



Inheritance analysis of copy number variation polymorphisms in swine genome

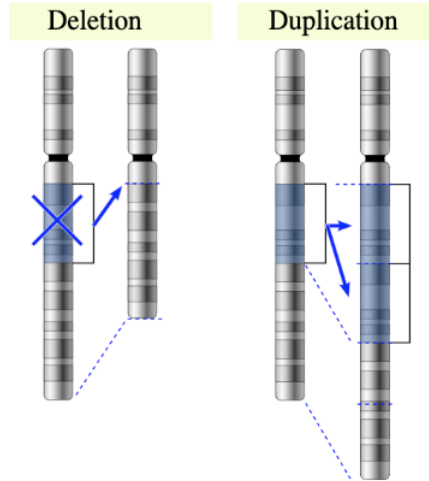
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Objectives

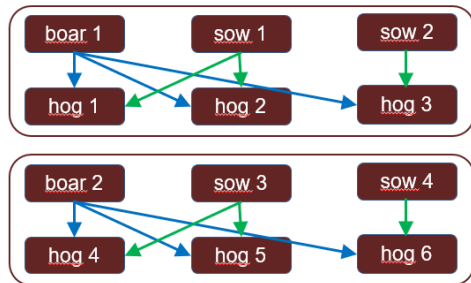
- to analyse of CNV inheritance in full and half siblings
- to determine the prevalence of CNVs formed *de novo* in the genomes of the offspring
- to describe the distribution of CNVs

Copy number variations



Material

- Whole genome sequence with Illumina HiSeq2000
- 12 swines (6 trios) Polish Large White breed:





Methods

Bioinformatics pipeline

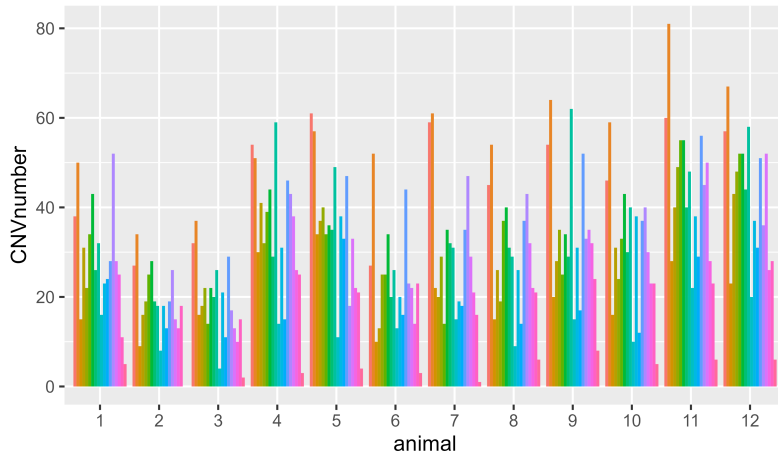
- Alignment to Sscrofa11.1 (BWA-MEM)
- Post alignment filtering (Picard & Samtools)
- CNV detection (CNVnator, Pindel)
- Functional annotation (VeP)

Statistical analysis

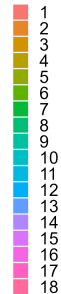
- Descriptive statistics
- Kolmogorov-Lilliefors test
- Wilcoxon signed rank test
- Permutation test
- U- Mann - Withney test
- Multidimensional scalling
- Test for fraction
- Correspondence analysis



