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New insight in genomic inbreeding assessment in domestic animals

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Inbreeding

- Mating of closely related individuals
- Unavoidable due to small effective population size (N_e)
 - Used also for **↑ productivity**

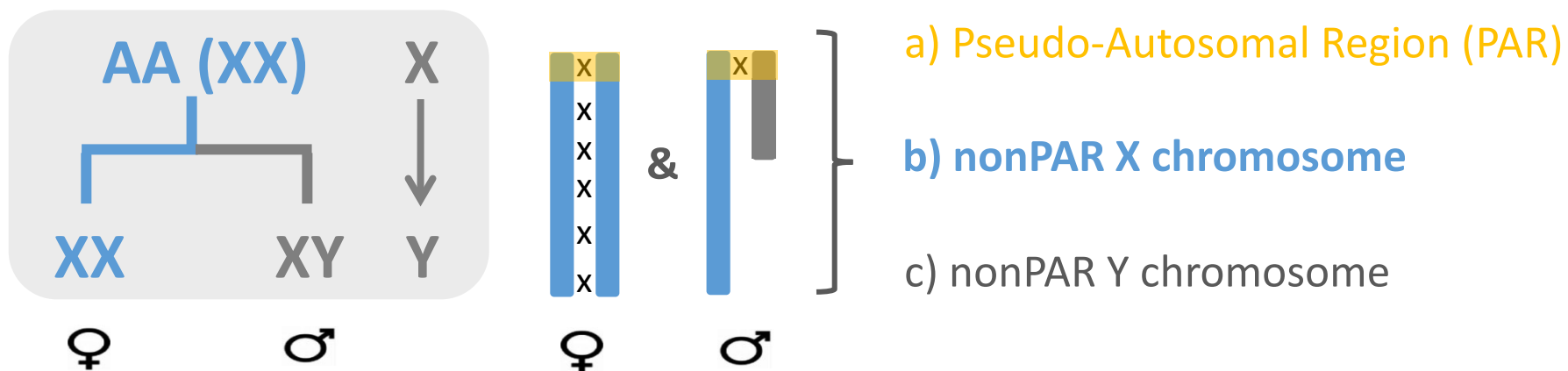
↑ the proportion of homozygosity (autozygosity)

NEGATIVE CONSEQUENCES:

- ✓ Higher frequency of detrimental genetic disorders
 - ✓ Inbreeding depression

– central point of population genetics/genomics –

Inbreeding & X chromosome - limited information available

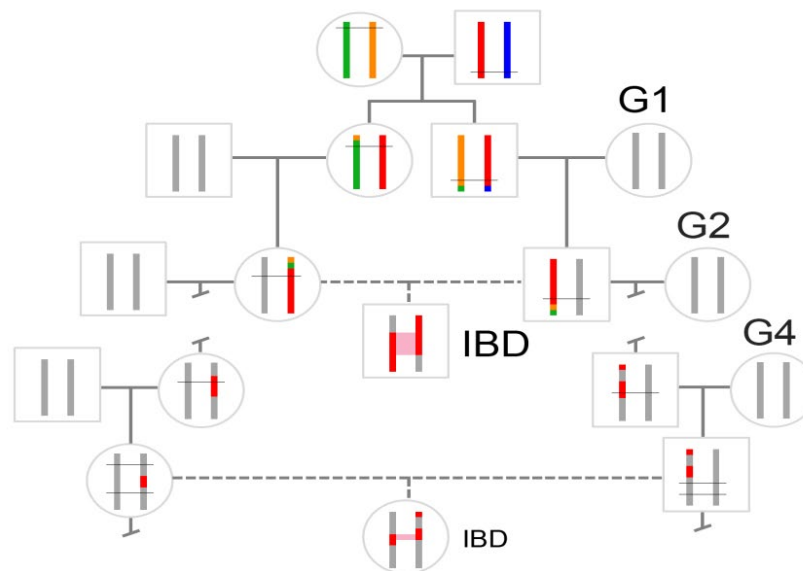


nonPAR X chromosome

- ↑ Genetic drift
- ↓ Recombination rate
- ↑ Linkage disequilibrium
- ↓ Mutation rate
- ↓ Ne
- ↓ Genetic diversity

Inbreeding estimation

- Inbreeding coefficient (F): 0 - 1

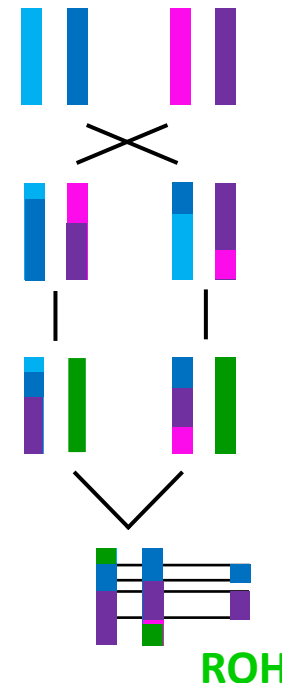
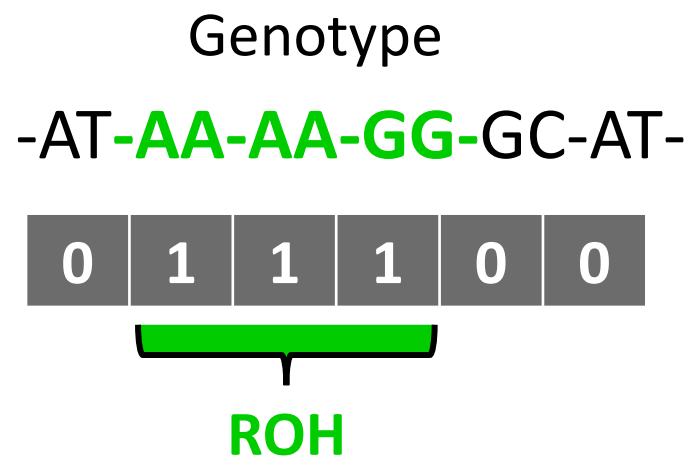


THROUGH HISTORY – Through the Pedigree
MODERN AGE – **Genomic assessment**

- markers representing variable sites of the genome (SNPs)
- **F_{ROH}** method leads

Genomic inbreeding coefficient - F_{ROH}

ROH - long homozygous regions in a genome
- represent autozygous segments



ROH incidence matrix

ID1	1	1	1	1	0	0	1	1	1	0	0	0	0	0	1	1	1	$F_{ROH} = 0.56$
ID2	0	0	1	1	0	0	1	1	1	0	1	1	1	0	0	0	0	$F_{ROH} = 0.44$
ID3	1	1	1	1	0	1	1	0	0	0	0	0	1	1	1	0	0	$F_{ROH} = 0.50$
ID4	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	0	0	$F_{ROH} = 0.28$

