UNIVERSITAS RERUM NATURALIUM WRATISLAVIENSIS

Constructing gene networks underlying traits routinely recorded in dairy cattle

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1. Motivation
2. Data
3. Gene selection
4. Gene network
5. Results
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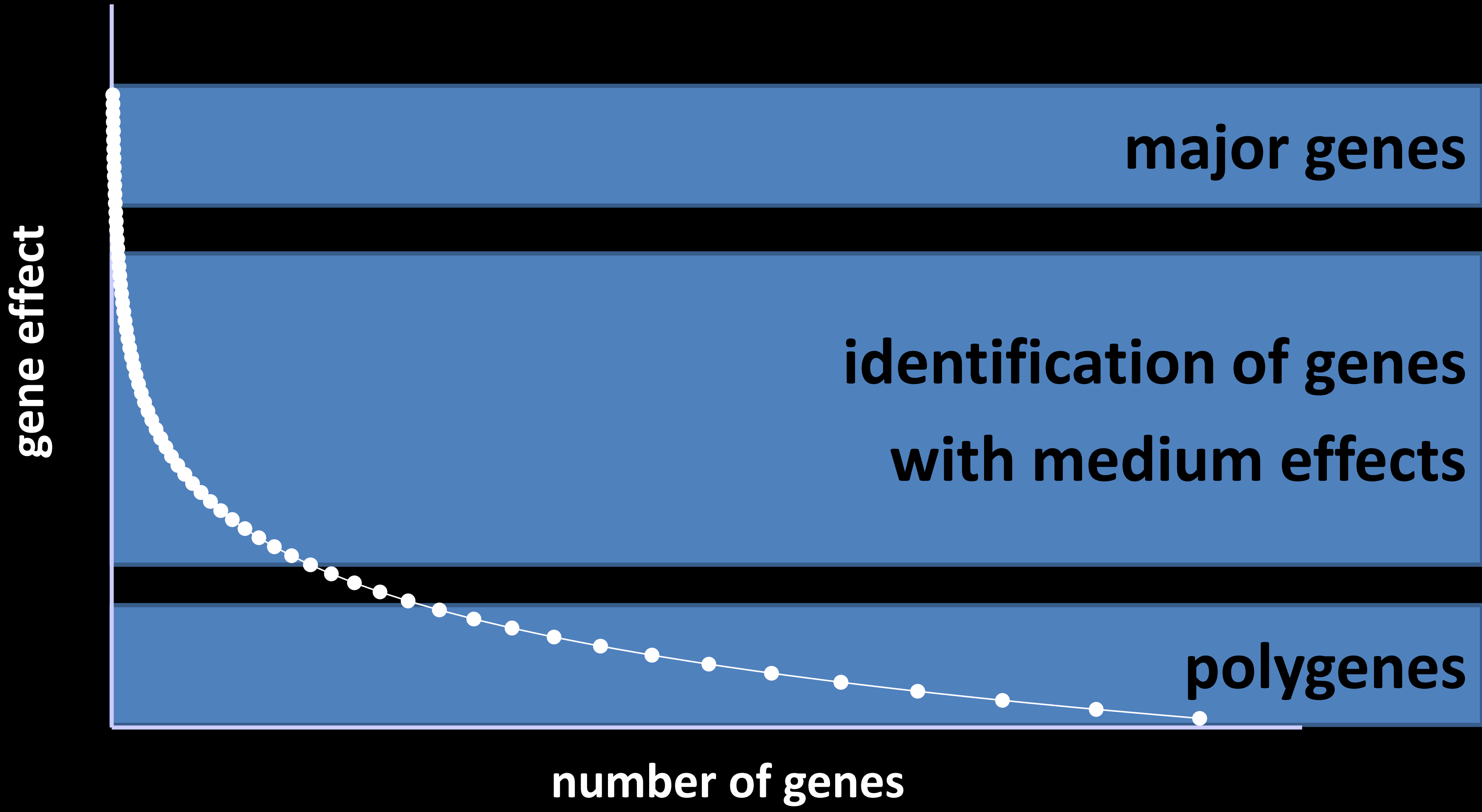
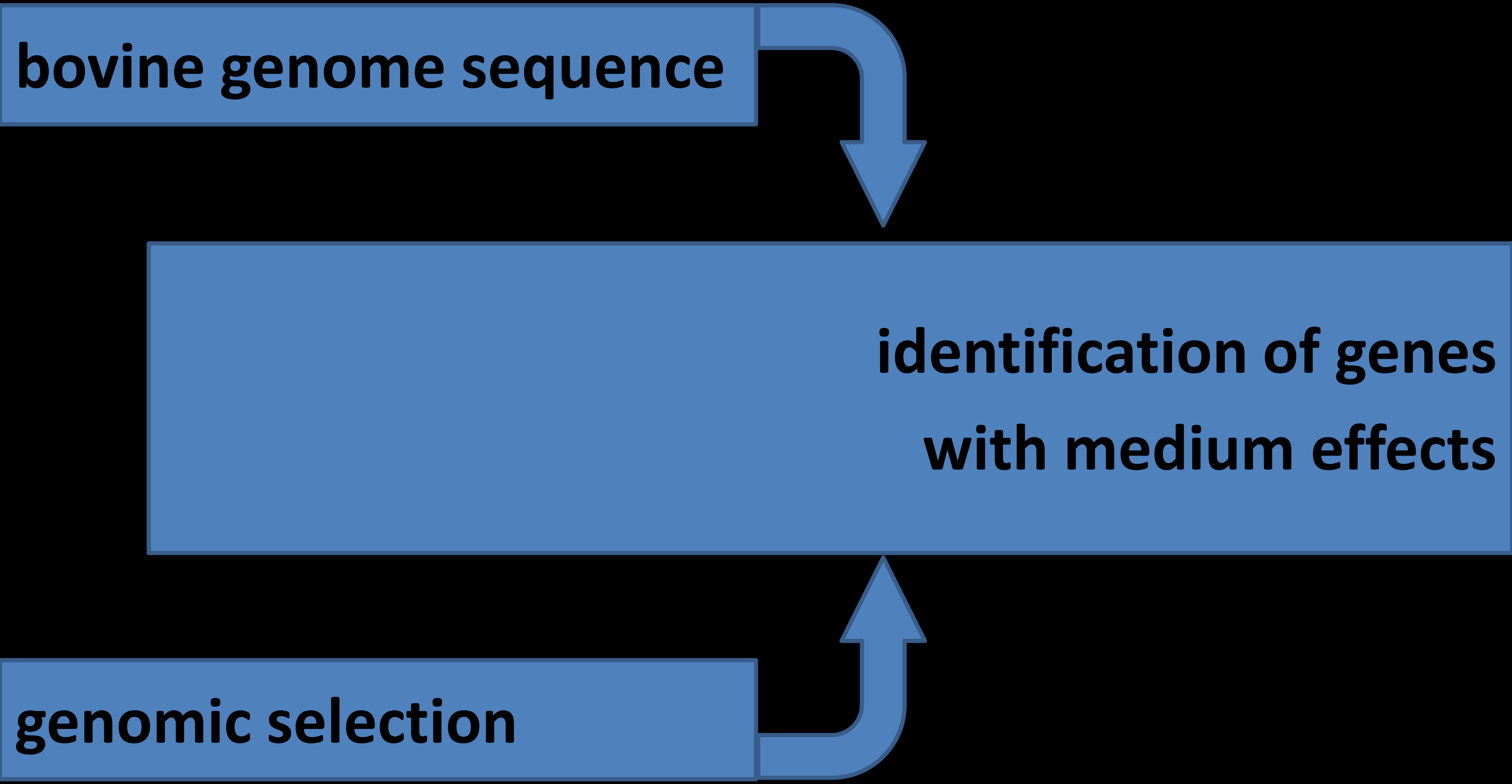
Motivation


