animals

Supplementary Materials: Investigating the Effect of Imputed Structural Variants from Whole-Genome Sequence on Genome-Wide Association and Genomic Prediction in Dairy Cattle

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Table S1. Summary of genome coverage read depth and insert size of SV for the whole-genome sequenced animals.

Population	Sample Number	Fold Coverage			Insert Size (bp)		
		Min	Mean	Max	Min	Mean	Max
Holstein	415	2.21	11.46	44.52	250	334.3	514
Jersey	63	2.65	10.57	25.68	250	352.3	502

Table S2. Summary of SV set output.

	TWICE_SEQ	FAM_HOL	FAM_JER	POP_HOL	POP_JER
SV Counts					
Deletions	10604	4182	116	13119	2113
Insertions	164	10	0	656	0
Inversion	145	132	15	5185	571
Duplications	249	347	12	2074	334
SV covered region (Mb)					
Deletions	4.71	3.09	0.10	9.39	2.25
Insertions	0.01	0.00	0.00	0.04	0.00
Inversion	0.27	0.22	0.02	8.50	0.82
Duplications	0.38	0.29	0.03	2.05	0.38

TWICE_SEQ: SV set from twice-sequenced individuals. FAM_HOL: SV set from Holstein sire-son pairs. FAM_JER: SV set from Jersey sire-son pairs. POP_HOL: SV set from Holstein population. POP_JER: SV set from Jersey population.

Table S3. Summary of reference panel datasets used for imputation.

Reference Panel *	Number of Markers	Description
1. BovineHD (200)	632,003	SNPs and genotypes from Illumina BovineHD BeadChip
2. WGS_800K_SNP (478)	609,259	BovineHD SNP locations with genotypes from whole-genome sequence
3. WGS_SNP (478)	12,475,948	SNPs from whole-genome sequence with MAF >0.05

* Panel 1: 200 individuals which have whole-genome sequence and BovineHD BeadChip; Panel 2 and 3: 478 individuals who were whole-genome sequenced only once.

Table S4. Summary of imputation scenarios with different reference panels and variant sets.

	SV Set to be Imputed				SNP
Reference panel	TWICE_SEQ	FAM_HOL	POP_HOL	POP_JER	Randomly selected SNPs from sequencing data
Panel 1	√	√			
Panel 2	√	√	√	√	√
Panel 2 (Exclude)	√	√			
Panel 3	√	√			
Panel 3 (Exclude)	√	√			

Panel 1. SNP genotypes from Illumina BovineHD BeadChip; Panel 2. SNP locations from BovineHD and genotypes from whole-genome sequences; Panel 3. SNP genotypes from whole-genome sequences with minor allele frequency (MAF>0.05). TWICE_SEQ: SV set from twice-sequenced individuals. FAM_HOL: SV set from Holstein sire-son pairs. POP_HOL: SV set from Holstein population. POP_JER: SV set from Jersey population. Exclude represents excluding SNPs inside SV regions from the corresponding panel. The randomly selected SNPs were retrieved from Panel 3 WGS SNPs (MAF>0.05).

Table S5. Genes within ±500 kb distance of the four significant SVs.

Gene	Chr	Start	End	SV Position			Distance in KB
LMO3	Chr5	93693960	93757645	Chr5	93504218	93505234	188.726
MGST1	Chr5	93926898	93942185				421.664
LOC781988	Chr6	86676446	86713666	Chr6	87209737	87211122	-496.071
UGT2A3	Chr6	86810491	86835733				-374.004
SULT1B1	Chr6	86917971	86942950				-266.787
SULT1E1	Chr6	87035918	87094959				-114.778
CSN1S1	Chr6	87141555	87159096				-50.641
CSN2	Chr6	87179506	87186022				-23.715
HSTN	Chr6	87189735	87204440				-5.297
STATH	Chr6	87229655	87239003				18.533
CSN1S2	Chr6	87262456	87280936				51.334
ODAM	Chr6	87327027	87335880				115.905
CSN3	Chr6	87378400	87392750				167.278
CABS1	Chr6	87469515	87471615				258.393
AMBN	Chr6	87694424	87705731				483.302
C14H8orf33	Chr14	1487365	1489409	Chr14	1299687	1299831	187.534
ZNF34	Chr14	1491980	1497904				192.149
RPL8	Chr14	1505029	1507626				205.198
COMMD5	Chr14	1531490	1533526				231.659
ARHGAP39	Chr14	1563865	1600378				264.034
MIR2308	Chr14	1566932	1567001				267.101
C14H8orf82	Chr14	1602473	1604999				302.642
LRRC24	Chr14	1604104	1609477				304.273
LRRC14	Chr14	1610261	1613725				310.43
RECQL4	Chr14	1614026	1620509				314.195
MFSD3	Chr14	1620565	1622643				320.734
GPT	Chr14	1623901	1626907				324.07
PPP1R16A	Chr14	1628813	1633988				328.982
FOXH1	Chr14	1654700	1656256				354.869
KIFC2	Chr14	1656360	1663803				356.529
CYHR1	Chr14	1664422	1665518				364.591