1 = IBD

nSNPs = 18

mean $F_{ROH} = 0.45$

$$F_{ROHk} = \frac{\sum_k \text{Length} (ROH_k)}{L_{\text{genome (info used)}}$$

Aim of the study

to describe and demonstrate the possibility of gaining insight into regional variation in inbreeding

highlight regions with differences between sexes

highlight regions with differences on the same chromosome

Materials & Methods

Three case studies

Sheep

Croatian sheep breeds

606 K SNPs (Illumina)
202 individuals
8 breeds; metapopulation



Cattle

Croatian cattle breeds

777 K SNPs (Illumina)
112 individuals
3 breeds; metapopulation



Dog

Labrador Retriever

172 K SNPs (Illumina)
276 individuals
(Binversie *et al.*, 2020)



After Quality Control

201 individuals - 410 508 SNPs

101 ♀ 391 532 - auto
100 ♂ 18 976 - chrX

112 individuals - 641 019 SNPs

79 ♀ 610 457 - auto
33 ♂ 30 562 - chrX

271 individuals - 114 179 SNPs

125 ♀ 111 198 - auto
146 ♂ 2981 - chrX

Materials & Methods

Runs Of Homozygosity (ROH)

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Min. ROH = 1 Mb

Min. SNP = 15

het. and missing per class
(Ferenčaković *et al.*, 2013)

RZooROH

1 cM = 1 Mb

Bertrand *et al.* (2019)

Regional Genomic Inbreeding (F_{ROH})

in males and
females separately
&
in females only

- { a) Autosomal (F_{ROH})
b) X chromosomal (F_{ROH_X}) }

sliding window
of
PAR length (by 0.2 Mb)

Cattle = 5.80 Mb
Dog = 6.59 Mb
Sheep = 7.03 Mb

Results

1. Regional F_{ROH} - Highest sex difference
2. X chromosome regional F_{ROH} variation
3. Regional F_{ROH} - Highest autosomal difference

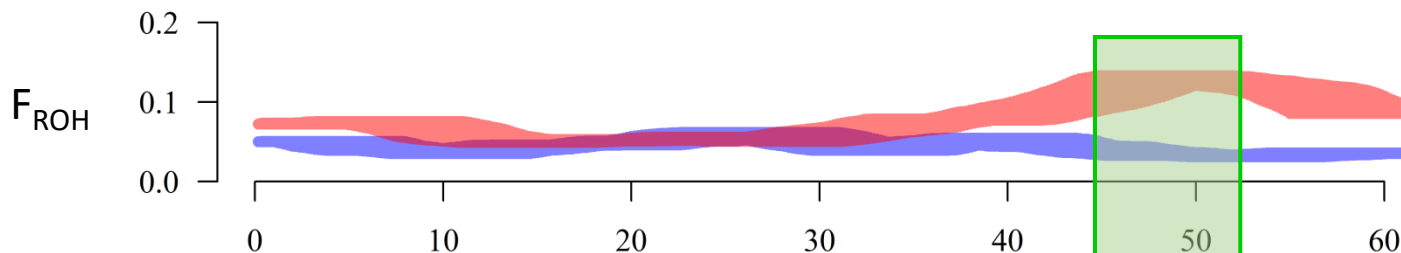
a)

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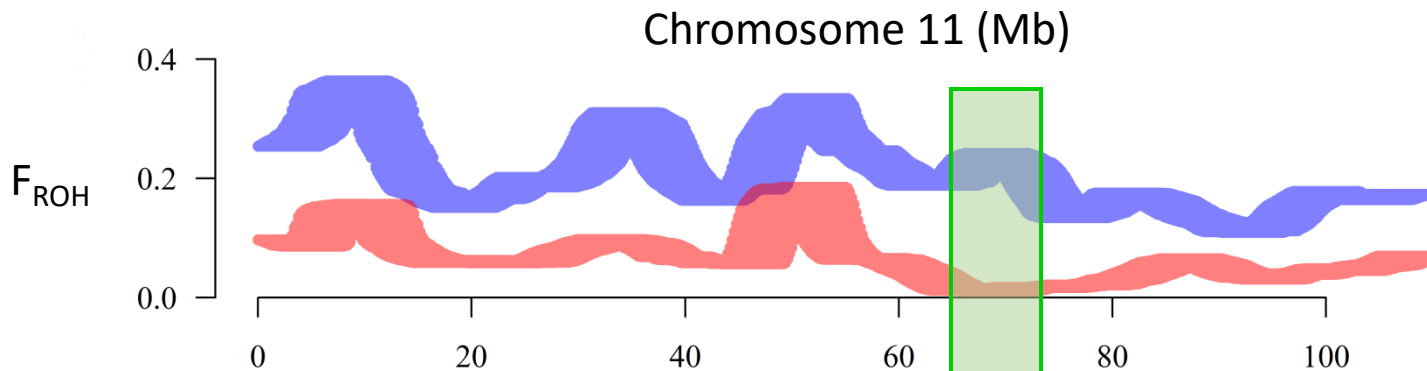
b)

RZooROH

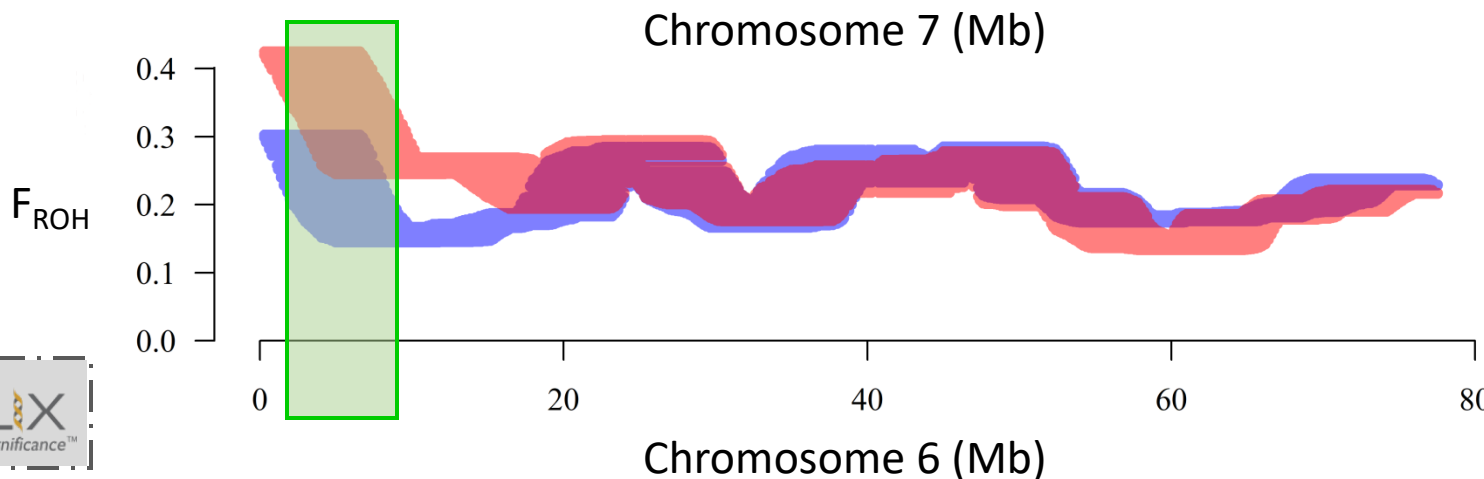
Regional F_{ROH} - Highest sex difference



