Biology-driven WGS genomic predictions for feed efficiency within and across-breeds

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BovReg
Understanding cattle genomes

EuroFAANG

Outline

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5. Investigating QTLs
6. Across-breed results
7. Usage of ATAC-seq narrow peaks
8. BayesLV models
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1. Biology-driven genomic predictions

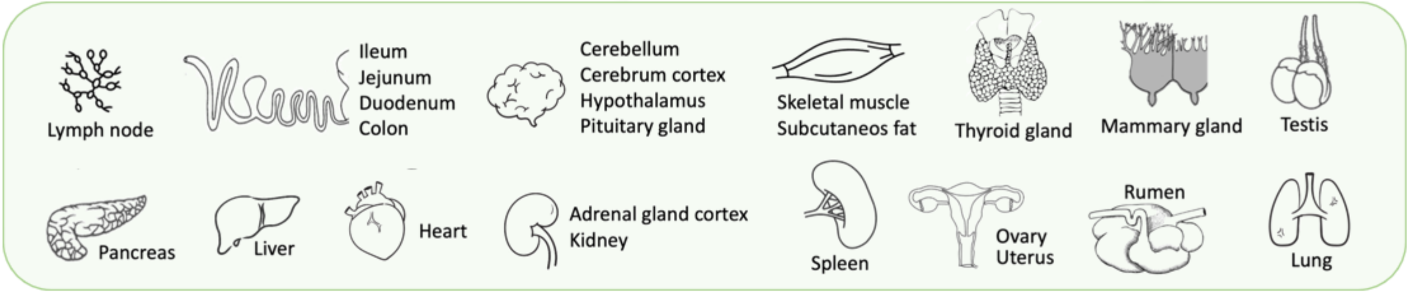
- WGS: millions of variants → pinpoint **causal variants** affecting traits of interest
- Key traits: **biological efficiency**, e.g. **feed efficiency**
- BovReg: catalogue of functionally active **genomic features (GF)** in cattle
- **Functional GF** → SNP prioritization → **Biology-driven genomic predictions**
- **AIM**: Validation of within- and across-breed **biology-driven genomic predictions** using **genomic features** for **dry matter intake (feed efficiency)**

2. Data available for genomic predictions

	NLD	**CAN**
Breed	Holstein	Beef crosses
Dependent variable	DRP on DMI	Pre-corrected DMI
n. animals DMI & geno (training - validation)	~3k (2.2k and 850)	~5.5k (4k and 1.5k)

