

The effect of ancestral and SNP panel genotyping on genomic inbreeding coefficients from imputed SNP in Holstein-Friesian dairy cows

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Introduction

Meyermans et al. *BMC Genomics* (2020) 21:94
https://doi.org/10.1186/s12864-020-6463-x

BMC Genomics

METHODOLOGY ARTICLE

Open Access

How to study runs of homozygosity using PLINK? A guide for analyzing medium density SNP data in livestock and pet species

R. Meyermans[†], W. Gorsen[†], N. Buys and S. Janssens[†]



Villanueva et al. *Genet Sel Evol* (2021) 53:42
https://doi.org/10.1186/s12711-021-00635-0



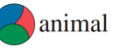
Open Access

The value of genomic relationship matrices to estimate levels of inbreeding

Beatriz Villanueva^{1*}, Almudena Fernández¹, María Saura¹, Armando Caballero², Jesús Fernández¹, Elisabeth Morales-González¹, Miguel A. Toro³ and Ricardo Pong-Wong⁴



Animal, page 1 of 11 © The Animal Consortium 2020
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Comparative evaluation of genomic inbreeding parameters in seven commercial and autochthonous pig breeds

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Caballero et al. *Genetics Selection Evolution* (2022) 54:82
https://doi.org/10.1186/s12711-022-00772-0

RESEARCH ARTICLE



A comparison of marker-based estimators of inbreeding and inbreeding depression

Armando Caballero^{1*}, Almudena Fernández², Beatriz Villanueva² and Miguel A. Toro³



Open Access

RESEARCH

Detecting inbreeding depression for reproductive traits in Iberian pigs using genome-wide data

María Saura^{1*}, Almudena Fernández², Luis Varona², Ana I Fernández², María Angeles R de Cara³, Carmen Barragán¹ and Beatriz Villanueva¹

Detection and quantification of inbreeding depression for complex traits from SNP data

Loic Yengo^{a,1}, Zhihong Zhu^a, Naomi R. Wray^{a,b}, Bruce S. Weir^c, Jian Yang^{a,b}, Matthew R. Robinson^{a,d}, and Peter M. Visscher^{a,b,1}

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Genomic inbreeding debate

Management of Genetic Diversity in the Era of Genomics

Theo H. E. Meuwissen^{1*}, John A. Woolliams¹, Anna K. Sonesson¹, Gebreyohannes Gebregiorgis¹ and Theo Meuwissen^{1*}

Human Heredity

Inbreeding Coefficient Estimation with Dense SNP Data: Comparison of Strategies and Application to HapMap III

Steven Gazal^{a,c}, Mourad Sahbatou^d, Hervé Perdry^{b,e}, Sébastien Letort^{f,g}, Emmanuelle Génin^{f,g}, Anne-Louise Leutenegger^{a,h}

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ORIGINAL RESEARCH
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Controlling Coancestry and Thereby Future Inbreeding by Optimum-Contribution Selection Using Alternative Genomic-Relationship Matrices

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Population Aspects of Consanguinity

Hum Hered 2014;77:49–62
DOI: 10.1159/000358224

Published online: July 29, 2014

Introduction

Why to study genomic inbreeding?

- ❑ Plethora of estimators (single SNP vs. continuous homozygous blocks)
- ❑ Plethora of SNP panels (LD, MD, HD)
- ❑ Variability in QC of SNP data (i.e., different data filtering)
- ❑ Simulation studies and/or with few genotyped data

Real case scenario in breeding programs: **SNP imputation**

Depends upon:

- ❑ The relationship between the core animals genotyped in HD and those to be imputed from LD/MD to HD
- ❑ The distribution along the genome and the number of SNP in the LD/MD panels
- ❑ The linkage disequilibrium between SNP in the LD/MD and SNP in the HD

Introduction

Research on **genomic inbreeding coefficients** using **imputation SNP** (i.e., genotyped + imputed)

Compare SNP genomic inbreeding coefficients (f_{SNP}):

1. Different estimators
2. SNP panels used to genotype cows

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<https://doi.org/10.3168/jds.2021-21125>

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Genomic inbreeding coefficients using imputed genotypes: Assessing different estimators in Holstein-Friesian dairy cows