CYHR1	Chr14	1674620	1677519				374.789
TONSL	Chr14	1681493	1692499				381.662
VPS28	Chr14	1693642	1698621				393.811
SLC39A4	Chr14	1719731	1724221				419.9
CPSF1	Chr14	1728206	1742668				428.375
ADCK5	Chr14	1742710	1756301				442.879
SLC52A2	Chr14	1763992	1766621				464.161
SCRT1	Chr14	1782900	1790463				483.069
DGAT1	Chr14	1795424	1804838				495.593
PARP8	Chr20	28315520	28506629	Chr20	28914471	28915027	-407.842
HCN1	Chr20	29121454	29567228				206.427

Table S6. Genomic prediction accuracies (standard errors) from cross-validations for milk yield, fat yield, protein yield, fertility and overall type of 5115 bulls with BayesR.

Sample Set	**Model**	**Trait**				
		FY	MY	PY	Fertility	Overall type
Holstein + Jersey	SNP	0.773(0.013)	0.929(0.001)	0.902(0.003)	0.618(0.034)	0.561(0.030)
	SNP+SV	0.773(0.013)	0.929(0.001)	0.902(0.003)	0.618(0.034)	0.561(0.030)

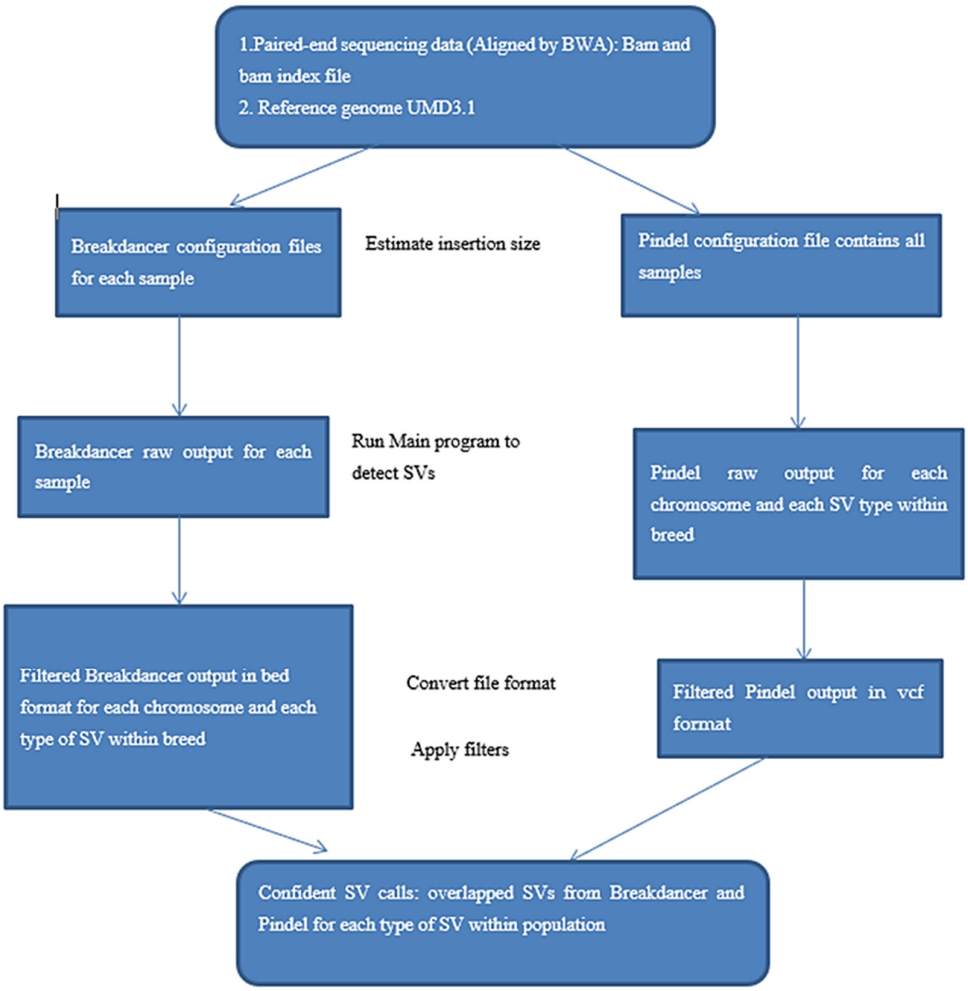