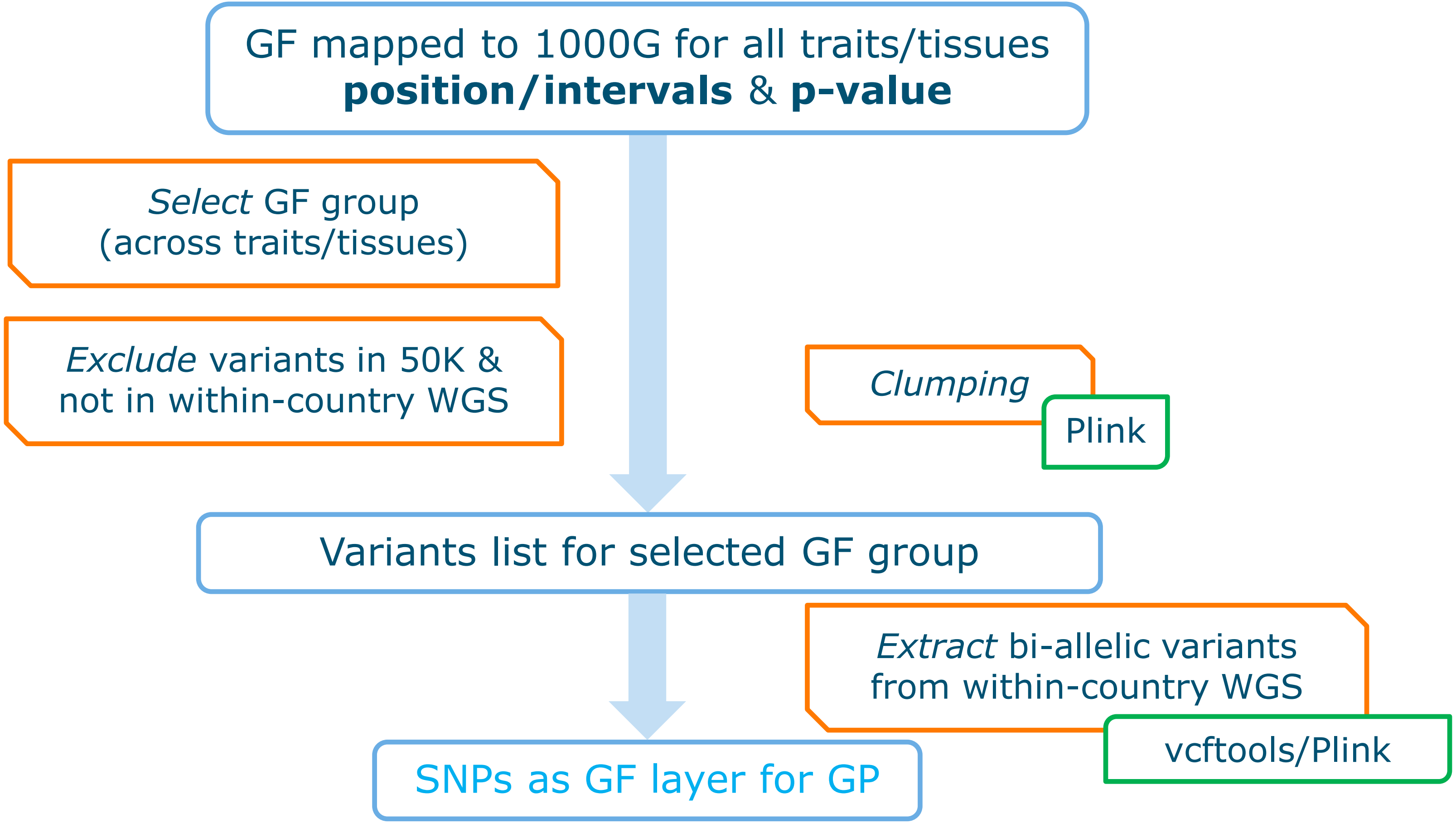
- **forward-in-time validation** (SE via bootstrapping): accuracy and bias
- 50k to imputed WGS (*Beagle*) → prioritize variants based on **GF**

2. Genomic features used

GF	Traits / Tissues
QTL (WP4)	Meat quality, Growth, Milk production, Morphology, Fertility, Health, Feed efficiency, Methane
eQTL (WP4)	(Gene, Transcript, Splice) Jejunum, Blood, Liver, Mammary Gland, Adipose, Muscle, Milk, Rumen
ATAC-seq (WP2)	

From GC Moreira et al., EAAP #939

2. Selection of genomic features



GF mapped to 1000G for all traits/tissues
position/intervals & **p-value**

Select GF group
(across traits/tissues)