Christos Dadousis,^{1*} Michela Ablondi,¹ Claudio Cipolat-Gotet,¹ Jan-Thijs van Kaam,² Maurizio Marusi,² Martino Cassandro,^{2,3} Alberto Sabbioni,¹ and Andrea Summer¹

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Genomic inbreeding coefficients using imputed genotypes: assessing differences among SNP panels in Holstein-Friesian dairy cows

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Objective

Investigate the **effect of ancestral genotyping** (and the **interaction with SNP panel**) used to genotype the cow for **estimating SNP inbreeding coefficients** derived after **SNP imputation** in Holstein cows

Material and Methods



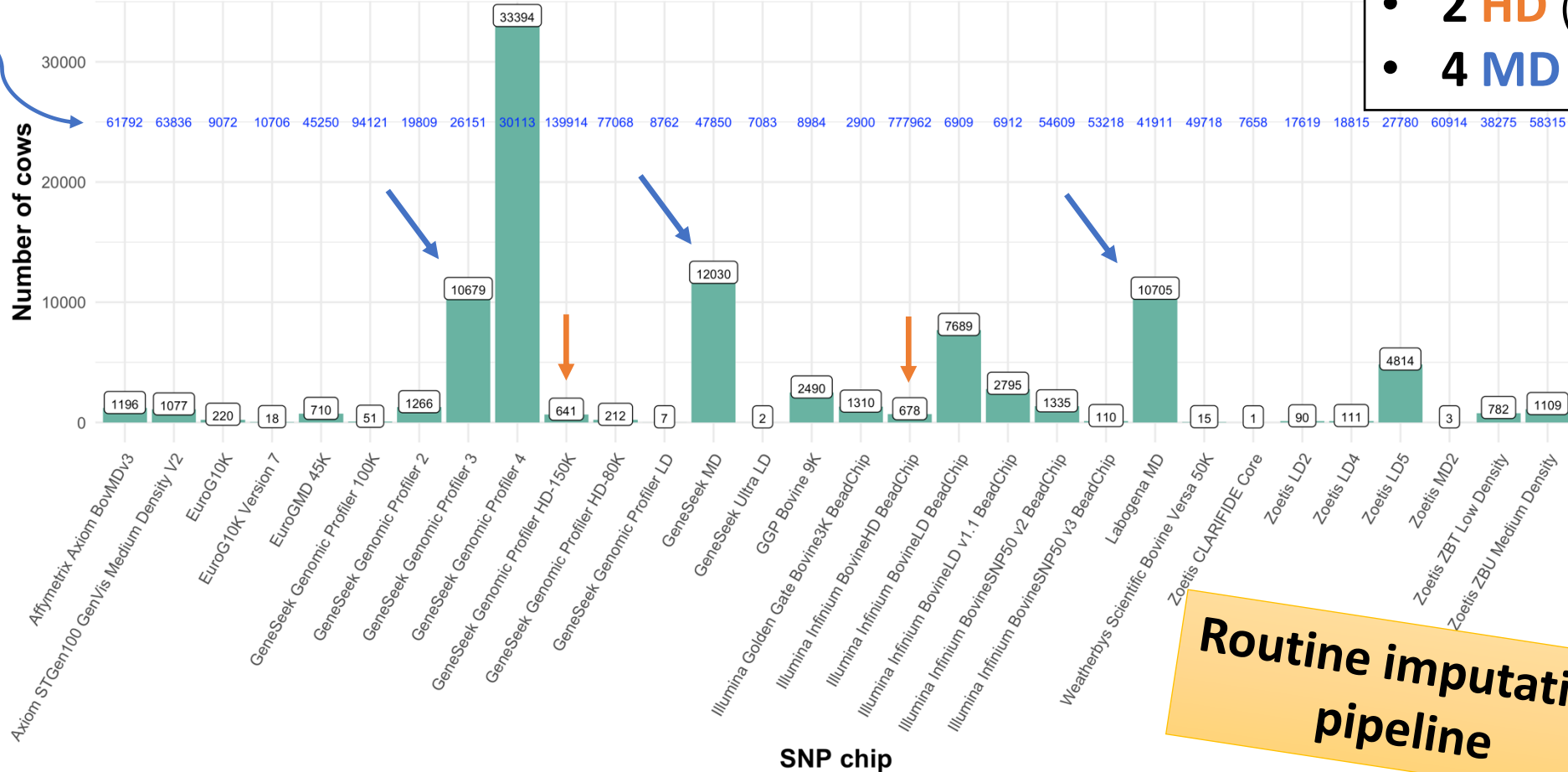
68,127 cows

84,445 imputation SNP

6 SNP panels

SNP/panel

- Select:
- 2 HD (~600 cows)
 - 4 MD (~10-30k cows)



Routine imputation pipeline

Material and Methods

Estimators:

- GRM
 - VanRaden (method 1 & 3; Fgrm & Fgrm2, respectively)
- F *plink* (plink imports the algorithms from GCTA)
