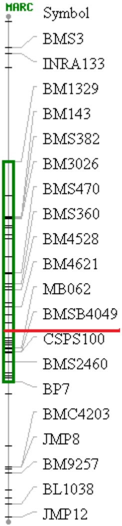




No.	Marker	Map distance (cM)	Alleles
1	BM1329	0.00	6
2	BMS2508	8.54	7
3	BMS1242	17.44	7
4	BM143	18.33	7
5	BMS518	23.57	4
6	BM4322	28.47	7
7	BMS470	32.00	4
8	ILSTS097	37.04	2
9	RM028	43.79	4
10	BM415	46.56	7
11	ILSTS035	51.87	9
12	ILSTS087	54.34	3
13	BMS2460	58.06	4
14	BP7	63.50	5

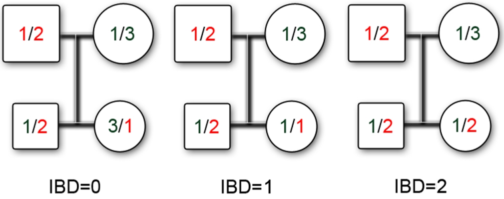
First model – α and ρ constant in time

$$y = X\beta + Z_\alpha\alpha + Z_\rho\rho + \epsilon,$$

where

- y – vector of lactation milk yields
- β – vector of fixed effects
- α – random additive polygenic effect, $\alpha \sim \mathcal{N}\left(0, A\sigma_\alpha^2\right)$
- ρ – random QTL effect, $\rho \sim \mathcal{N}\left(0, IBD\sigma_\rho^2\right)$
- ϵ – residual, $\epsilon \sim \mathcal{N}\left(0, I\sigma_\epsilon^2\right)$

Technical aspects – IBD



- Calculated using Citius ($http : //jay.au.poznan.pl/ \sim mcszyd/citius/citius.pdf$)
- Coefficient of relatedness = expected fraction of alleles shared that are IBD

$$\lambda = \frac{1}{2} P(IBD = 1) + P(IBD = 2)$$

Second model – α varies in time

$$y_{ij} = \beta + \sum_{m=0}^{k_\alpha} \alpha_{im}\phi_m(\tau_{ij}) + \rho_i + \xi_i + \epsilon_{ij},$$

where

- y_{ij} – jth test day record for individual i
- $\phi_m(\tau_{ij})$ – mth Legendre polynomial at time point τ_{ij}
- α_{im} – mth random regression coefficient for additive polygenic effect, $\alpha \sim \mathcal{N}(0, A \otimes G_\alpha)$
- ξ – random permanent environmental effect, $\xi \sim \mathcal{N}\left(0, I\sigma_\xi^2\right)$

Third model – α, ρ and ξ vary in time

$$y_{ij} = \beta + \sum_{m=0}^{k_\alpha} \alpha_{im}\phi_m(\tau_{ij}) + \sum_{m=0}^{k_\rho} \rho_{im}\phi_m(\tau_{ij}) + \sum_{m=0}^{k_\xi} \xi_{im}\phi_m(\tau_{ij}) + \epsilon_{ij},$$

where

- ρ_{im} – mth random regression coefficient for QTL effect, $\rho \sim \mathcal{N}\left(0, IBD \otimes G_\rho\right)$
- ξ_{im} – mth random regression coefficient for permanent environmental effect, $\xi \sim \mathcal{N}\left(0, I \otimes P_\xi\right)$

Likelihood

- Model 1

$$
\begin{aligned}
-2\log L &= \mathrm{const} + n\log\sigma_\epsilon^2 + \log|A| + n\log\sigma_\alpha^2 + \log|IBD| + \\
&+ n\log\sigma_\rho^2 + n\log\sigma_\xi^2 + log|C| + y^T S y
\end{aligned}
$$

Likelihood

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$$
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\end{aligned}
$$

- Model 2

$$
\begin{aligned}
-2\log L &= \text{const} + n\log\sigma_\epsilon^2 + 4\log|A| + n\log|G_\alpha| + \log|IBD| + \\
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Likelihood

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\end{aligned}
$$

- Model 3

$$
\begin{aligned}
-2\log L &= \text{const} + n\log\sigma_\epsilon^2 + 4\log|A| + n\log|G_\alpha| + 4\log|IBD| + \\
&+ n\log|G_\rho| + n\log|G_\xi| + log|C| + y^T S y
\end{aligned}
$$