Results

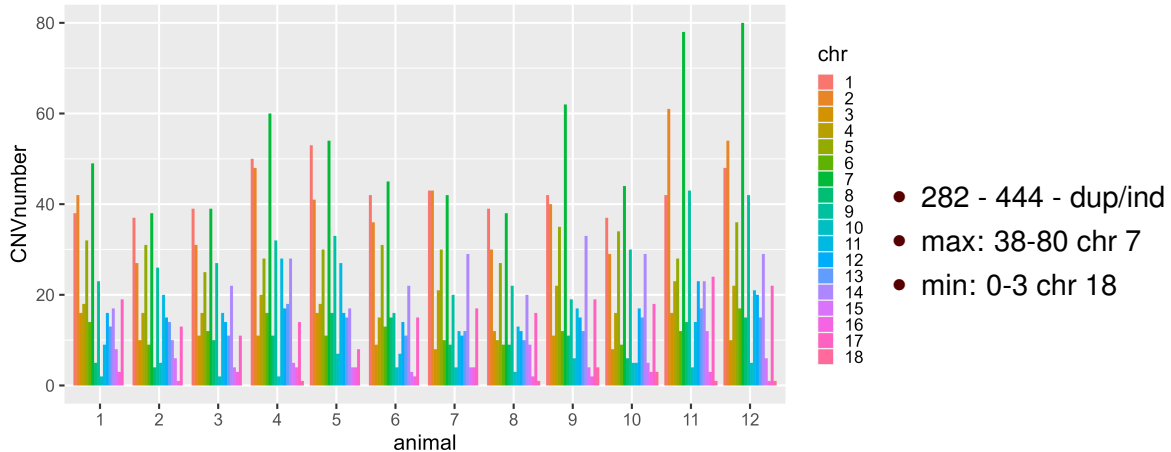


chr



- 325 - 753 - del/ind
- max: 34 - 81 chr 2
- min: 0-8 chr 18

Results



Results

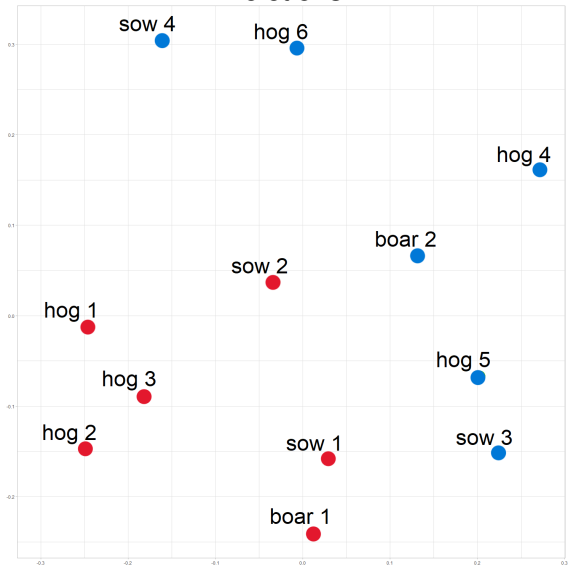
The length of CNVs

- deletions: 600 - 195000 bp (average 6662 ± 13001.5)
- duplications: 1200 - 561400 bp (average 10036 ± 33438.1)