Figure S1. Flowchart for population SV pipeline.This flowchart illustrates the pipeline for generating population SV calls for Holstein and Jersey populations. In the filtering step, for both Breakdancer and Pindel, only SVs that were detected in at least 2 animals and > 50 bp regions from genome gaps were included. A few filters were further applied to the raw output of Pindel by setting: minimum coverage as 1; minimum SV event size as 50; minimum supporting reads as 5; maximum supporting reads as twice as the genome coverage for deletions, inversions and insertions and as 4 times of the genome coverage for tandem duplications. The final confident SV sets were then overlapped from filtered Breakdancer and Pindel output set by each SV type, respectively.

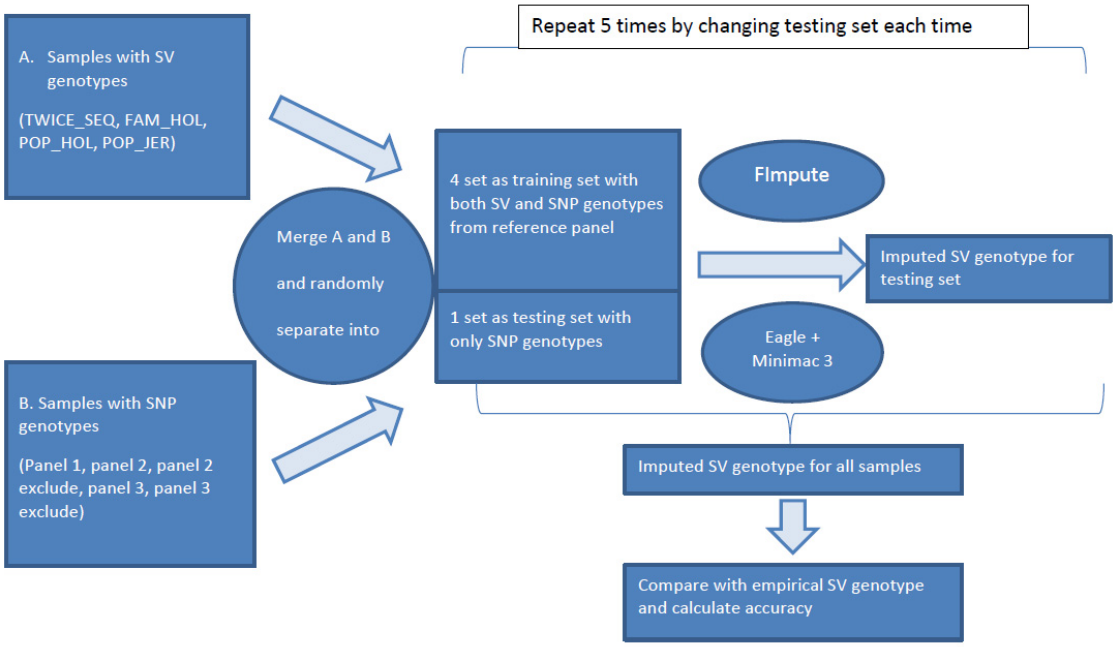


Figure S2. Flowchart of 5-fold cross-validation of imputation pipeline.