Exclude variants in 50K &
not in within-country WGS

Clumping

Plink

Variants list for selected GF group

Extract bi-allelic variants
from within-country WGS

vcftools/Plink

SNPs as GF layer for GP

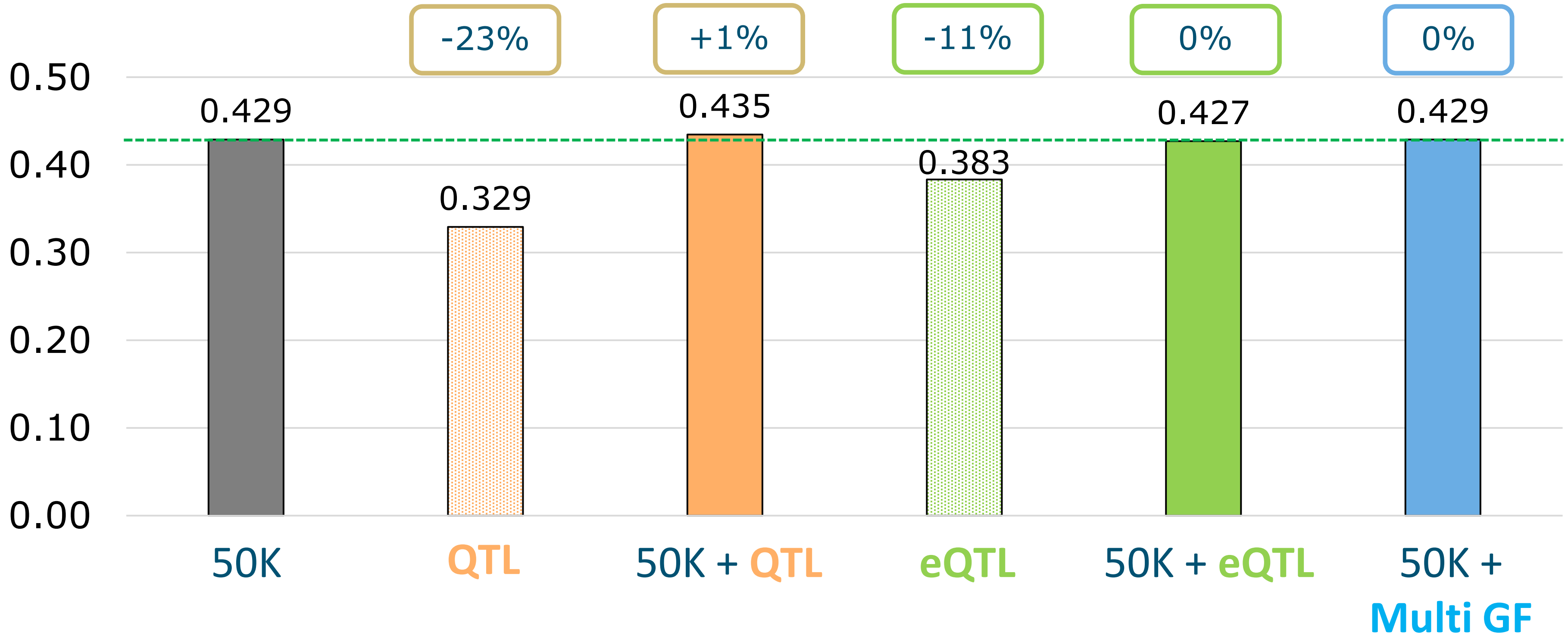
3. Scenarios and software

Scenario	**NLD**	**CAN**
50K	48K	46K
50K + **QTL**	48K + 5,416	46K + 4,222
50K + **eQTL**	48K + 12,401	46K + 11,884
50K + **(QTL, eQTL, ATAC)**	48K + 17,796	46K + 16,089

- *NextGP.jl* [1]
- Base 50K: SNPBLUP (BayesC_0) common variance across SNPs