$F_{ROH} = 0.033$
 $F_{ROH} = 0.133$ } **0.1**
 45.0 Mb – 52.0 Mb



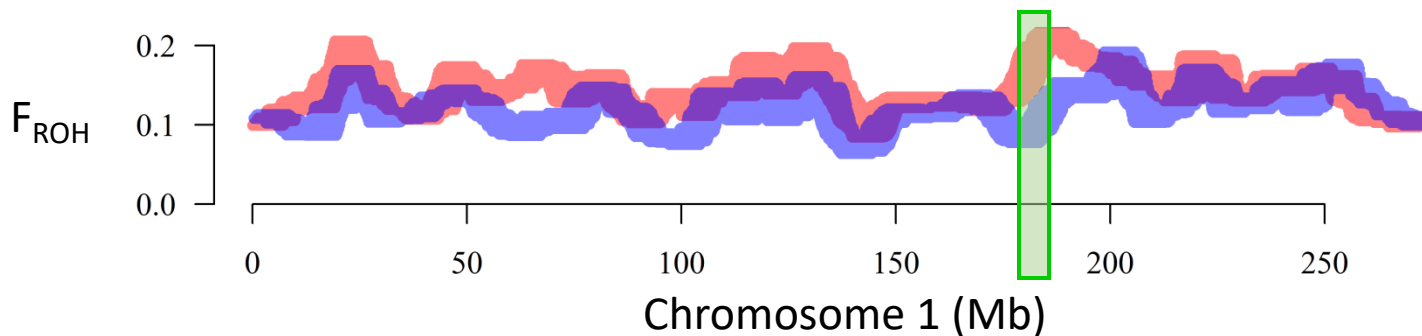
$F_{ROH} = 0.242$
 $F_{ROH} = 0.010$ } **0.232**
 66.20 Mb – 72.0 Mb



