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Milk metabolites and their genetic variability

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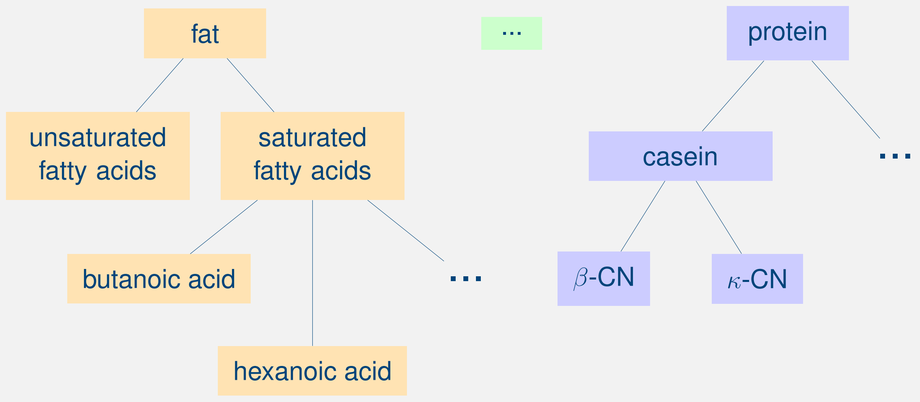
Motivation

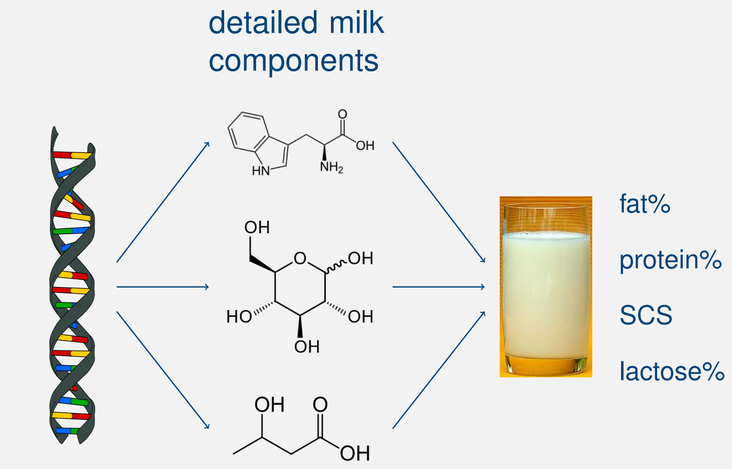


Refine division into subgroups. More than 2 000 milk components exist[1]!

Decomposition of milk into its metabolic components

- ➜ assess energy status of cow
- ➜ explore metabolic (production) diseases (e.g. ketosis, milk fever etc.)
- ➜ study heritability and mode of inheritance of novel milk traits

Two Approaches

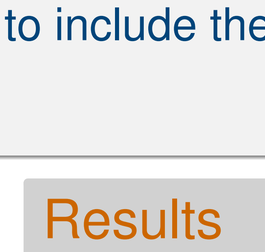


❶ genome to metabolites

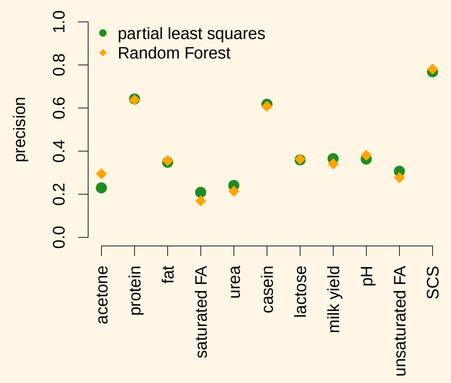
❷ metabolome to milk

Experimental Data

- milk sample of 1 295 Holstein cows
- first lactation between 21st–120th day
- half sibs (192 sires) on 18 farms
- genotypes at 37 180 SNPs
- pedigree with 23 819 animals
- 190 metabolites measured via GC-MS