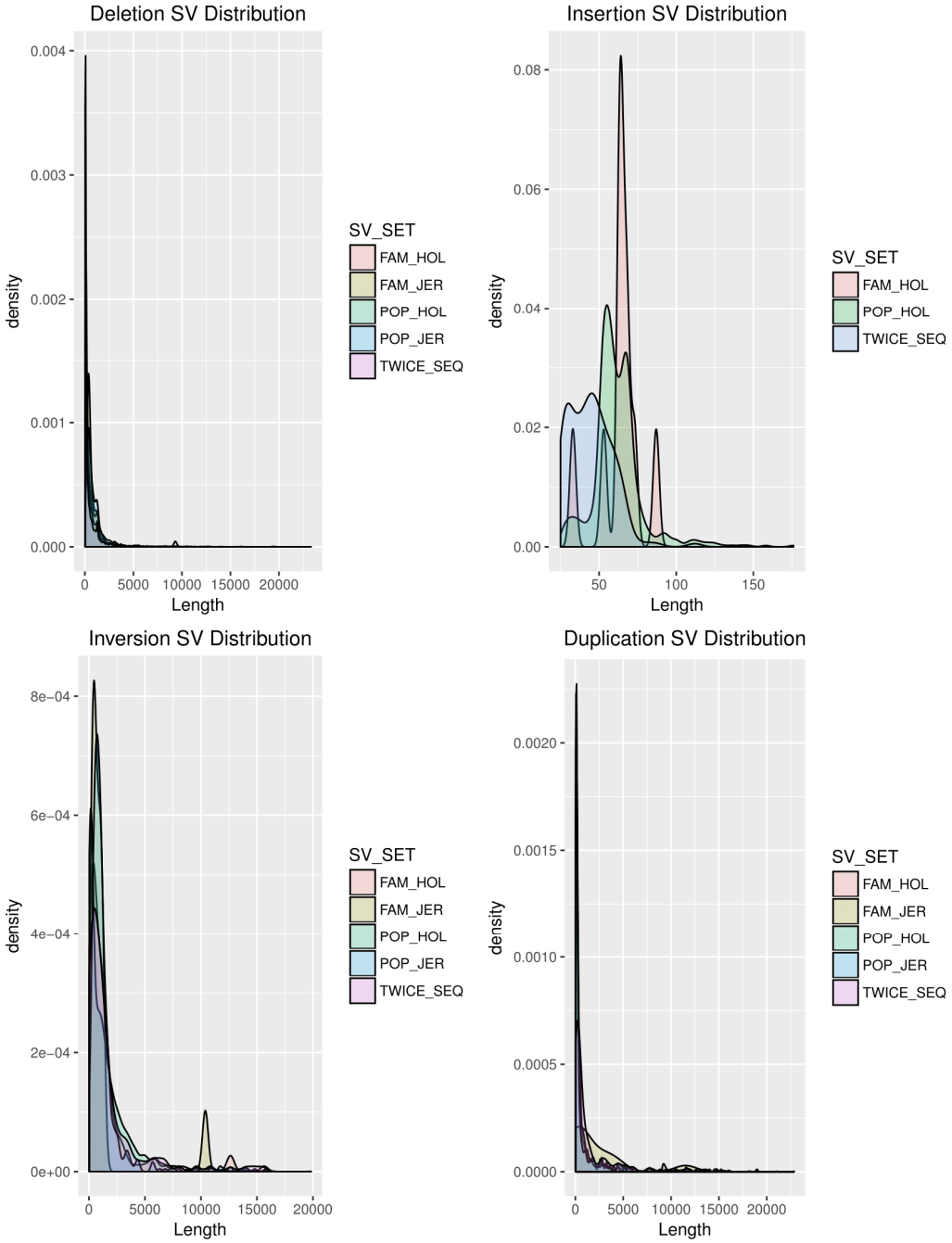
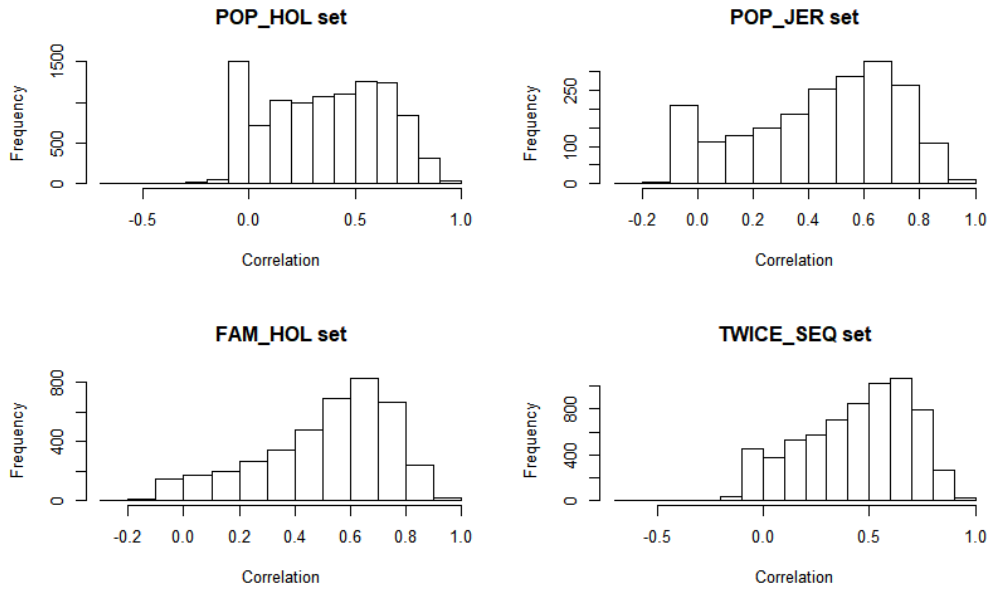