$F_{ROH} = 0.193$
 $F_{ROH} = 0.335$ } **0.142**
 2.44 Mb – 8.98 Mb

Females / Males

Regional F_{ROH} - Highest sex difference

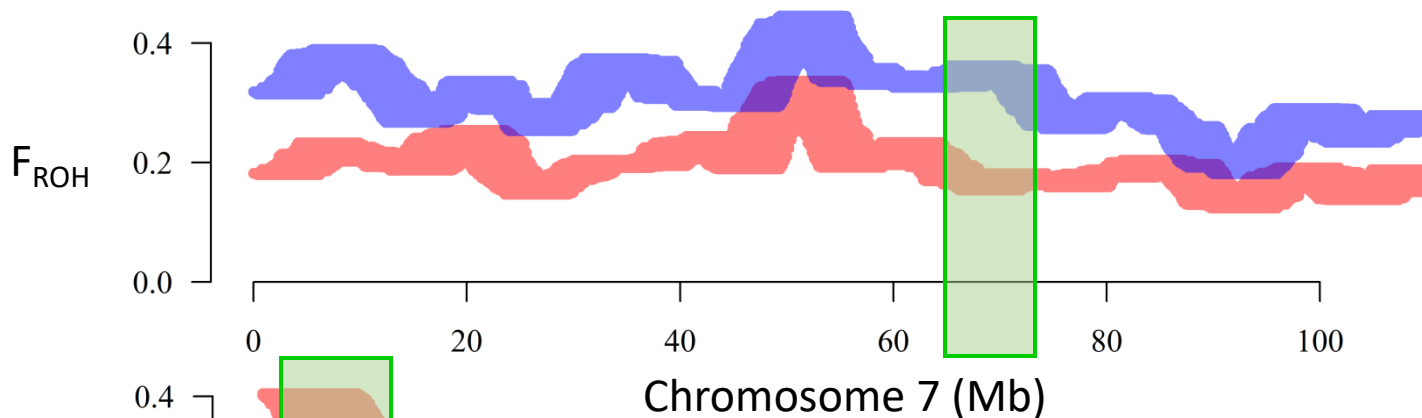


$F_{ROH} = 0.095$

$F_{ROH} = 0.195$

0.1

179.20 Mb – 186.23 Mb

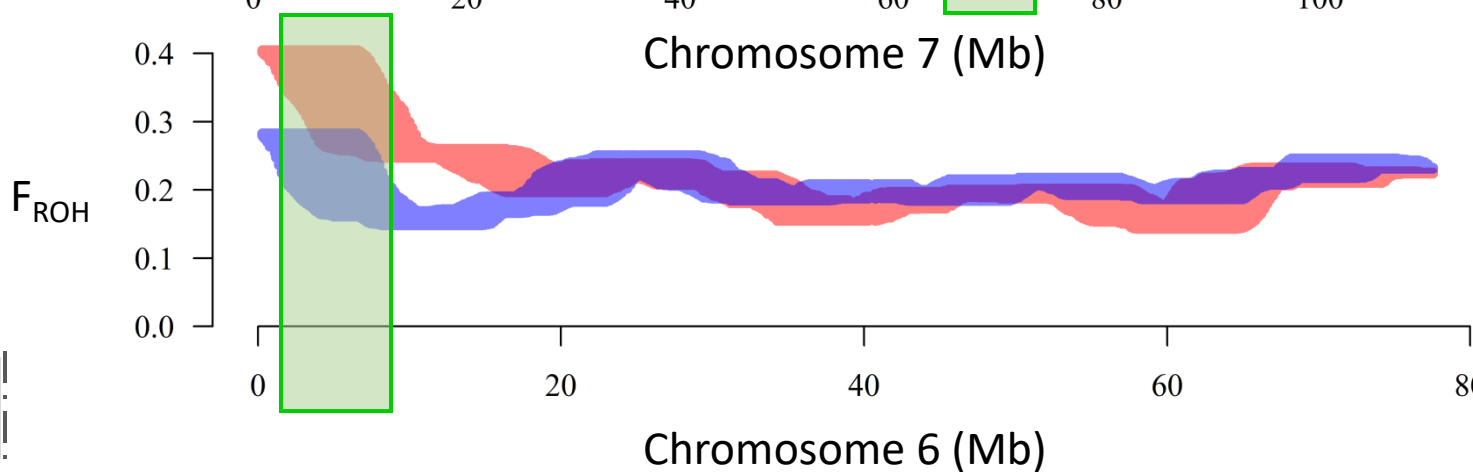


$F_{ROH} = 0.359$

$F_{ROH} = 0.156$

0.203

66.20 Mb – 72.0 Mb



$F_{ROH} = 0.197$

$F_{ROH} = 0.333$

0.136

2.44 Mb – 8.98 Mb

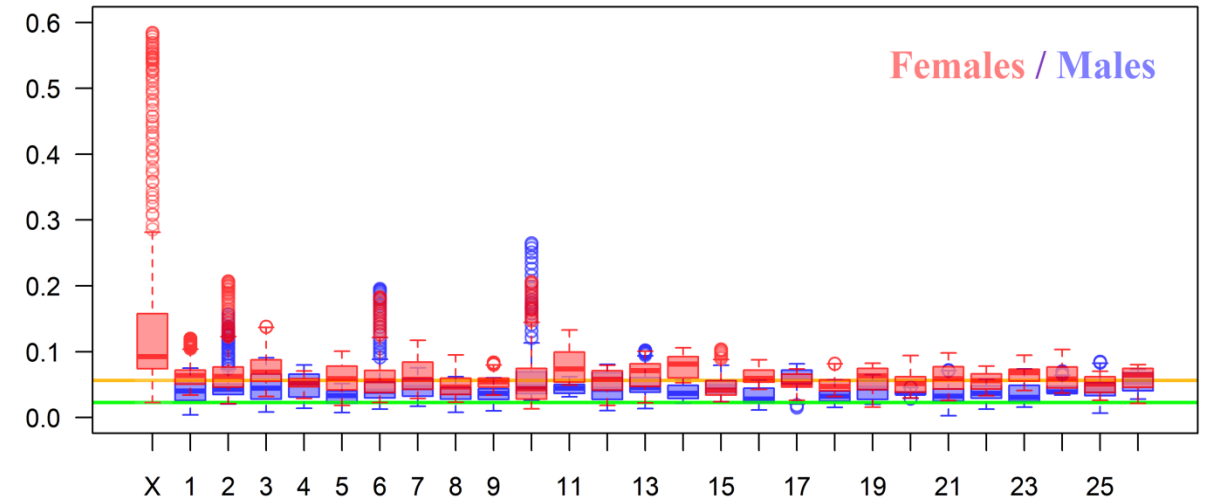
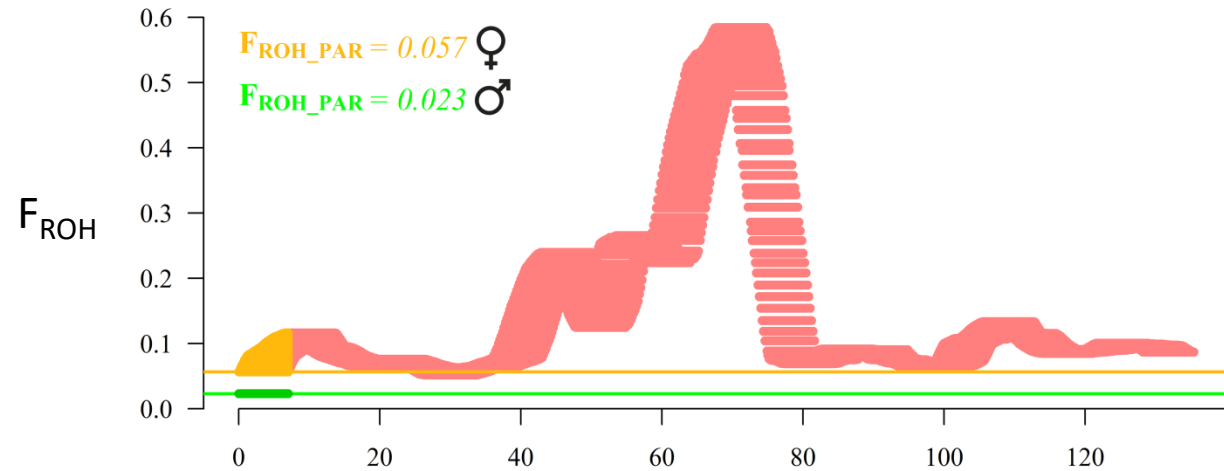
RZooROH

Females / Males

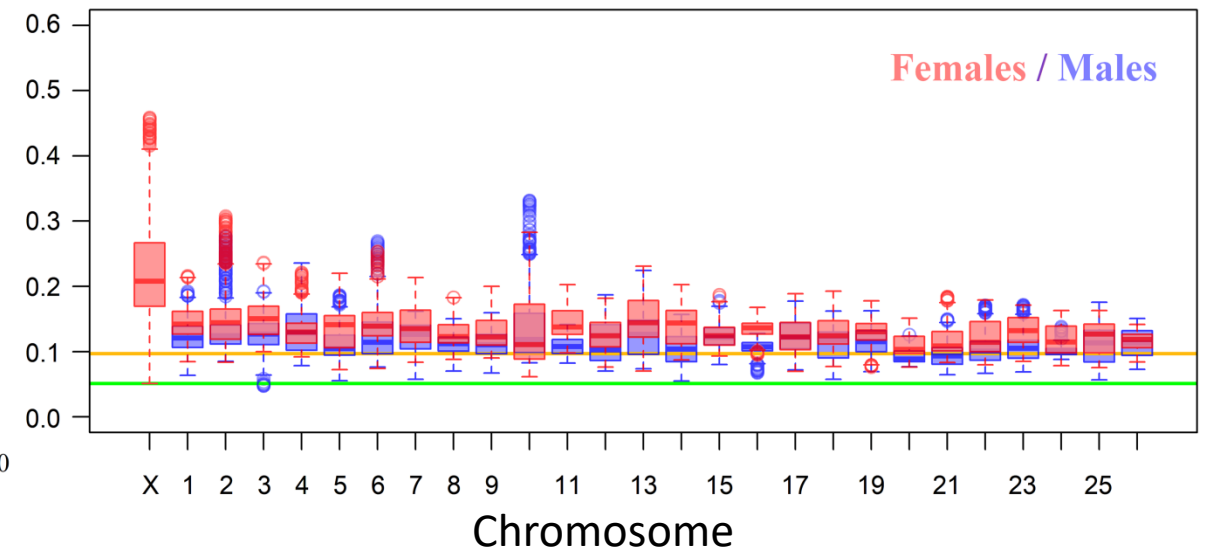
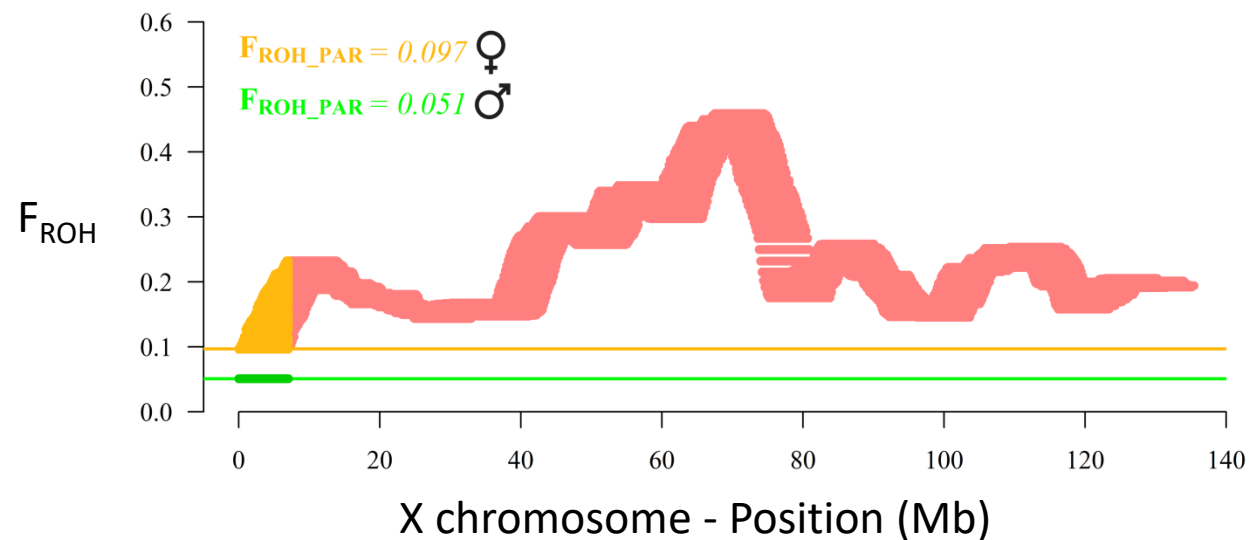
X chromosome regional F_{ROH} variation -