 - F method of moments based on observed and expected autosomal homozygous genotype counts for each sample $[(\text{obs.hom.count} - \text{exp.count}) / (\text{total obs} - \text{exp.count})]$
 - F_{hat1} (usual variance-standardized relationship minus 1, VanRadens' 2nd) (--het flag)
 - F_{hat2} ($\cong F$)
 - F_{hat3} (based on the correlation between uniting gametes)
- FROH (consecutiveRUNS.run, *detectRUNS*, R)
 - ROH definition: minSNP = 20, maxGap = 10^6 , minLengthBps = 10^6 , maxOppRun = 1, maxMissRun = 1

Allelic frequency dependent

Allelic frequency independent
Regressed on Fped

(--ibc flag)

Cow ancestral genotype information

- Sire, dam, maternal grandsire
- G: genotyped, N: not genotyped, M: missing information

Metrics comparing genotyped vs. imputation f_{SNP} :

- Pearson and spearman correlations
- Regression coefficients

Confusion of nomenclature in the literature...

Villanueva *et al.*, 2021
PMID: 33933002
Caballero *et al.*, 2022
PMID: 36575379

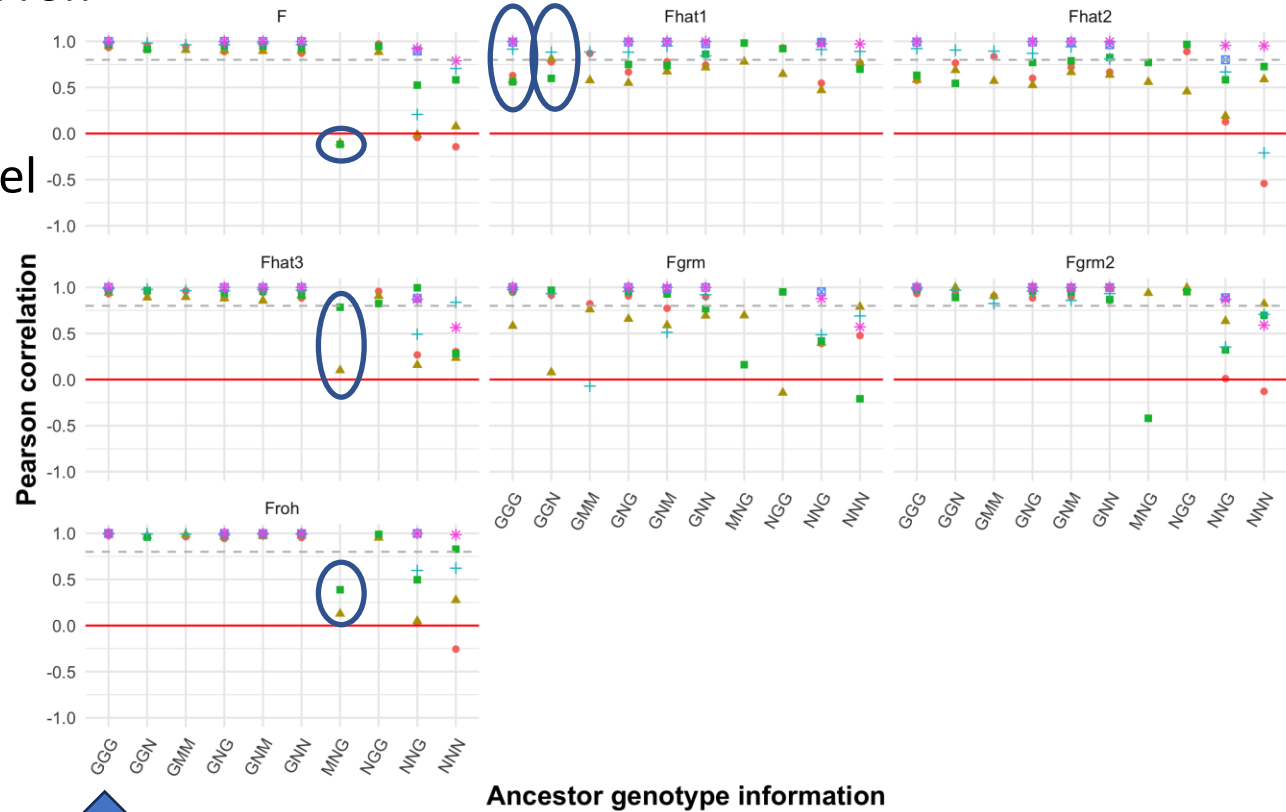
Table 1 Summary of the names given to different genomic inbreeding coefficients in the literature