Figure S3. Plot of size distribution in base pairs of deletions, insertions, inversions and duplications in FAM_HOL, FAM_JER, POP_HOL, POP_JER and TWICE_SEQ.



b.

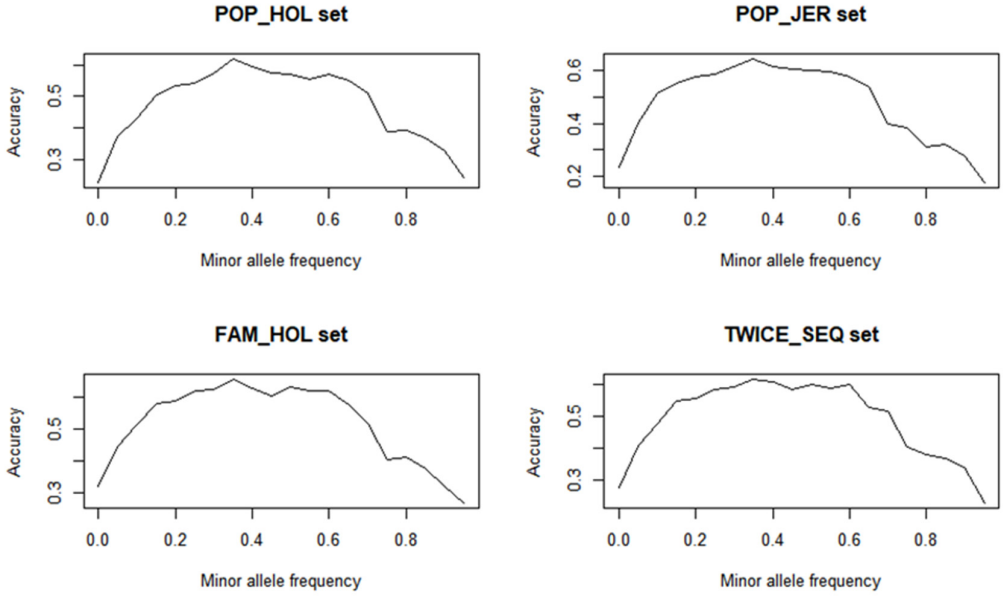


Figure S4. Imputation accuracy for deletions in POP_HOL, POP_JER, FAM_HOL and TWICE_SEQ sets. a. Distribution of imputation accuracy. b. Imputation accuracy versus MAF where imputation accuracy is calculated as the mean in each 0.05 MAF bin.