- Additional GF layer: SNPBLUP or Bayesian (2 mixture model – no advantage)
- QTL, eQTL, ATAC → Multi-GF: overlapping GF (in NLD: 57% within ATAC), BayesRCπ (2 classes)

[1] https://github.com/datasciencetoolkit/NextGP.jl

4. Results – NLD: prediction accuracy



- SE: ±0.03
- No impact on dispersion (slope = 0.68 for 50k)

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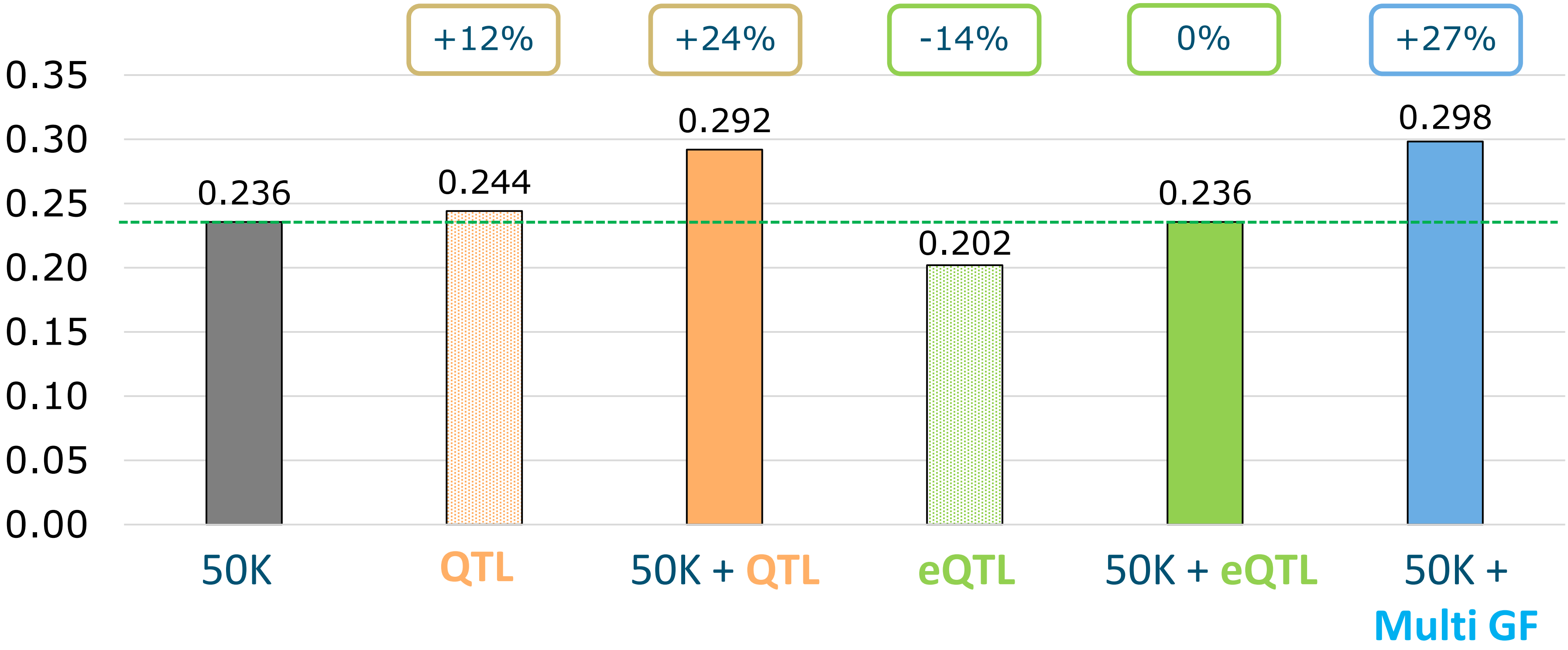
4. Results – CAN: prediction accuracy