Nomenclature used in this paper	Nomenclature used in the literature	References
F_{NEJ}	F_{IH}	[19]
	F_M	[20]
	F_{MOL}	[33]
	Homozygosity	[21]
	F_{HOM}	[28, 35]
	HOM_{SNP}	[37]
	SNP-Similarity* SIM*	[29] [47]
$F_{L&H}$	F_x or F_{I1}	[11, 25, 40]
	F_{SP}	[26]
	F_{HOM}	[27, 33, 36, 41, 42, 46, 55]
	F_{EHOH}	[35]
	F_{PLINK}	[31]
	F_G	[45]
	F_{EH} L&H L&H*	[34] [22] [47]
F_{VR1}	F_{GRM}	[19, 41]
	F_{GRM1}	[35]
	F_{VR}	[34]
	F_G	[17]
	VR1*	[47]
	$\hat{\rho}_{hat1}, F^I$	[18, 42, 54]
F_{VR2}	F_{GRM}	[27, 33]
	F_{GRM2}	[35]
	VR2*	[47]
	$\hat{\rho}_{hatIII}, F^{II}$	[18, 42, 54]
	F_{GR}	[11, 40]
F_{YAN}	GRM_F, F_{GRM}	[21, 28, 31]
	F_{UNI}	[27, 35, 36, 41, 55]
	F_{grm}	[31]
	SNP-Yang*	[29]
	YAN*	[47]

*Self-relationship or self-coancestry

Results and Discussion

- Similar patterns for F, Fhat3, Fgrm2 and Froh
- Robust results for F, Fhat3, Fgrm2 and Froh
- At least one genotyped parent needed for F, Fhat3, Fgrm2 and Froh
- Effect of ancestral genotype – SNP panel interaction on Fhat1-2, and Fgrm