major genes
identification of genes
with medium effects
polygenes
gene effect
number of genes

Motivation



bovine genome sequence

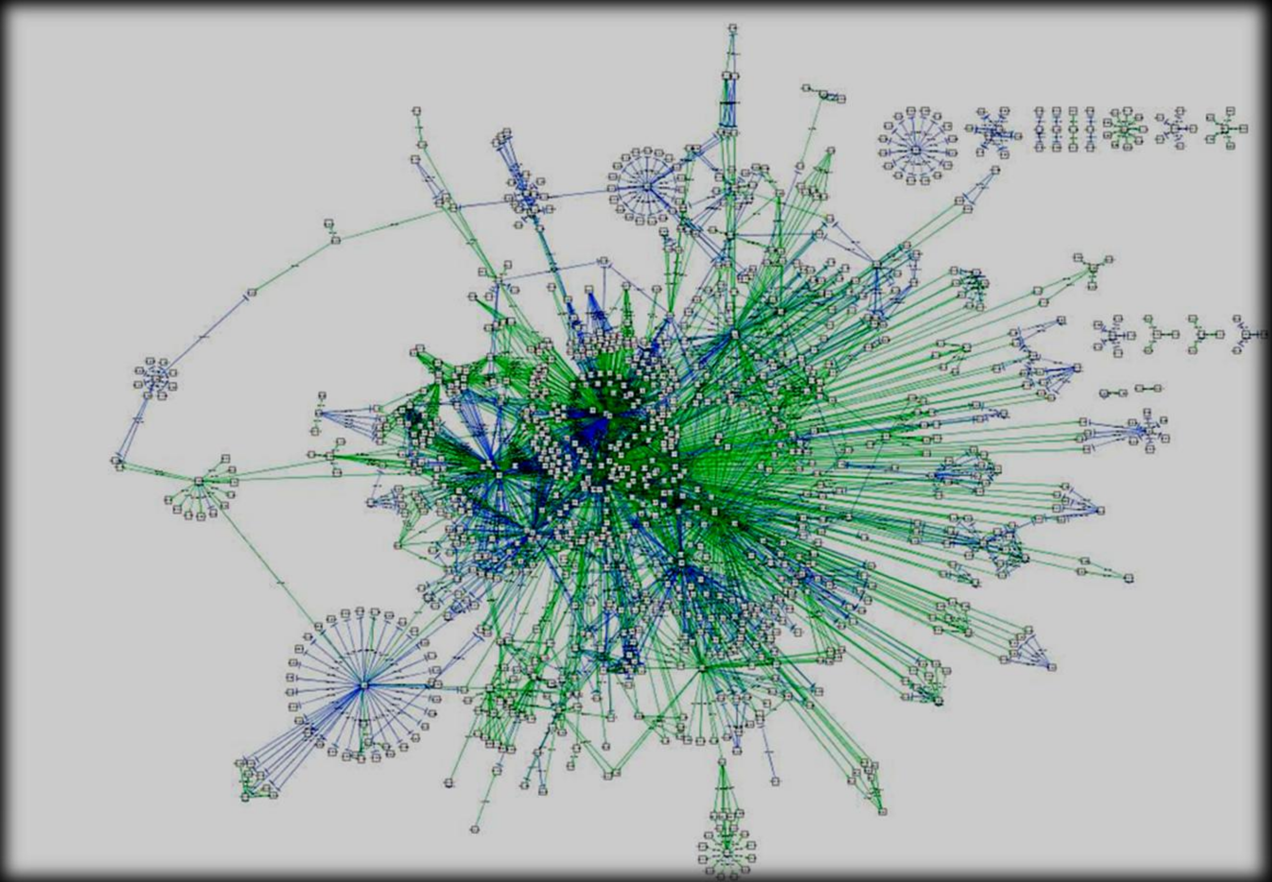
identification of genes

with medium effects

genomic selection

Motivation

gene regulatory network anchored on known genes



protein yield
fat yield

Data set

2461 HF bulls

genotypes:

Illumina 50K chip

phenotypes:

EBV for 29 traits

Gene selection procedure: 1. SNP effect estimation

$$y = \mu + Zq + e$$

- y deregressed EBV
- μ general mean
- **q SNP** $\sim N\left(0, \mathbf{I}\sigma_q^2\right)$
- Z $\in\{-1, 0, 1\}$
- e residual