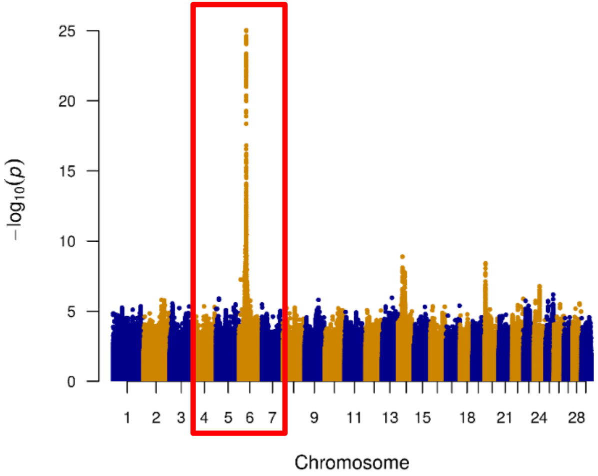


- SE between ±0.02 and ±0.03
- Similar pattern for dispersion (slope = 0.56 for 50k)

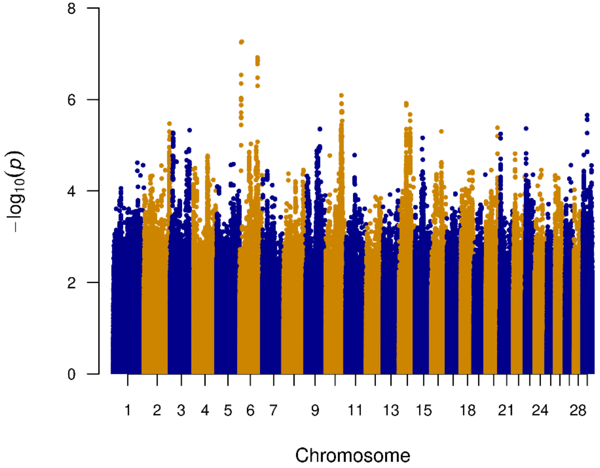
5. Investigating QTL effects in CAN

Gredler-Grandl *et al.* 2022, WCGALP

ALL
10,539 animals
Beef, Holstein, Finnish Red
~30M variants

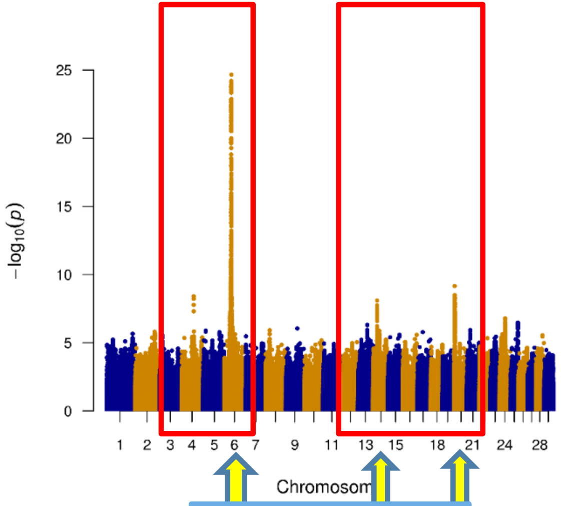


HOL
2,368 animals
Only Holstein
~20M variants



BEEF
7,805 animals
Only Beef
~28M variants

Zhang *et al*. 2020, BMC genomics

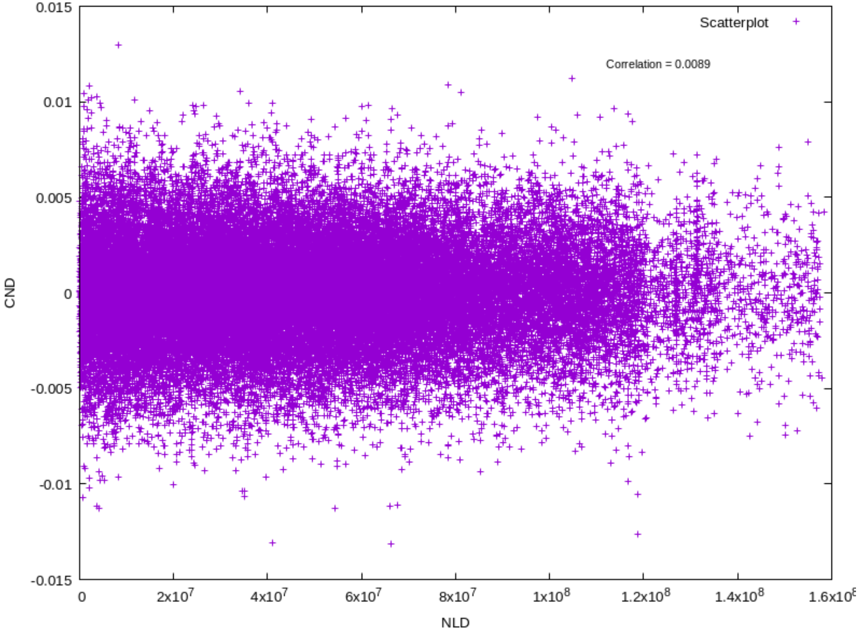


chr 6, 14, 20

🇨🇦 data → filter SNPs with $2pq\alpha^2 \geq 0.0001$

chr	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
count	1	16	6	0	19	21	0	0	1	1	2	0	0	30	6	3	2	1	2	13	0	0	0	2	1	0	1	0	1

6. Across-breed genomic predictions

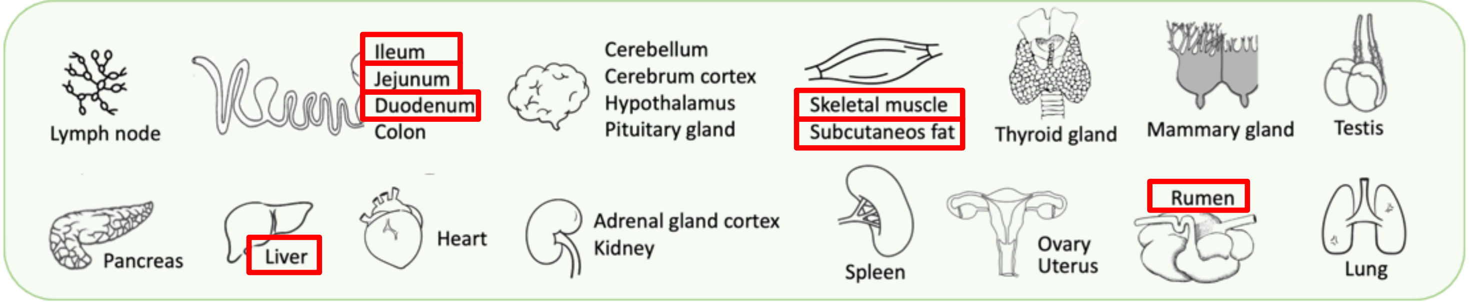


SNP effects from NLD data, prediction on CAN data

Scenario	Number of SNPs overlapped	Prediction accuracy
50K only	46K	0.00
QTL only	2,431	-0.02
eQTL only	11,505	0.00
50K + QTL	46K + 2,431	-0.02
50K + eQTL	46K + 11,505	0.00