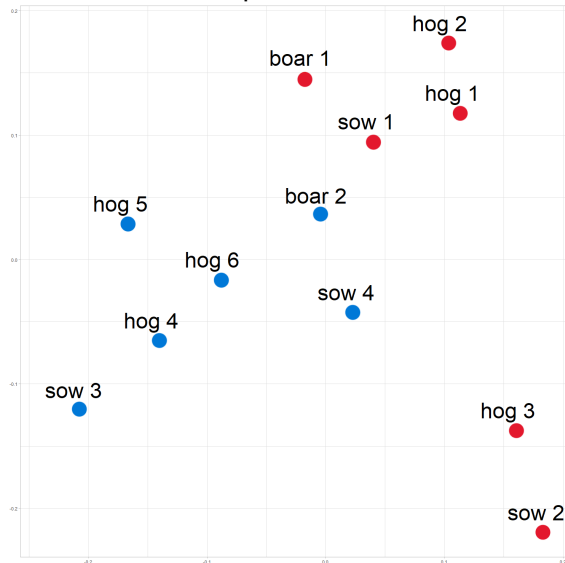
The percentage of genome covered

- deletions: 0.11% - 0.21%
- duplications: 0.26%-0.35%

Deletions

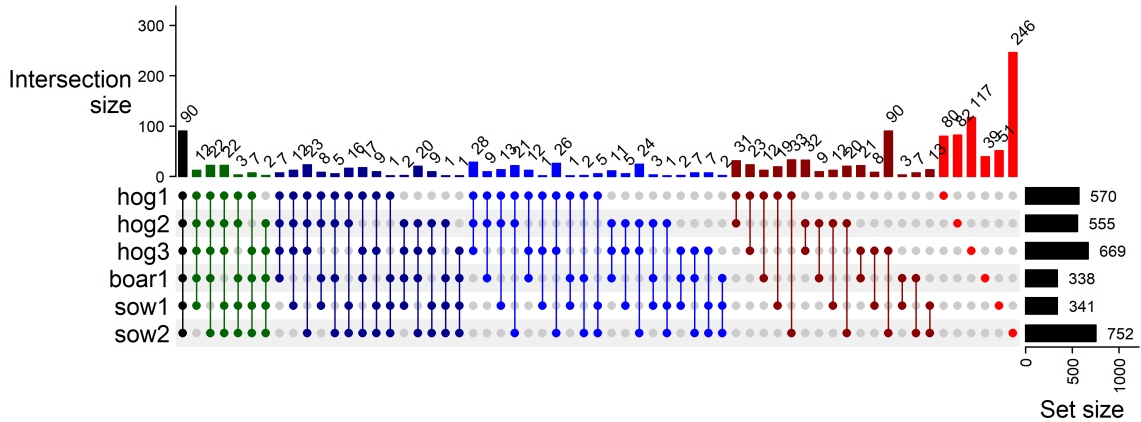


Duplications



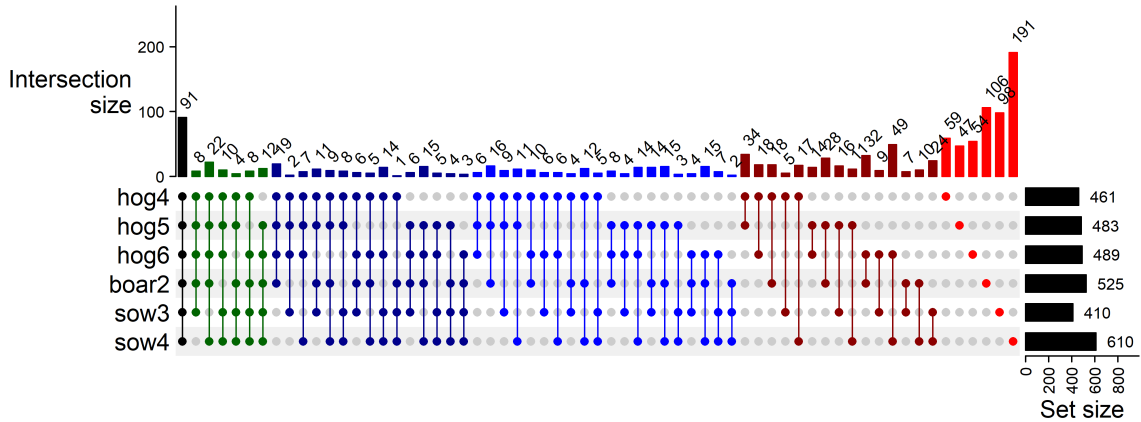


Results - common deletions