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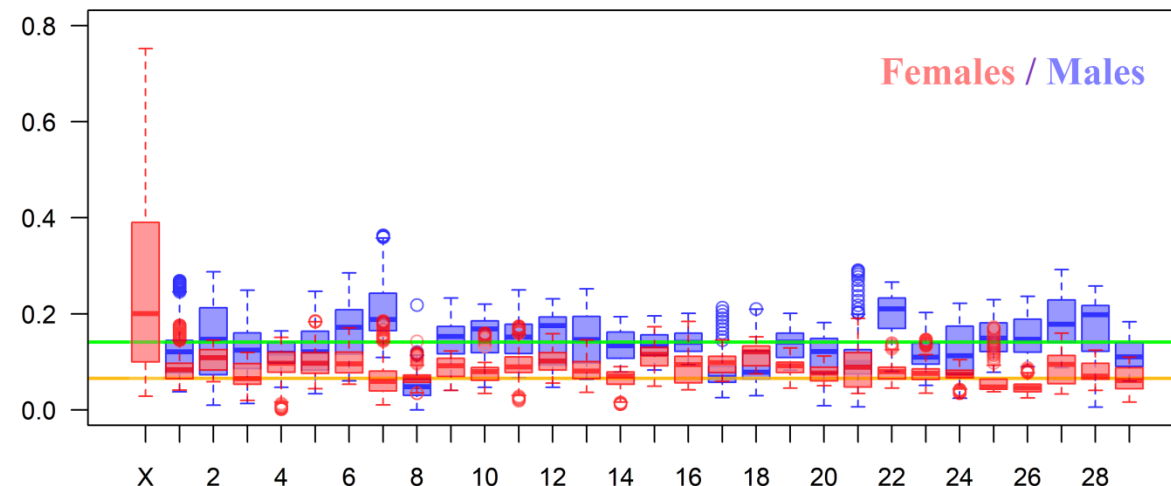
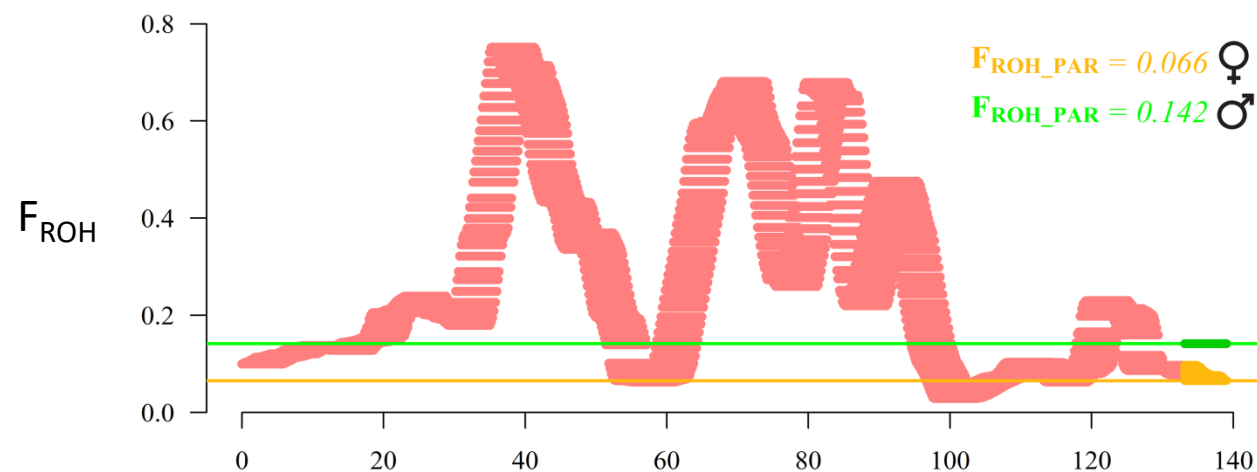
RZooROH



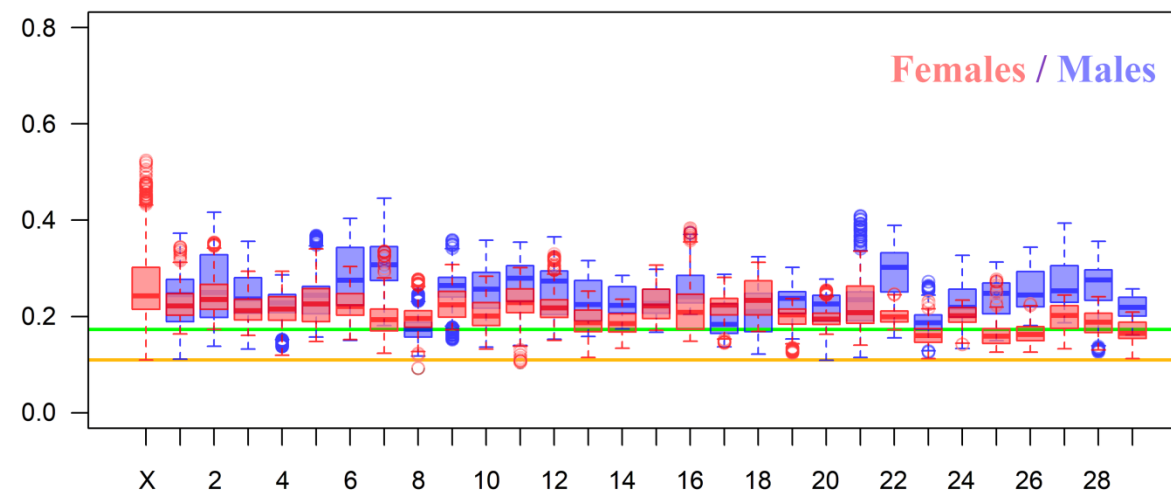
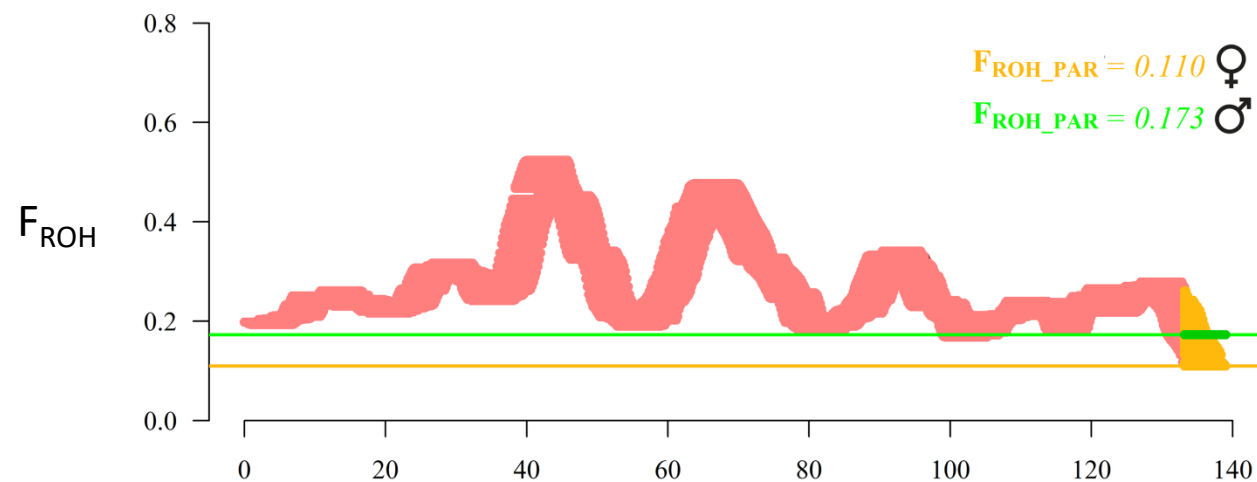
X chromosome regional F_{ROH} variation -