Next: multi-breed NLD-CAN

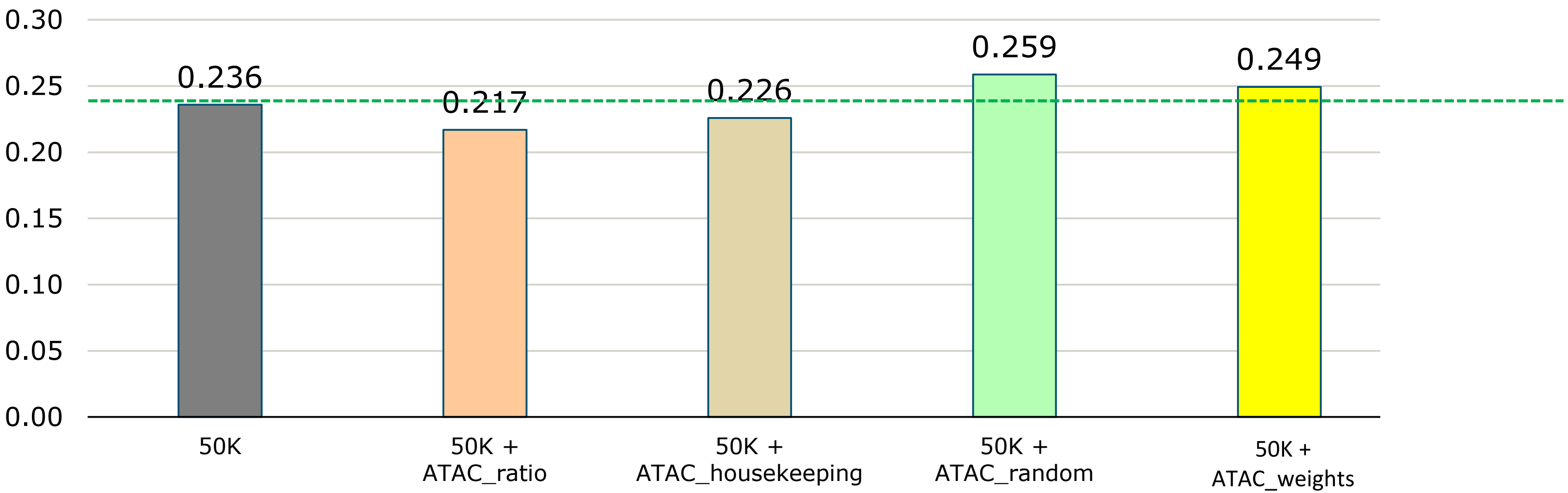
7. Use of narrow-peaks ATAC-seq



Different scenarios implemented using *ATAC-seq* narrow peaks for selected tissues

Scenario	Description	SNPs
ATAC_ratio	Top 10K variants from narrow peaks **ratio** (overlaps selected/ total tissues) **+ adjacent SNPs (200Kb)**	210,919 → 19,523 (LD pruning)
ATAC_housekeep	Top 10K variants that overlaps across all narrow peaks ("**housekeeping" set**)	10,000
ATAC_random	**Random** selection	3,318
ATAC_weights	**Higher weights on less frequent variants** (e.g., QTLs)	390

7. Narrow-peaks ATAC-seq results



- SNPBLUP models
- Randomly selected variants gave same or higher accuracy than ATAC-seq scenarios (# SNPs)
- ATAC-seq modelled as additional SNP layer → model narrow-peaks as different layers into NextGP annotation matrix