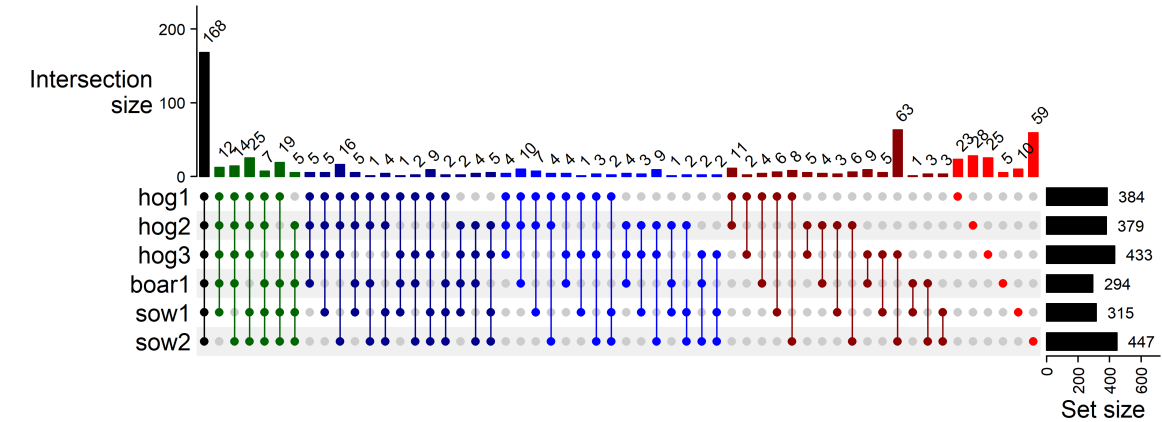


Results - common deletions



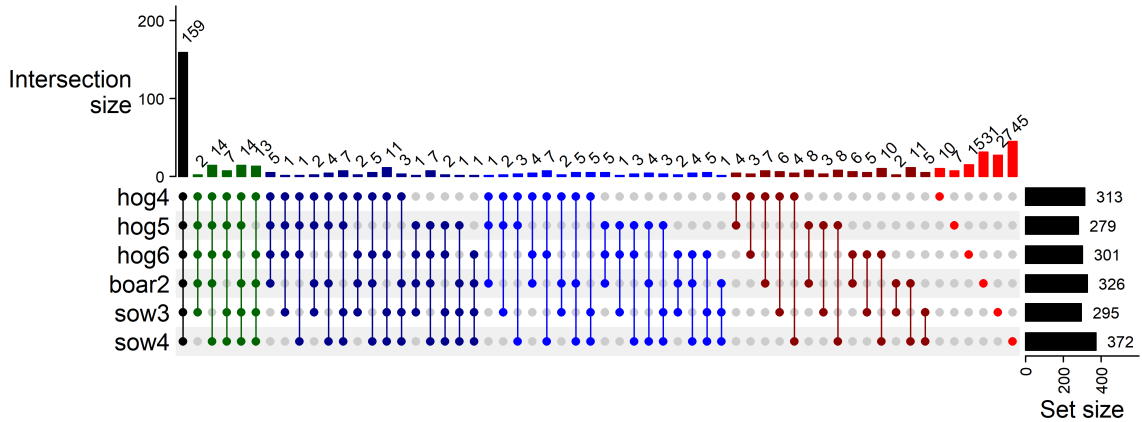


Results - common duplications





Results - common duplications



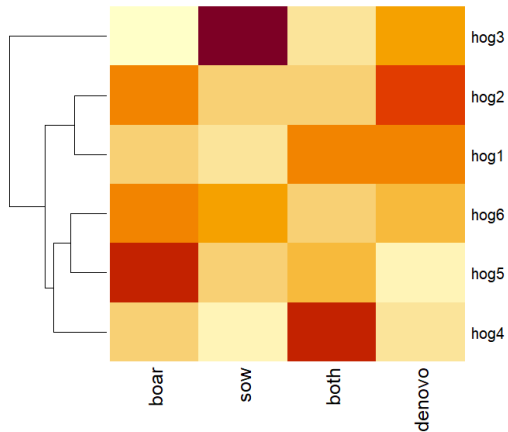
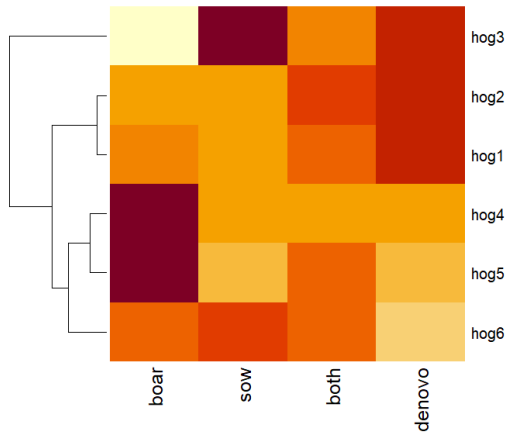