❯

estimates of 46 267 additive effects of 29 traits

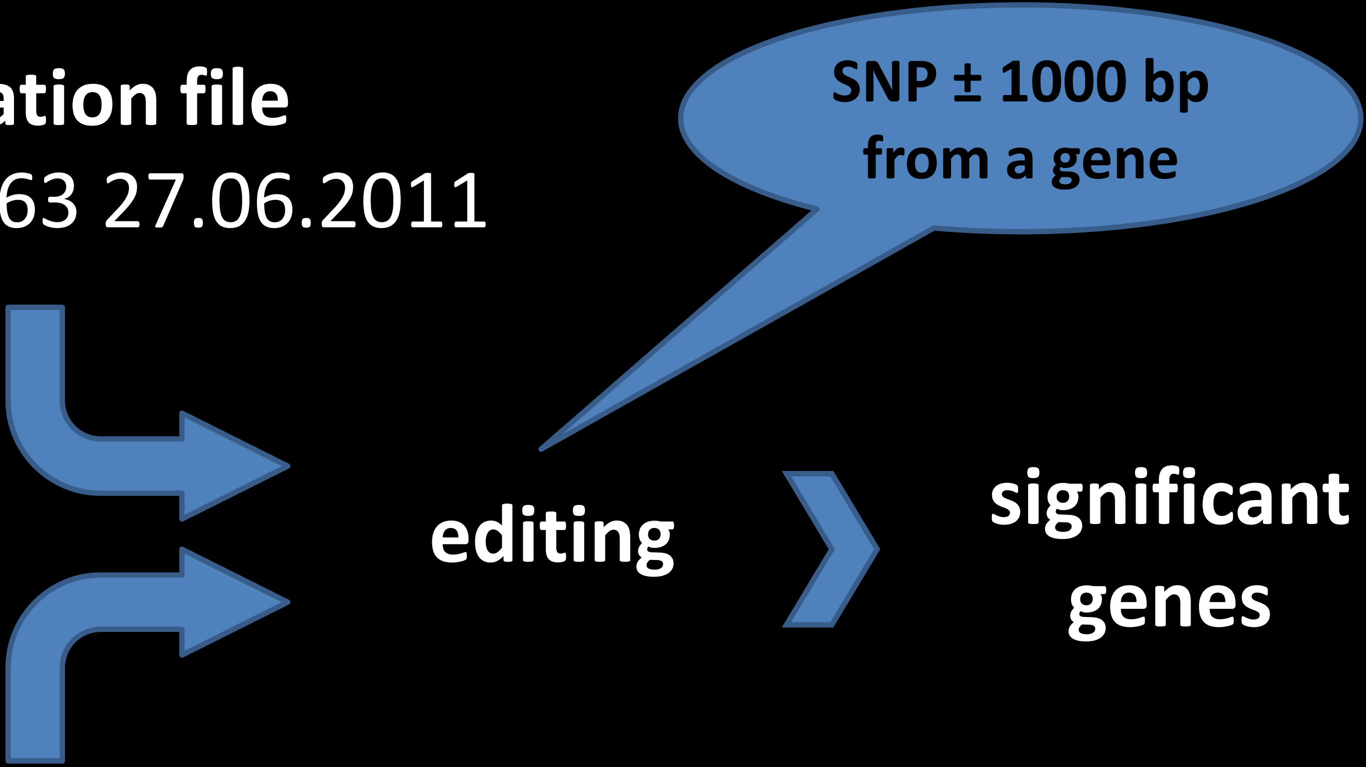
Gene selection procedure: 2. SNP selection

q SNP $\sim N\left(0, \mathbf{I}\sigma_q^2\right)$

CV for α=0.20

Bonferroni
N=46 267

Gene selection procedure: 3. SNP annotation



annotation file
ENSEMBL v. 63 27.06.2011

SNP ± 1000 bp from a gene

editing

significant genes

significant SNPs
genomic evaluation 04.2011

Gene network construction

gene list

Cytoscape

Cytoscape: An Open Source Platform for Complex Network Analysis and Visualization

Bisogenet

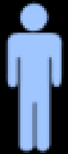
Martin et al. 2010 BMC Bioinformatics

- **NCBI**
- **UniProt**

- **KEGG pathway**
- **Gene Ontology**

- **protein interaction**
- **gene interaction**

no cattle data →



human data used

Results: protein yield

- 5 significant SNP identified
- BTA: 1, 5, 6, 25
- 2 SNPs annotated within bovine genes