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RZooROH



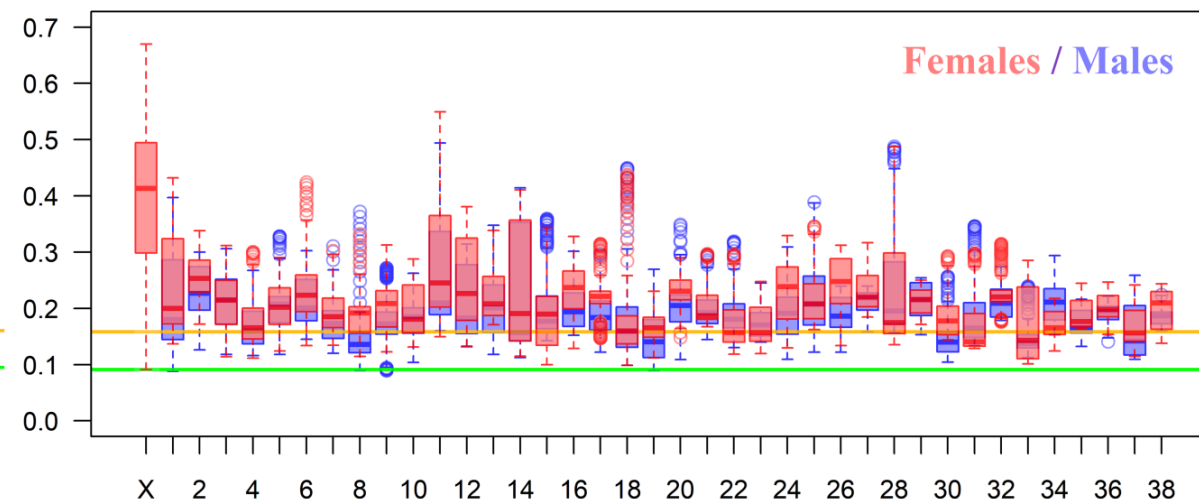
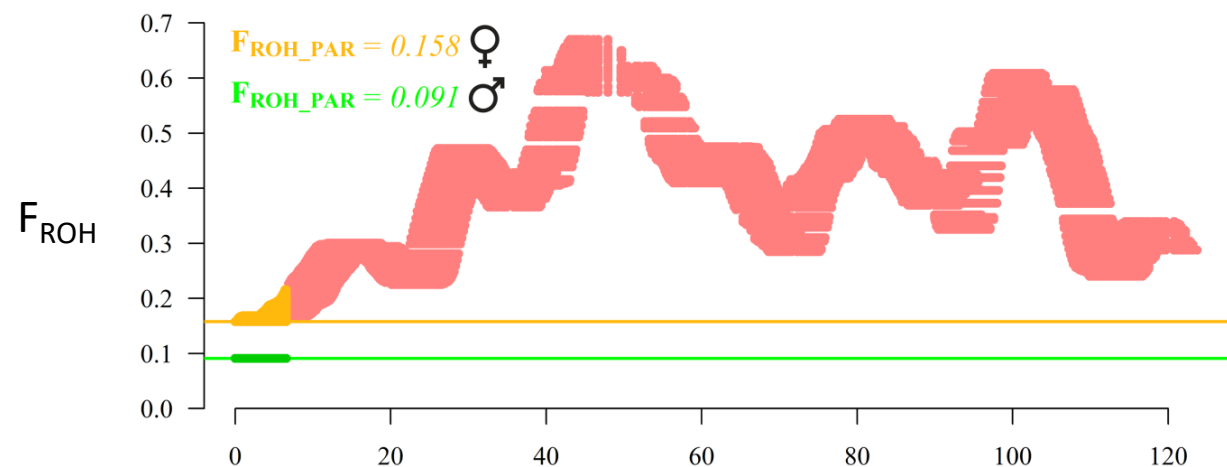
X chromosome - Position (Mb)