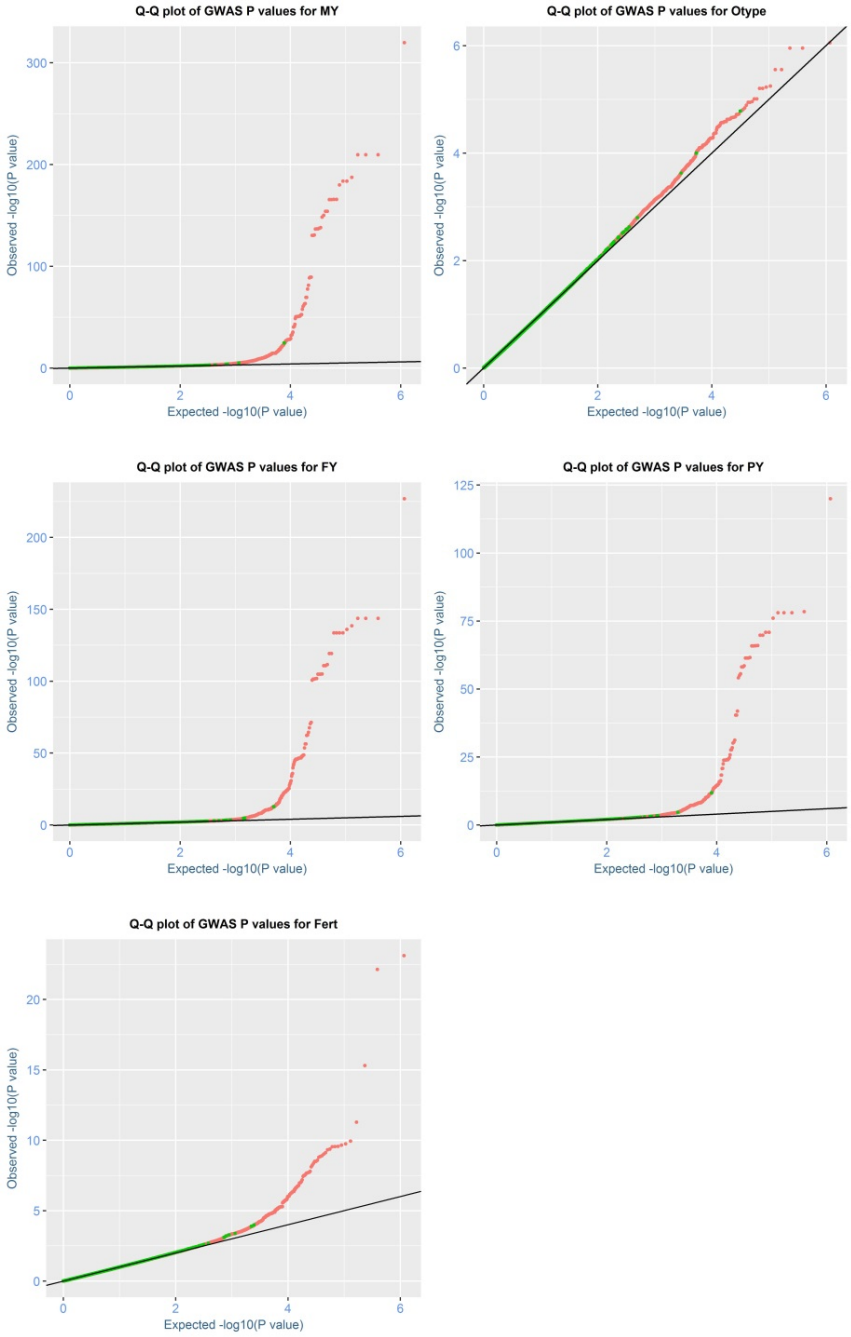


Figure S5. QQ plots for meta-analysis of single traits: fat yield, milk yield, protein yield, fertility and overall type with observed -log10(P-value) on vertical axis and expected -log10(P-value) on horizontal axis. Red dots are SNPs and green dots are SVs.