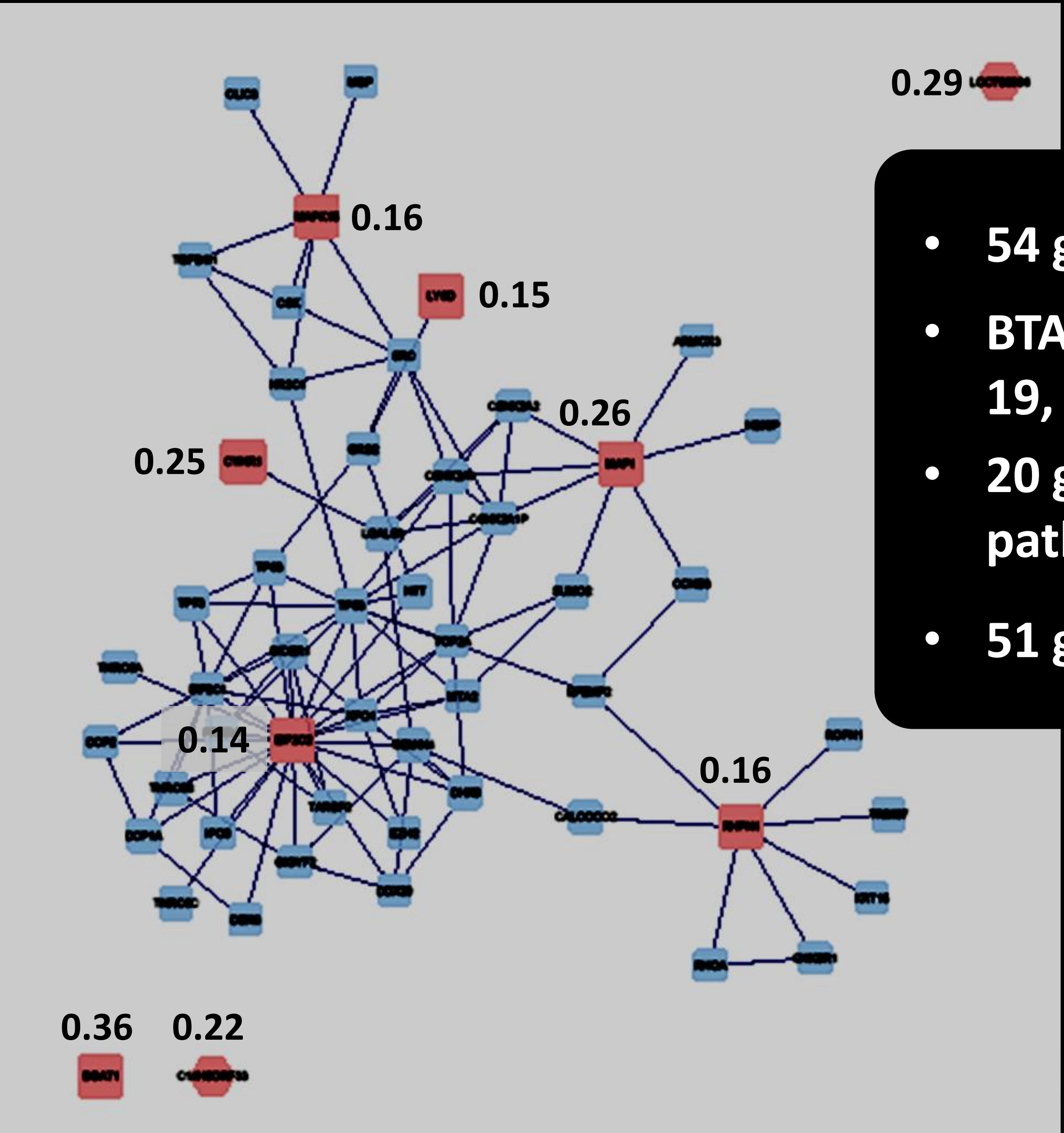
  → 1 locus unknown

  → 1 locus no interactions present

Results: fat yield

- 34 significant SNP identified
- BTA: 2, 3, 7, 14, 26
- 9 SNPs annotated within bovine genes