Chromosome

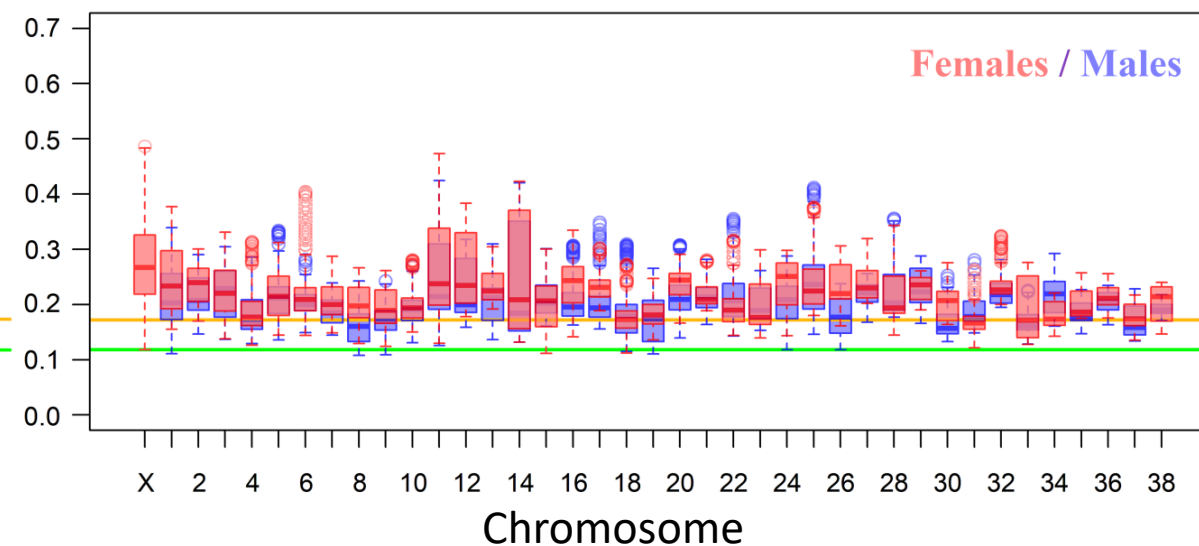
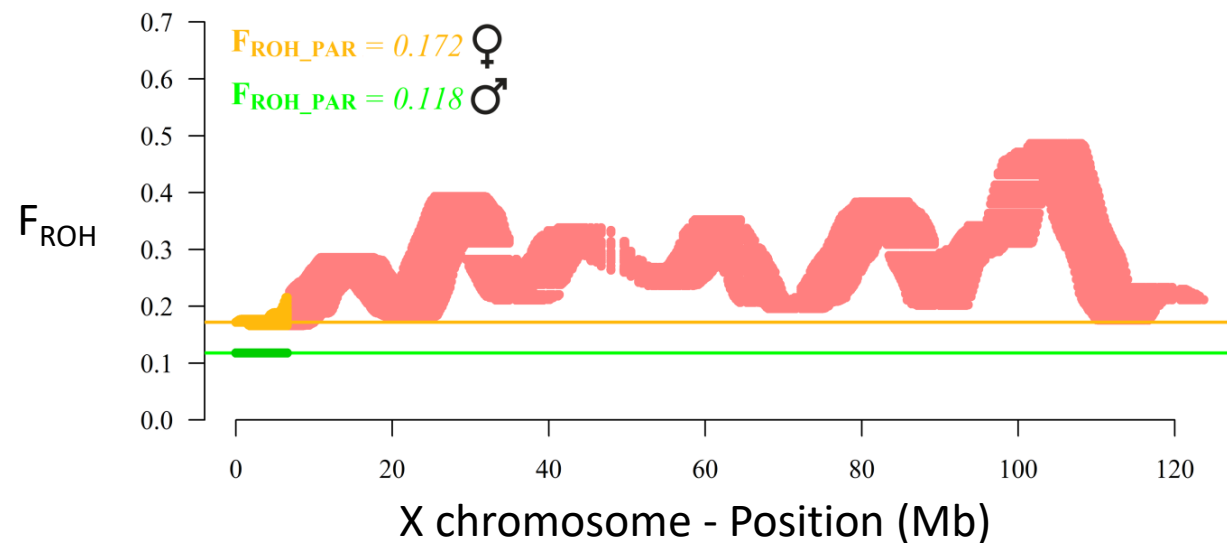
X chromosome regional F_{ROH} variation -



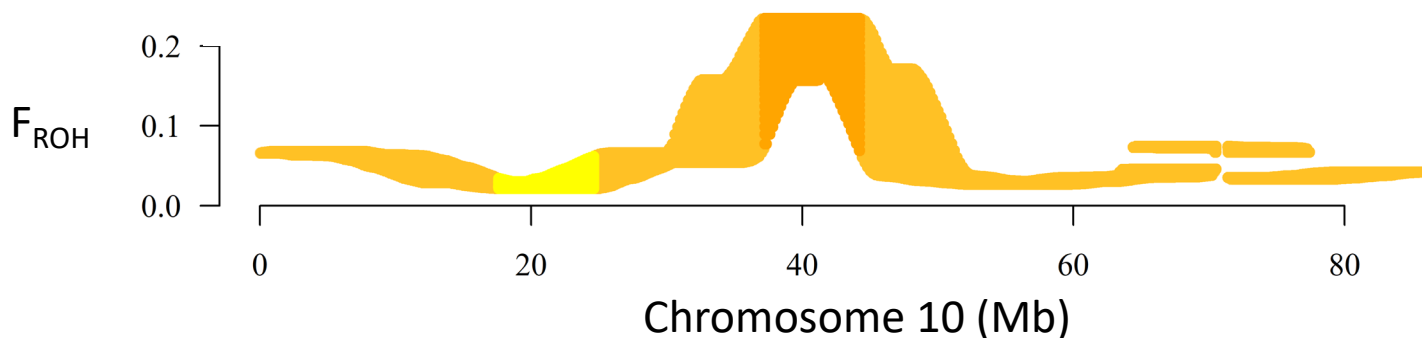
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RZooROH



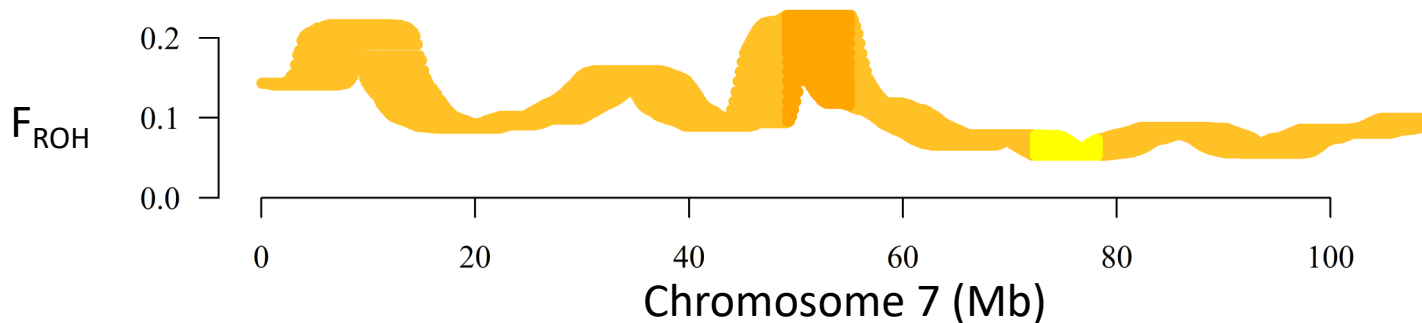
Regional F_{ROH} - Highest autosomal difference