Conclusions



➜ monitor some metabolites important for milk traits or diseases

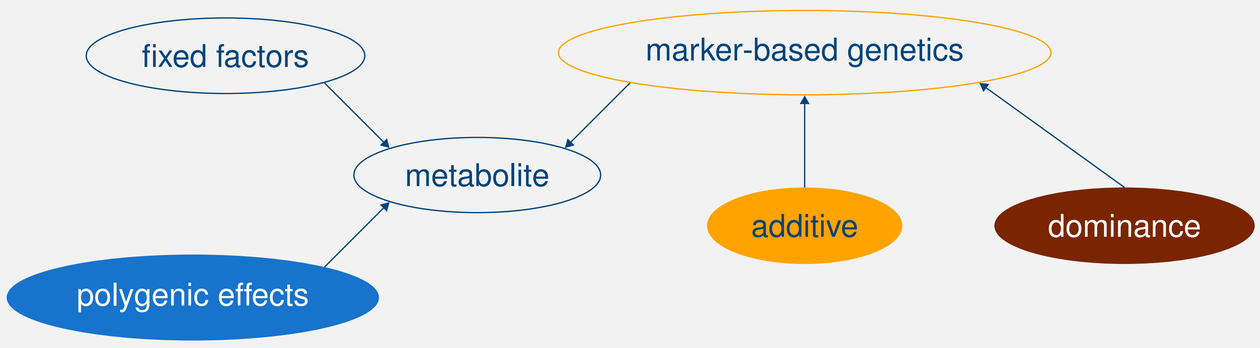
❶ GBLUP is suitable to study genetics of metabolic components

❶ small to intermediate level of inheritance, mainly due to additive genetic sources of variation

❷ Some milk traits are well predicted from metabolite profiles

➜ identify locus-specific effects on selected metabolites (see Melzer *et al.*, Session 12)

Theory



Linear mixed model (GBLUP)[2] on $\log_2$-transformed metabolite measurements with genomic (realised) and pedigree (expected) relationship was extended to include the correlation of dominance deviations.

Likelihood ratio tests[3] and FDR-corrected *P*-values

H_0: $\sigma^2_p = 0$ vs. H_A: $\sigma^2_p > 0$ (polygenic)

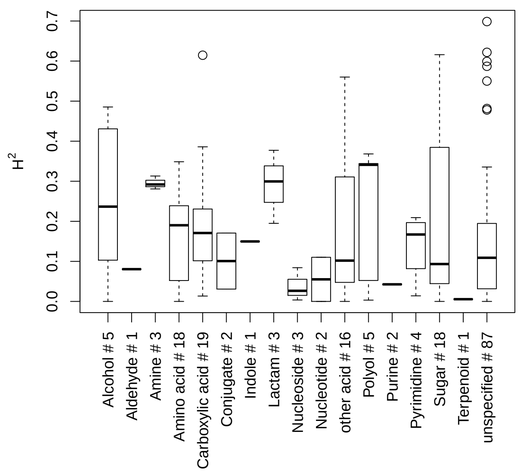
H_0: $\sigma^2_d = 0$ vs. H_A: $\sigma^2_d > 0$ (dominance)

$$RLRT \sim \tfrac{1}{2}\delta_0 + \tfrac{1}{2}\chi^2_1$$

H_0: $\sigma^2_a = 0 \wedge \sigma^2_p = 0$ vs. H_A: $\sigma^2_a > 0 \vee \sigma^2_p > 0$ (additive)

$$RLRT \sim \tfrac{1}{4}\delta_0 + \tfrac{1}{2}\chi^2_1 + \tfrac{1}{4}\chi^2_2$$

H^2 per chemical group



Results

- broad-sense heritability $0 \leq H^2 \leq 0.70$
- narrow-sense heritability $0 \leq h^2 \leq 0.57$
- 55 metabolites with significant additive genetic variation, mainly in sugars (6), amino (10) and carboxylic (6) acids
- no metabolite with significant dominance variation at 5 % level
- $\geq$ 80 % of phenotypic variation explained by GBLUP model (via leave-one-out cross-validation)

References

[1] Töpel (2004) *Behr's Verlag*
[2] VanRaden (2008) *JDS* 91:4414
[3] Self & Liang (1987) *J. Am. Stat. Assoc.* 82:605

Cooperation partners

- LKV Güstrow
- Max Planck Institute for Molecular Plant Physiology, Potsdam-Golm
- vit Verden
- Helmholtz Zentrum München