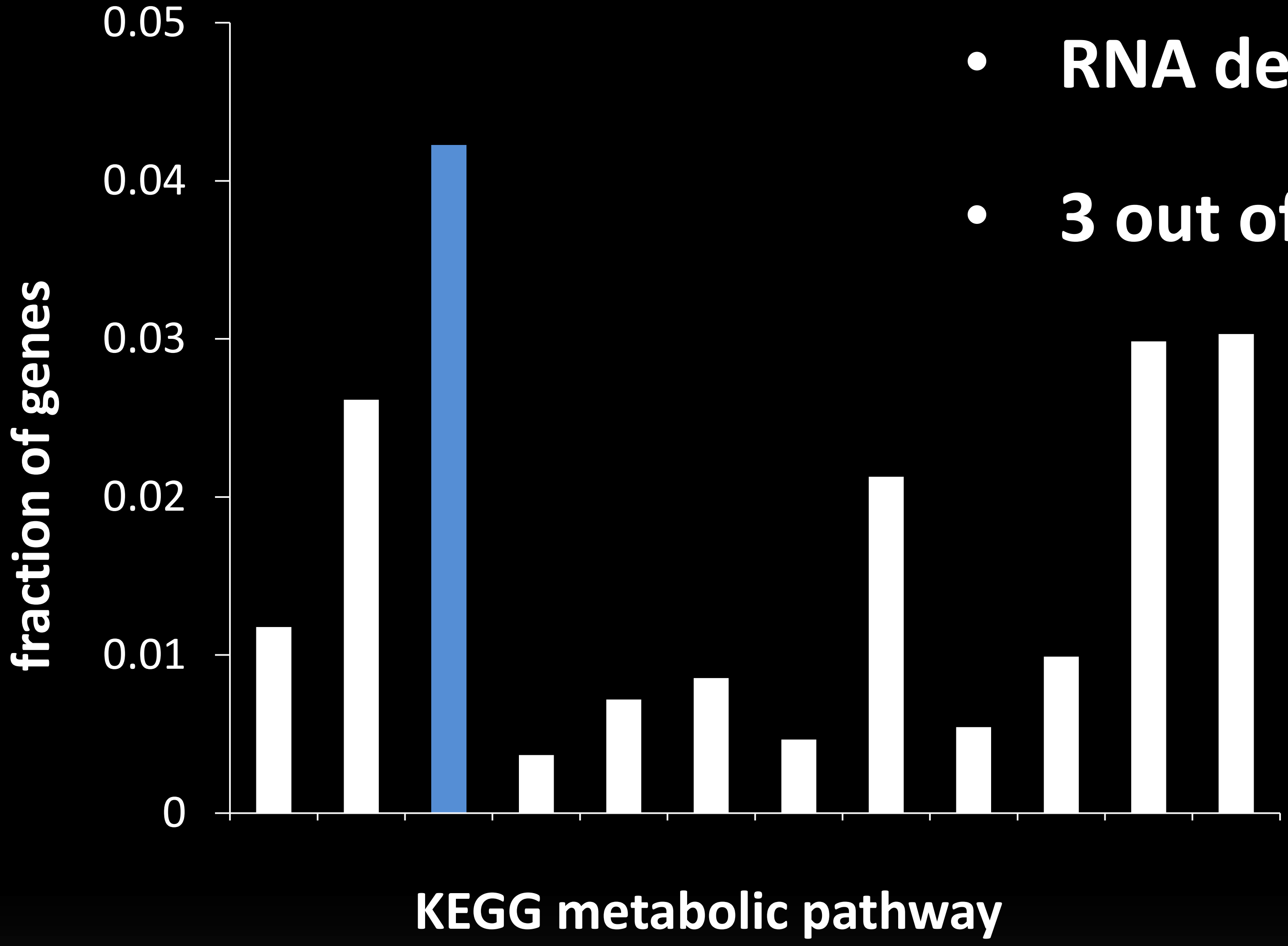
→ 2 loci unknown
→ 1 locus no interactions (DGAT1)
→ 6 loci interactions found



Results: fat yield

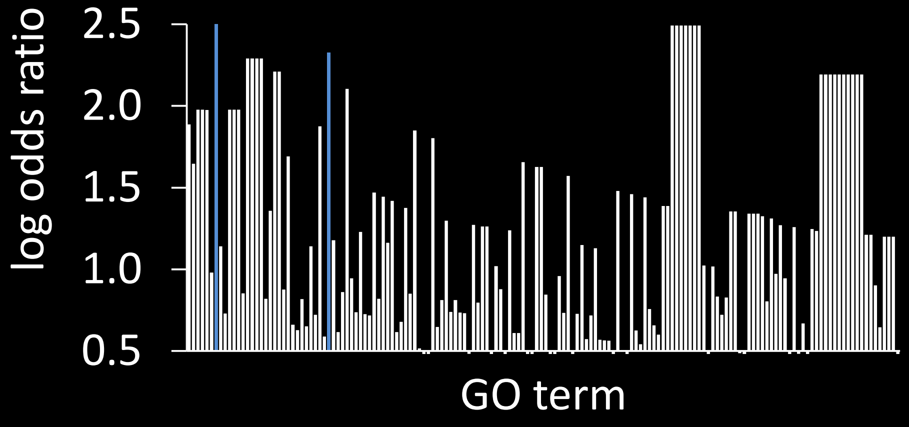
- 54 genes
- BTA: 1-7, 10-11, 13-16, 18-19, 21-25, 29
- 20 genes - metabolic pathways known
- 51 genes - GO terms known