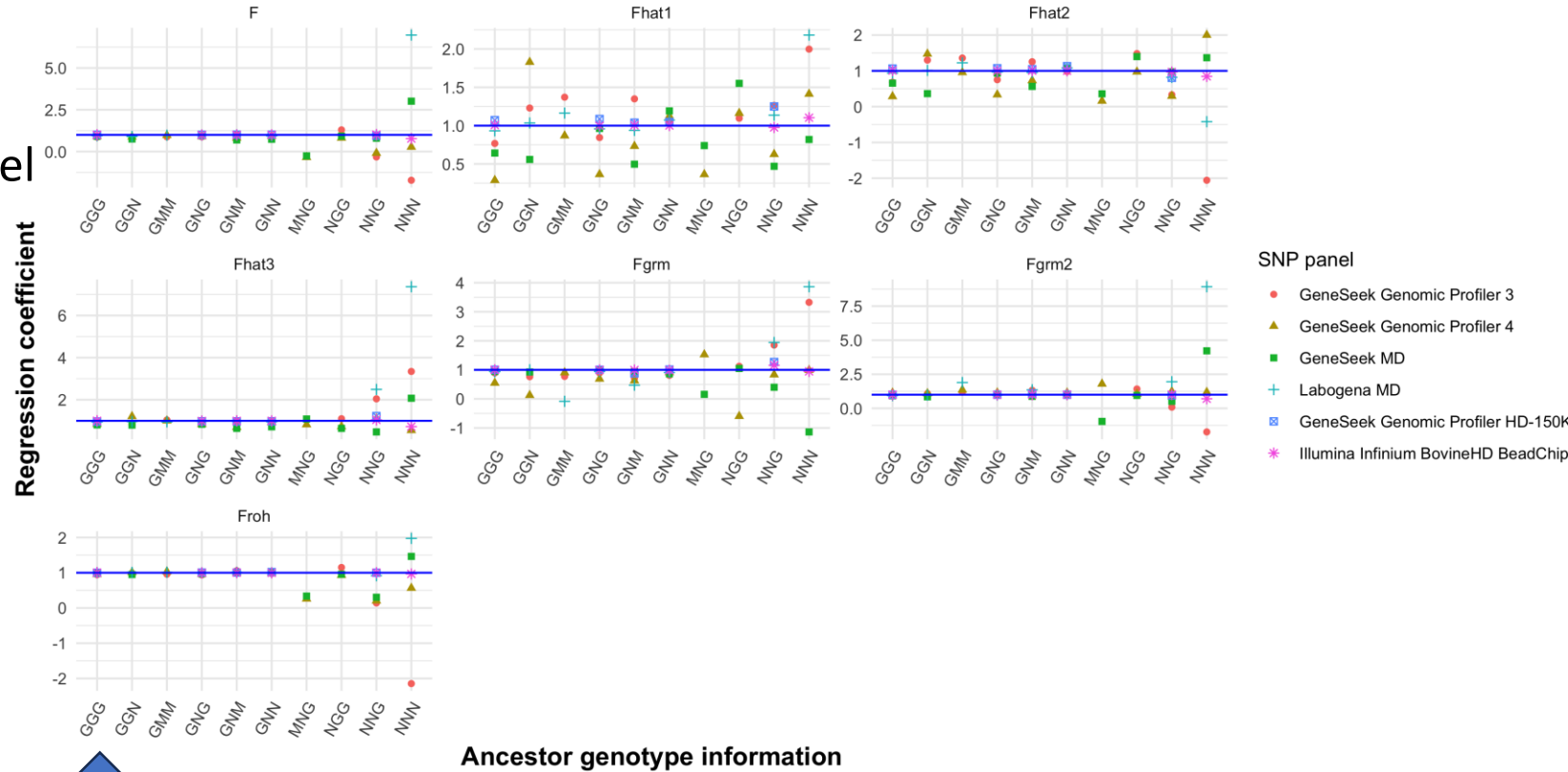


- Sire, dam, maternal grandsire
- G: genotyped, N: not genotyped, M: missing information

- Red horizontal line was set to zero.
- - Dashed grey horizontal line was set to 0.8.

Results and Discussion

- Similar patterns for F, Fhat3, Fgrm2 and Froh
- Robust results for F, Fhat3, Fgrm2 and Froh
- At least one genotyped parent needed for F, Fhat3, Fgrm2 and Froh
- Effect of ancestral genotype – SNP panel interaction on Fhat1-2, and Fgrm
- Depending upon SNP panel, there can be inflation or deflation of f_{SNP}



- Sire, dam, maternal grandsire
- G: genotyped, N: not genotyped, M: missing information