Results

- Most of inherited deletions - chromosome 11
- Most of inherited duplications - chromosome 5
- No differences in numbers of CNV inherited from sow and boar
 - deletions $P = 0.84$
 - duplications $P = 0.41$

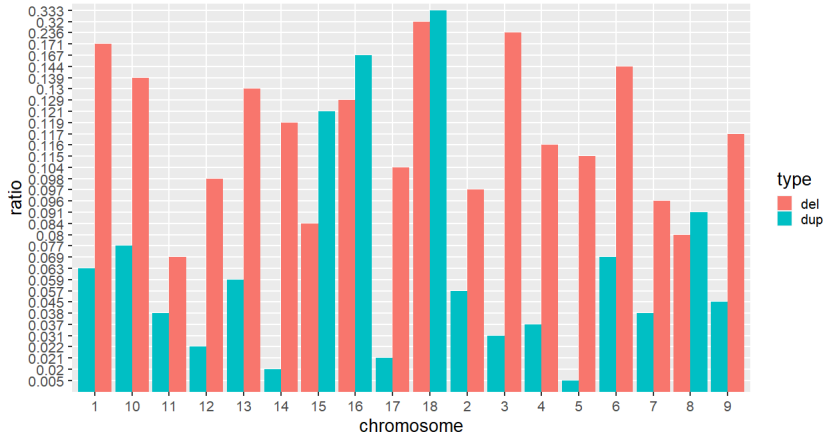


Results



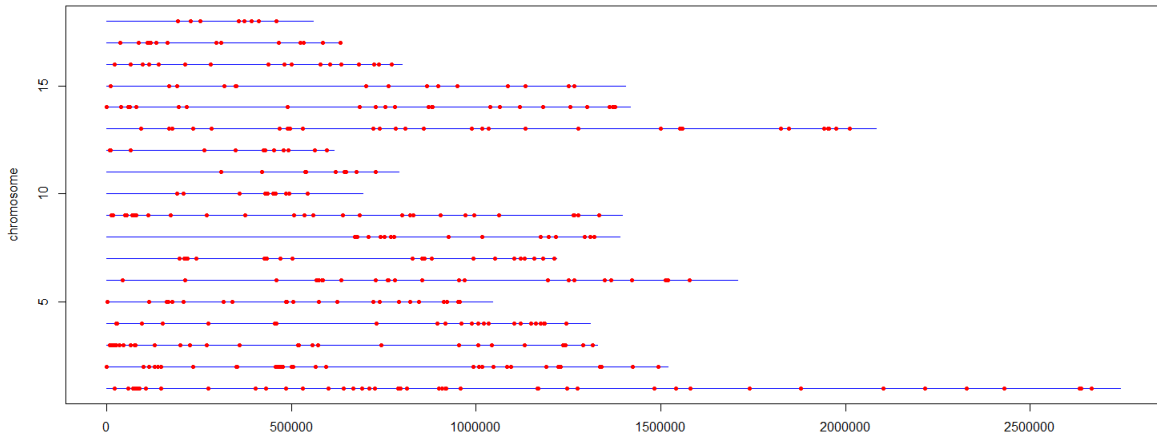
Results - *de novo* CNVs

- deletions
422 (47 – 117)
- duplications
96 (7 – 28)
- 72 CNV - chr 1
55 - del, 17 - dup



