Investigating relationships between fertility traits in Holstein Friesian cattle using Structural Equation Modelling.

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Investigate the relationships among fertility traits in Holstein-Frisian cattle, based on a data set of 1 393 Polish Holstein-Friesian bulls.

Structural Equation Modelling (SEM) - multivariate statistical analysis technique that is used to analyze structural relationships. It is used to analyze the structural relationship between measured variables and latent constructs.

- can decompose single nucleotide polymorphism (SNP) effects on a trait into direct or indirect components

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- one of methods that allows to determine the relationship between variables
- probabilistic graphical model that represents a set of variables and their conditional dependencies via a directed acyclic graph (DAG)
- nodes - variables; path - dependencies
- two stages: structure learning, parameter learning

Data
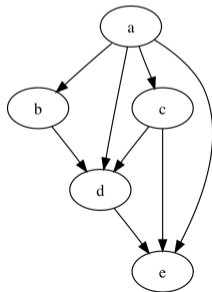
- 1 393 Polish Holstein-Friesian bulls.
- three fertility traits in the form of DRP were collected: conception rate of heifers, conception rate of cows, calving interval.
- genotyping: Illumina BovineSNP50 BeadChip Version 2
- filtration: minor allele frequency of at least 0.01, the technical quality of the chip, with a minimum call rate of 98%
- included 46 216 SNPs

Genetic parameters & Bayesian Network

Mixed model

$$y = X\beta + Z\alpha + e, \tag{1}$$

- y - trait values
- X - design matrix for β
- β - vector of fixed effects comprising a general mean
- α - vector of random additive polygenic effects
- Z - design matrix for α
- e - residuals

Bayesian Network:

- hill - climbing algorithm
- residuals from mixed model $\rightarrow$ posterior probability

Structural Equation Modeling

$$y = \Lambda y + Ws + X\beta + Xg + \epsilon \tag{2}$$

- y - vector of phenotypes
- Λ - matrix of regression coefficient obtained from learned structure of Bayesian network
- W - matrix of genotypes codes of SNP makers
- s - effect of SNP
- X - incidence matrix for β
- β - fixed effect
- Z - incidence matrix for random effect
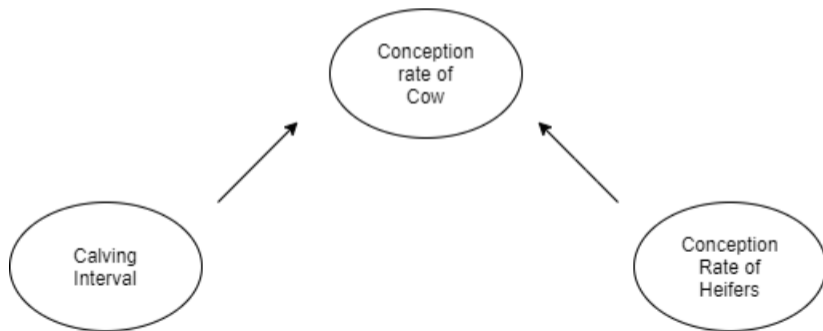- g - random effect

Annotation

- remaping to the newest genome - ARS_UCD1.2 (Remap)
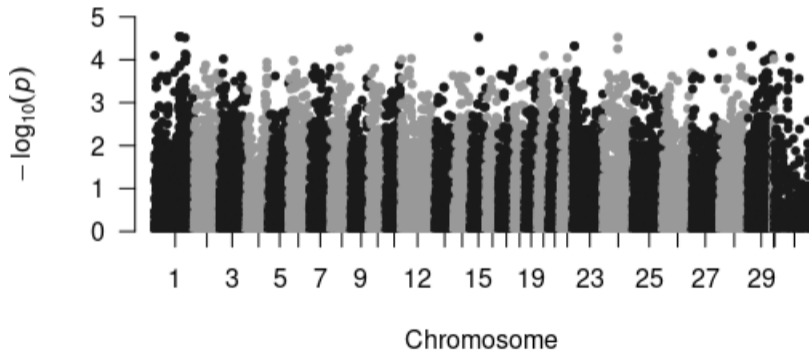- annotation to the genes - Varinat Efect Predictor

- conception rate of heifers → conception rate of cows: −0.238
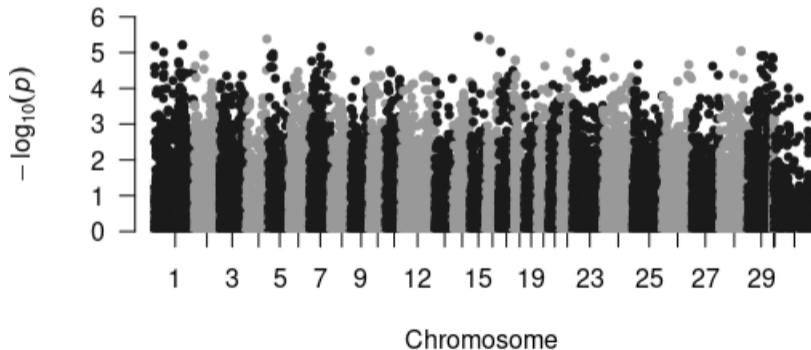- calving interval → conception rate of cows: −0.485

Manhattan plot for conception rate of heifers

Manhattan plot for calving interval

- for conception rate of heifers we didn't found any significant SNP
- for calving interval we found one SNP as significant - rs41631073 (p-value < 0.05).
  It's intergenic variant, located on chromosome 1.

Results - SEM

Gene	SNP
COL12A1	rs41610029
COL12A1	rs43583789
WDR49	rs43258719
WDR49	rs41578214
WDR49	rs43254920
WDR49	rs41968322
WDR49	rs42742620
NA	rs41642487
NA	rs42909957
NA	rs41610029

Table: Annotation for 10 most significant SNPs for Conception Rate based on nominal p-value

Gene	SNP
CFDP1	rs42201929
ROR2	rs42601532
ROR2	rs29012807
CLIC6	rs41609588
CLIC6	rs41632723
CLIC6	rs41751194
TRIM6	rs42495945
NA	rs11030464
NA	rs109715272
NA	rs41642487

Table: Annotation for 10 most significant SNPs for Calving Interval based on nominal p-value

- for Conception Rate 7 SNPs mapped to two genes: COL12A1 and WDR49
  - COL12A1: endodermal cell differentiation
  - WDR49: calcium ion binding
- for Calving Interval 7 SNPs mapped to four genes: CFDP1, ROR2, CLIC6, TRIM6
  - CFDP1: many roles during embryogenesis
  - ROR2: regulation and signalling pathways
  - CLIC6: dopamine receptor
  - TRIM6: gene and transcript regulation
- no indirect relationships were found
- influence of conception rate of heifers and calving interval on conception rate of cows is negative
- further research is needed $\rightarrow$ Include more traits and/or individuals

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THANK YOU FOR YOUR ATTENTION

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