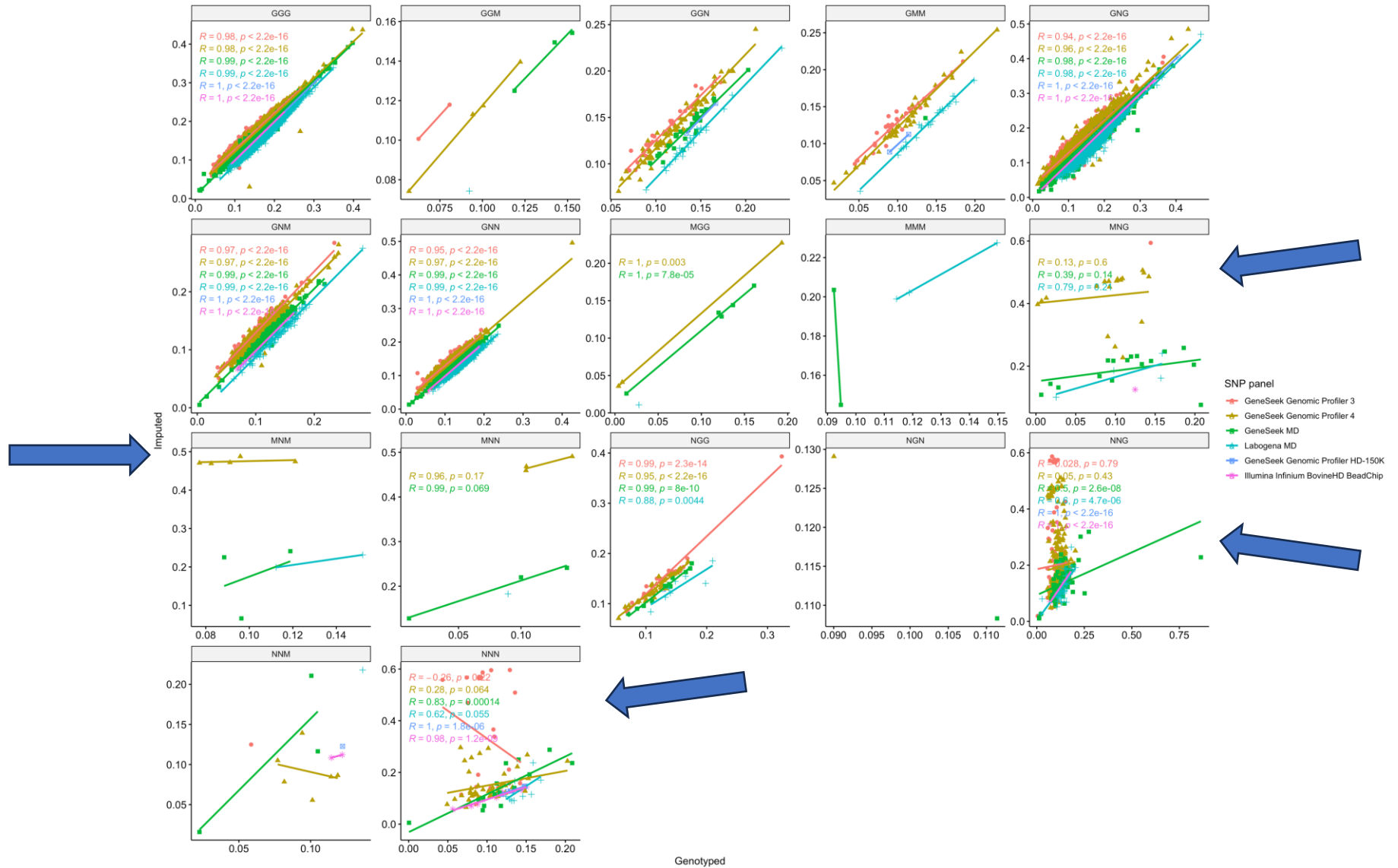


- Blue horizontal line was set to 1.