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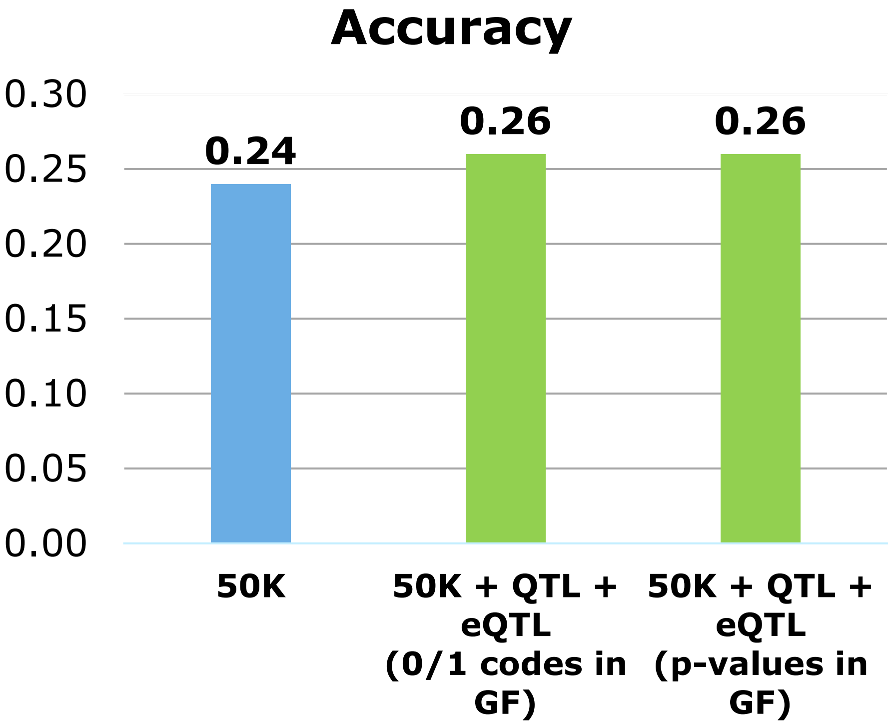
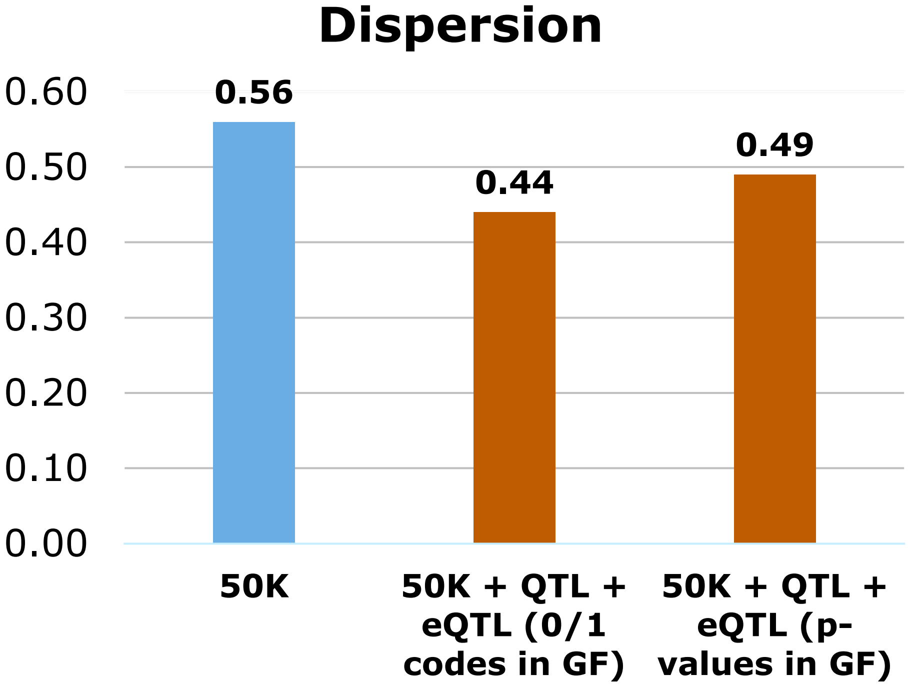
8. BayesLV (using p-value in GF layer)





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9. Conclusions

- Inclusion of **Genomic Features** could increase **genomic prediction accuracies** for **Dry Matter Intake**
- Results may vary across datasets
- No advantage using Bayesian (2 mixture model) over SNPBLUP for GF

Acknowledgments

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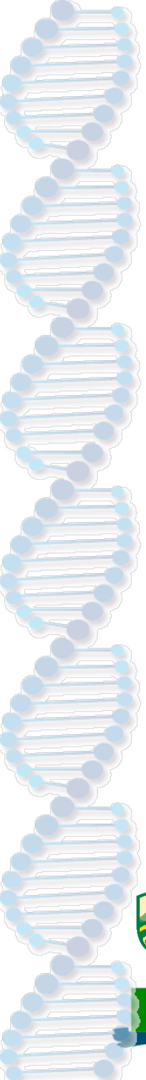

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Thank you for your attention

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