- $S = V^{-1} - V^{-1}X(X^T V^{-1} X)^{-1} X^T V^{-1}$

Technical aspects – EM

- Model 1 – Estimating 3 parameters

$$\sigma_\alpha^2,\ \sigma_\rho^2 \text{ and } \sigma_\epsilon^2$$

- Model 2 – Estimating 13 parameters

$$G_\alpha \text{ (Matrix } 4 \times 4\text{)},\ \sigma_\rho^2,\ \sigma_\xi^2 \text{ and } \sigma_\epsilon^2$$

- Model 3 – Estimating 31 parameters

$$G_\alpha,\ G_\rho,\ P_\xi \text{ and } \sigma_\epsilon^2$$

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$$G_\alpha,\ G_\rho,\ P_\xi \text{ and } \sigma_\epsilon^2$$

Gaussian elimination

EM – estimators

- $$\sigma_\alpha^{2[t+1]} = \frac{\widehat{\alpha}'^{[t]} A^{-1} \widehat{\alpha}^{[t]} + tr(A^{-1} C_\alpha^{-1[t]}) \sigma_\epsilon^{2[t]}}{q}$$

- $$\sigma_\rho^{2[t+1]} = \frac{\widehat{\rho}'^{[t]} IBD^{-1} \widehat{\rho}^{[t]} + tr(IBD^{-1} C_\rho^{-1[t]}) \sigma_\epsilon^{2[t]}}{q}$$

- $$\sigma_\xi^{2[t+1]} = \frac{\widehat{\xi}'^{[t]} \widehat{\xi}^{[t]} + tr(C_\xi^{-1[t]}) \sigma_\epsilon^{2[t]}}{q}$$

EM – estimators

- $\sigma_\alpha^{2[t+1]} = \dfrac{\widehat{\alpha}'^{[t]} A^{-1} \widehat{\alpha}^{[t]} + tr(A^{-1} C_\alpha^{-1[t]}) \sigma_\epsilon^{2[t]}}{q}$
- $G_{\alpha(kl)}^{[t+1]} = \dfrac{\widehat{\alpha}_k'^{[t]} A^{-1} \widehat{\alpha}_l^{[t]} + tr(A^{-1} C_{\alpha_k \alpha_l}^{-1[t]}) \sigma_\epsilon^{2[t]}}{q}$
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- $\sigma_\xi^{2[t+1]} = \dfrac{\widehat{\xi}'^{[t]} \widehat{\xi}^{[t]} + tr(C_\xi^{-1[t]}) \sigma_\epsilon^{2[t]}}{q}$
- $P_{\xi(kl)}^{[t+1]} = \dfrac{\widehat{\xi}_k'^{[t]} \widehat{\xi}_l^{[t]} + tr(C_{\xi_k \xi_l}^{-1[t]}) \sigma_\epsilon^{2[t]}}{q}$

EM – estimators

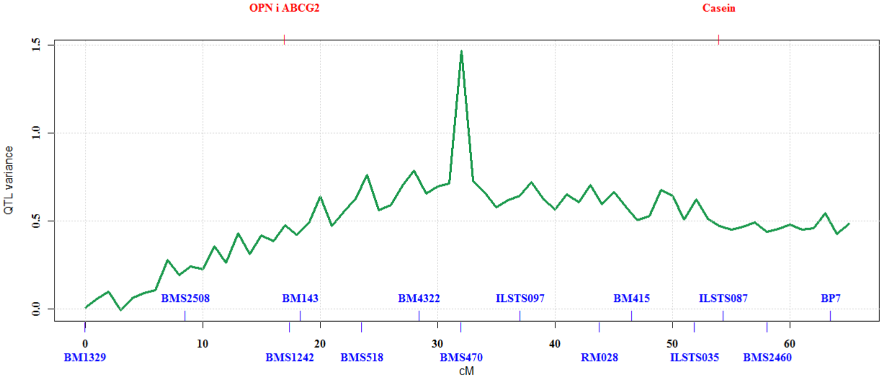
- Model 1

$$\sigma_\epsilon^{2[t+1]} = \frac{\widehat{\epsilon}'^{[t]}\widehat{\epsilon}^{[t]} + tr([X, Z_\alpha, Z_\rho]C^{-1[t]}[X, Z_\alpha, Z_\rho]')\sigma_\epsilon^{2[t]}}{n}$$