Results and Discussion

Froh genotyped vs. imputation f_{SNP}

- Inflation of imputation f_{SNP}



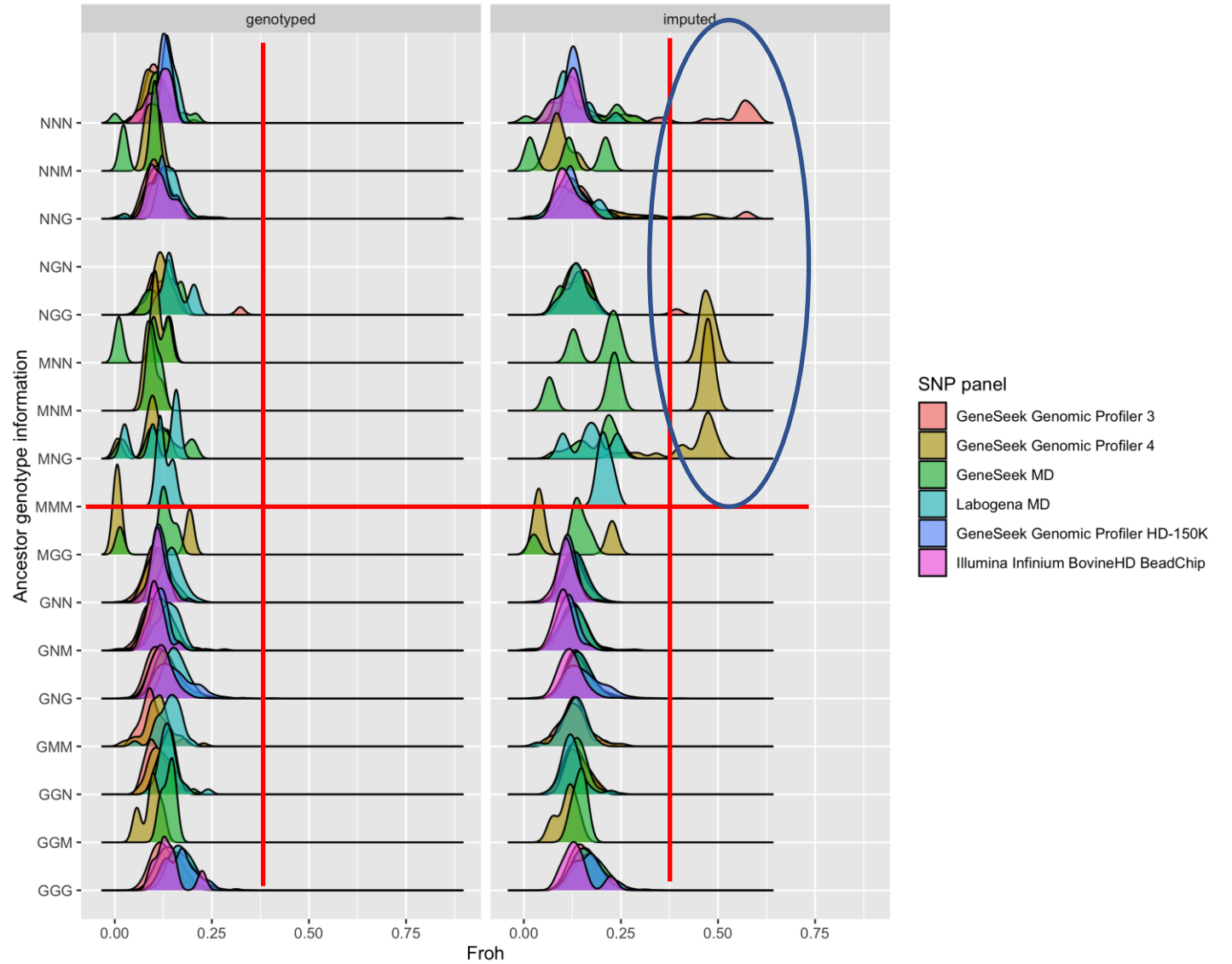
- Sire, dam, maternal grandsire
- G: genotyped, N: not genotyped, M: missing information

Results and Discussion

Froh

genotyped vs. imputation f_{SNP}

- Inflation of imputation f_{SNP}



- Sire, dam, maternal grandsire
- G: genotyped, N: not genotyped, M: missing information

Conclusion

- ❑ **FROH** was the most **robust** estimator
 - If **extreme f_{SNP}** found, check **SNP panel** of the **cow** and **ancestors** in the imputation process.
- ❑ **Fhat1-2**, and **Fgrm** are **influenced** by the **cow's SNP panel** and the **ancestral genotyping status**.
- ❑ **Downgrading HD SNP panels** to a set of carefully selected MD imputation SNP has, in general, **no effect** on f_{SNP} .
- ❑ The choice of **SNP panel for genotyping cows, parental genotyping** and **genomic inbreeding estimator** should be considered when designing imputation strategies for genomic analysis in dairy cattle

Thank you for your attention!