Results: fat yield, metabolic pathways



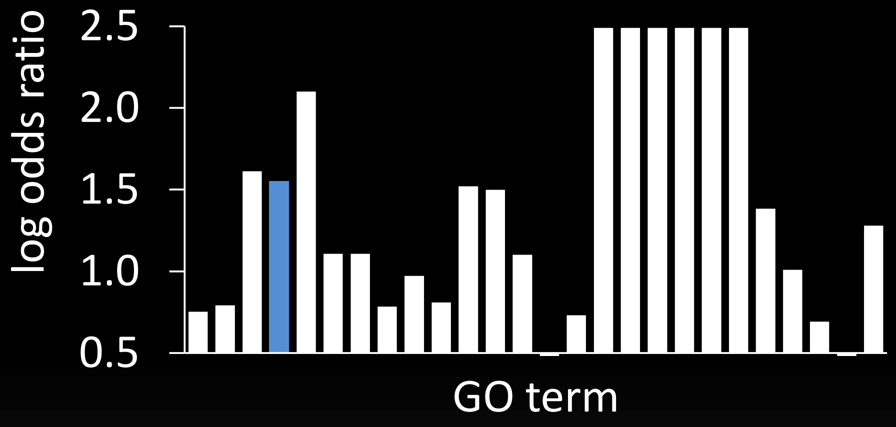
- **RNA degradation**
- **3 out of 71 genes**

Results: fat yield, gene ontology


Biological Process

- **150 GO with $P < 0.05$**
- **gene silencing**
- **8 out of 38 genes $P < 3^{-10}$**

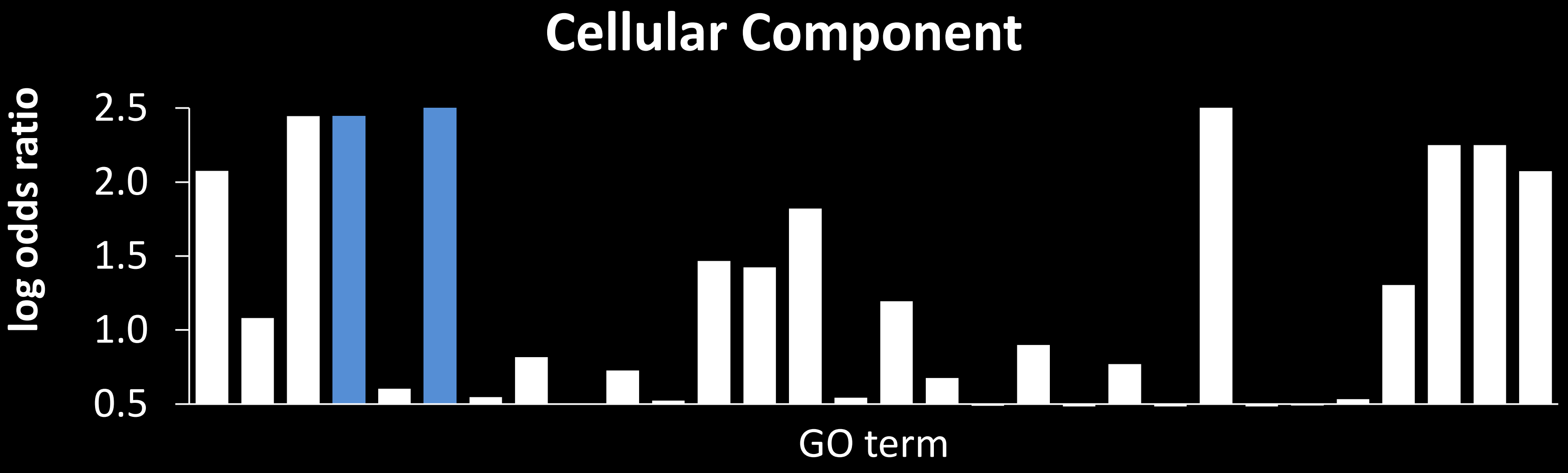
- **RNA interference**
- **3 out of 6 genes / 2 out of 4 genes**


Molecular Function

- **26 GO with $P < 0.05$**
- **protein binding**
- **44 out of 51 genes $P < 9^{-5}$**

- **small interfering RNA binding**
- **2 out of 7 genes**

Results: fat yield, gene ontology



- **29 GO with $P < 0.05$**
- **cytoplasmic mRNA processing body**
- **8 out of 38 genes $P < 5^{-11}$**