- Model 2 & 3

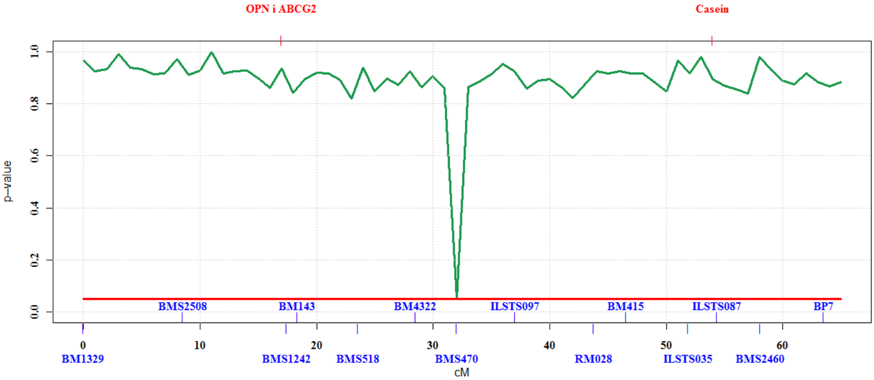
$$\sigma_\epsilon^{2[t+1]} = \frac{\widehat{\epsilon}'^{[t]}\widehat{\epsilon}^{[t]} + tr([X, Z_\alpha, Z_\rho, Z_\xi]C^{-1[t]}[X, Z_\alpha, Z_\rho, Z_\xi]')\sigma_\epsilon^{2[t]}}{n}$$

Results – Model 1

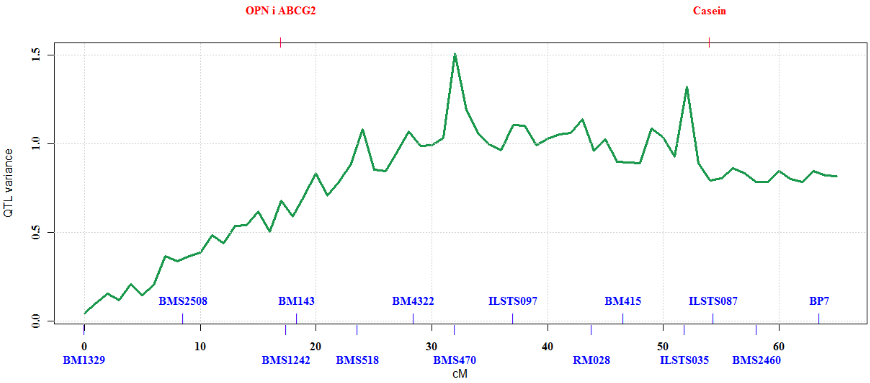


Results – Model 1

LRT $\quad H_0 : \widehat{\sigma}_q^2 = 0$ *vs.* $H_1 : \widehat{\sigma}_q^2 \neq 0$

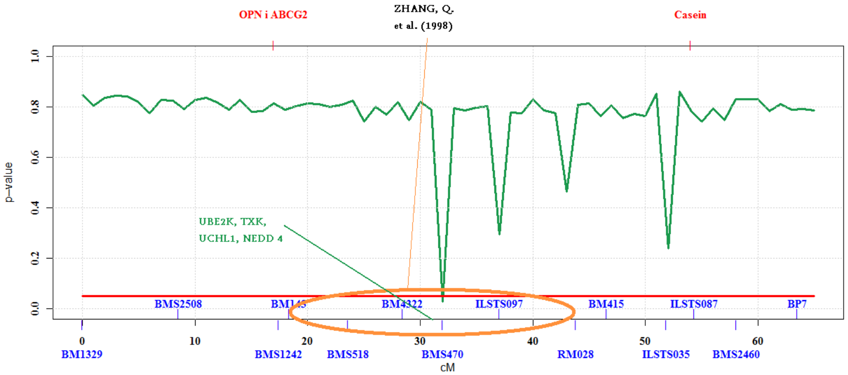


Results – Model 2



Results – Model 2

$$\text{LRT} \quad H_0 : \widehat{\sigma}_q^2 = 0 \ \textit{vs.} \ H_1 : \widehat{\sigma}_q^2 \neq 0$$



Conclusions

- QTL position for milk yield was mapped close to marker BMS470 (Model 1 & Model 2).

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- In the region near marker BMS470, QTL affecting milk yield have been reported in several previous studies (Szyda et al. 2003, Ihara et al. 2004 and Chen et al. 2006).

Conclusions

- QTL position for milk yield was mapped close to marker BMS470 (Model 1 & Model 2).

- In the region near marker BMS470, QTL affecting milk yield have been reported in several previous studies (Szyda et al. 2003, Ihara et al. 2004 and Chen et al. 2006).

- Possible position for second QTL was mapped close to marker ILSTS 087 (Model 2).

Thank You!