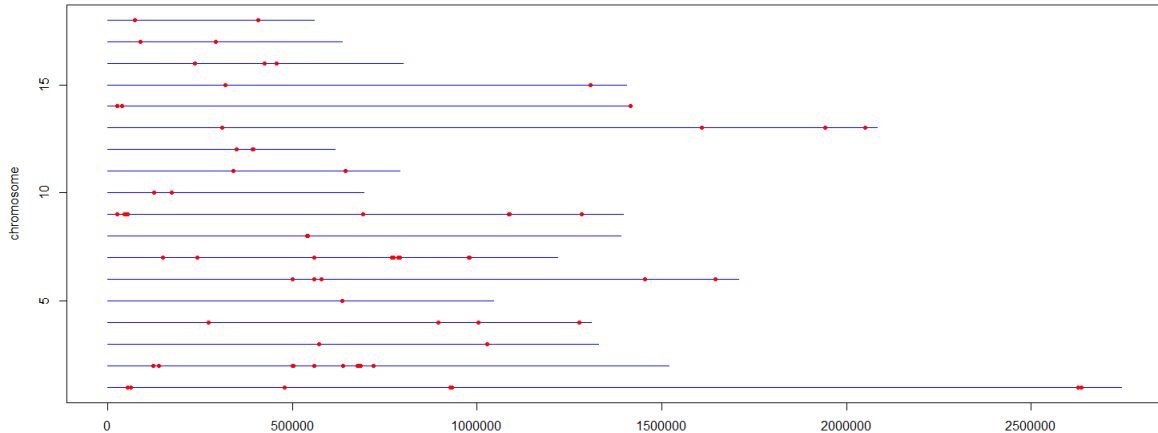


Results - density of *de novo* deletions along the genome





Results - density of *de novo* duplications along the genome



Results

- Significantly less CNVs arise *de novo* than inherited ($P=0.008$ for deletions, 0.006 for duplications)
- Fraction of *de novo* CNVs depends on animal in both deletions ($P=0.007$) duplications ($P=0.004$)

	hog 1	hog 2	hog 3	hog 4	hog 5	hog 6
deletion	0.129	0.131	0.150	0.111	0.089	0.094
duplication	0.058	0.072	0.045	0.018	0.021	0.044

Results

- *De novo* deletions are shorter than inherited in all animals.

	hog 1	hog 2	hog 3	hog 4	hog 5	hog 6
P-value	$3.76 \cdot 10^{-5}$	$1.26 \cdot 10^{-6}$	$6.49 \cdot 10^{-7}$	$0.13 \cdot 10^{-1}$	$0.17 \cdot 10^{-3}$	$8.18 \cdot 10^{-7}$

- no differences in length of *de novo* and inherited duplications

	deletions	duplications
variants	422	96
overlapped genes	268	81
intergenic variant	14%	21%
genic coding variants	4.2%	13%
others	81.8%	66%

Results - Enrichment analysis

- Common duplications in all 12 pigs are related to the regulation of basic biological processes (metabolic and olfactory receptor activity, as well as G protein-coupled receptor signaling pathway)
- No significant results found for common deletions
- No significant results found for *de novo* CNVs

Conclusions:

- CNVs formed *de novo* account for 2%-15% of all CNVs
- deletions formed *de novo* are shorter than inherited
- full siblings are more similar each other in structure of CNVs than to other individuals
- *de novo* CNVs are not uniformly distributed
- duplications in genes are considered to be essential sources of evolutionary innovation and duplications with beneficial effects are likely to be kept
- deletions bring severe consequences by interrupting gene products and causing loss of the biological functions; polymorphisms with large negative effects are likely to be removed from the population by natural selection

THANK YOU FOR YOUR ATTENTION!

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Acknowledgements:



Any questions?