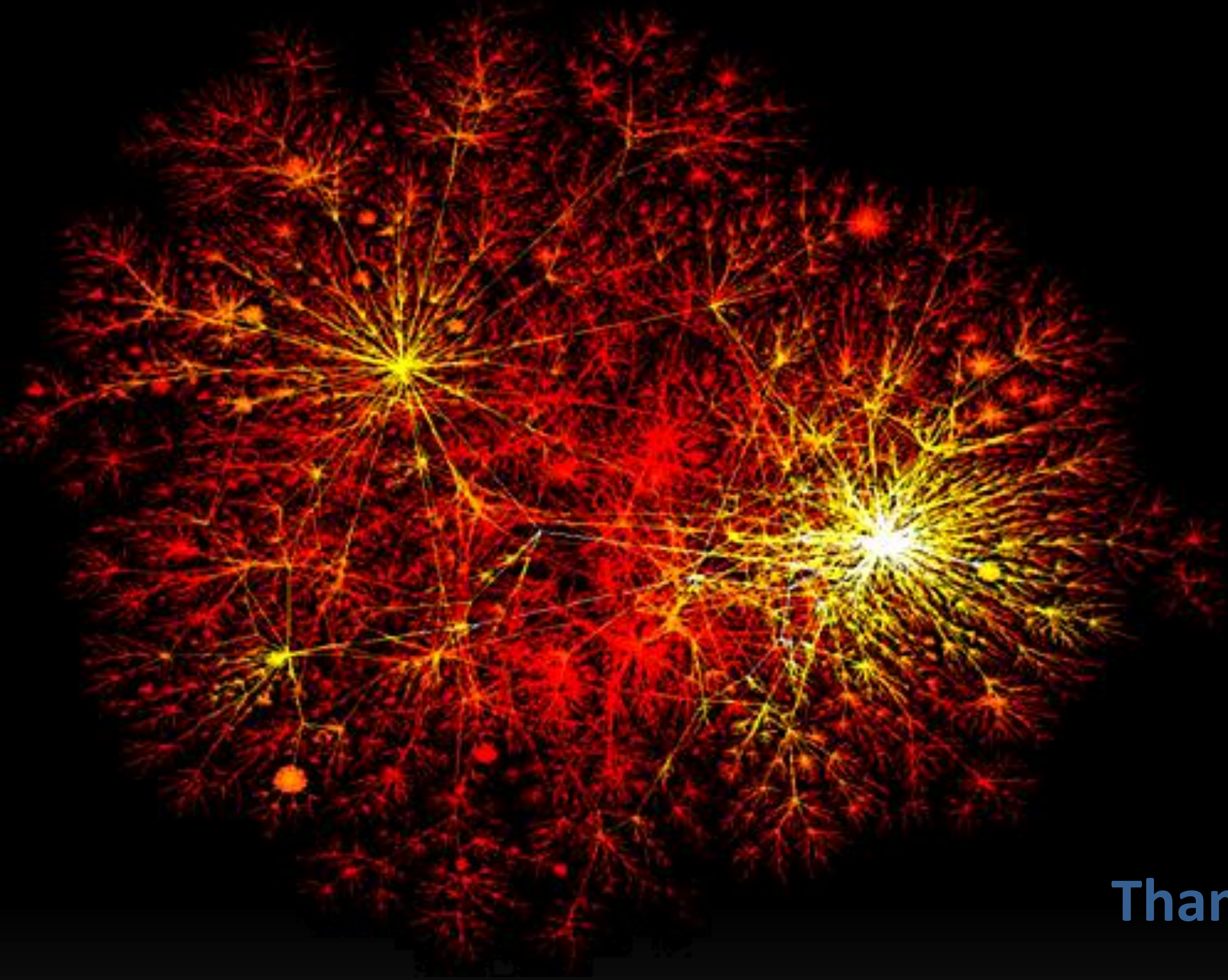
- **RNA-induced silencing complex / micro-ribonucleoprotein complex**
- **5 out of 10 genes / 2 out of 4 genes**

Conclusions

1. **Fat yield regulated by RNA genes ???**
2. **Poor resolution with 50K chip**
   - many SNPs outside genes
   - 777K better
3. **No data for *Bos taurus***

Questions

1. **SNP choice**
    - how many SNPs
    - consider LD
    - α
    - correct for multiple testing
2. **Network validation**
    - individual genotyping - expensive
    - Individual sequencing - even more expensive
    - permutation
    - replication across different (national) data sets



Thank you