$F_{ROH} = 0.235$

$F_{ROH} = 0.022$

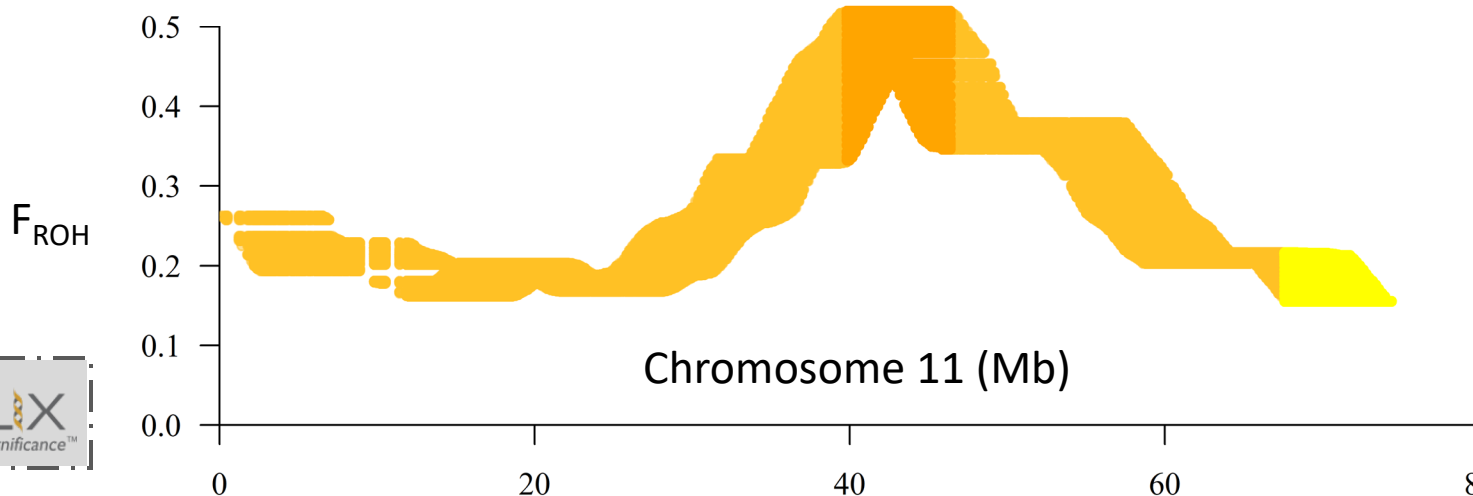
0.213



$F_{ROH} = 0.229$

$F_{ROH} = 0.054$

0.175



$F_{ROH} = 0.520$

$F_{ROH} = 0.155$

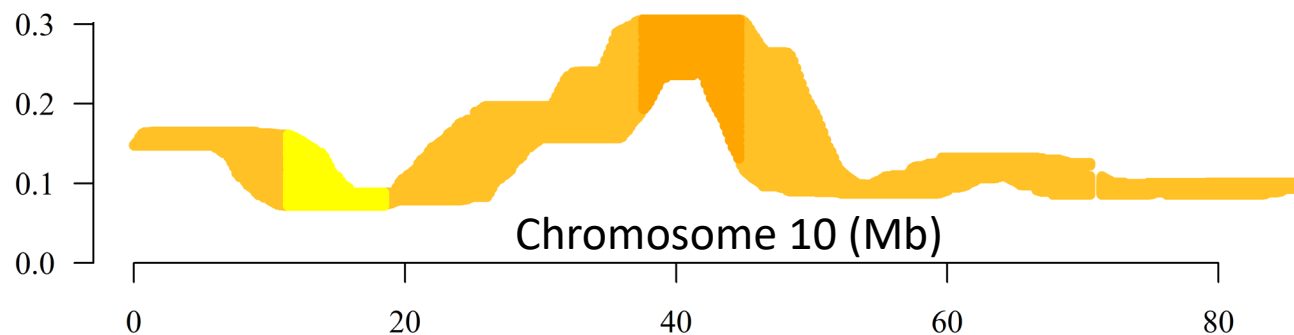
0.364

All individuals

Regional F_{ROH} - Highest autosomal difference



F_{ROH}



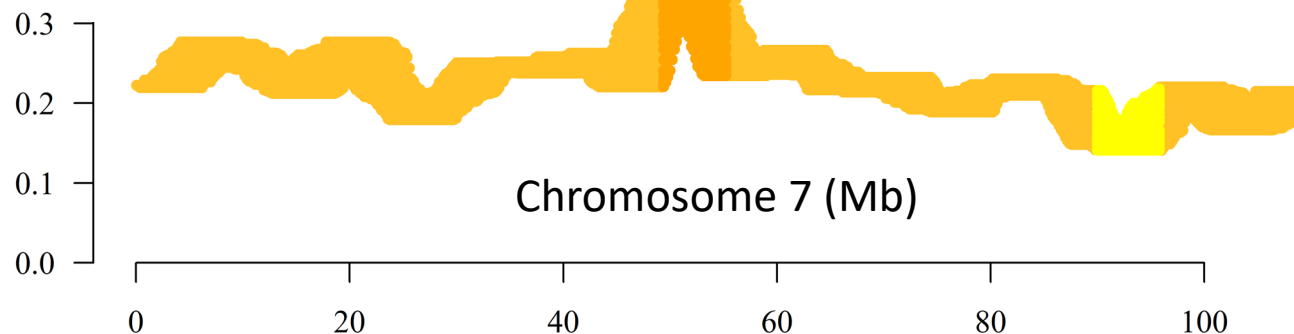
$F_{ROH} = 0.305$

$F_{ROH} = 0.072$

0.233



F_{ROH}



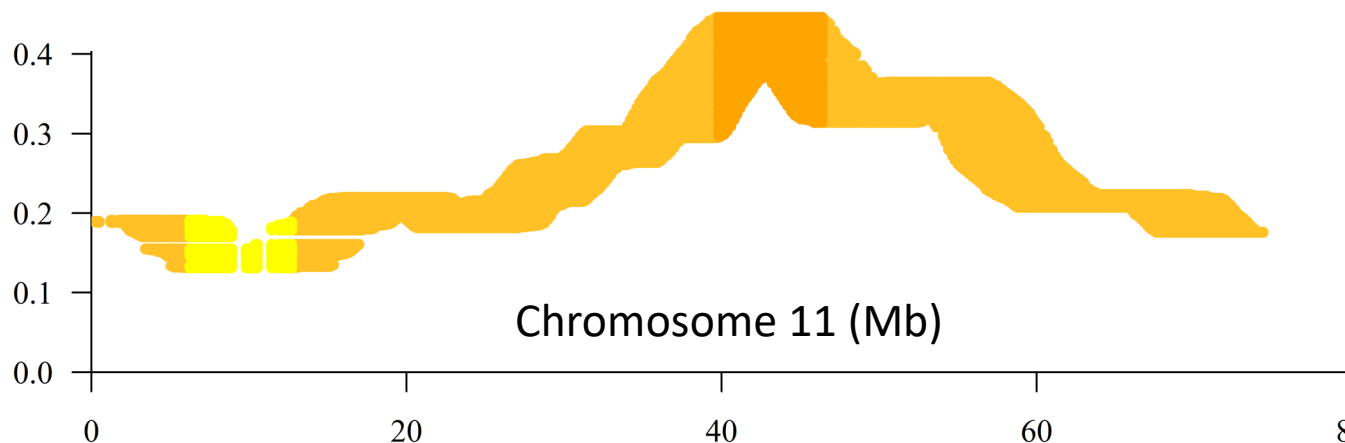
$F_{ROH} = 0.368$

$F_{ROH} = 0.141$

0.227



F_{ROH}



$F_{ROH} = 0.446$

$F_{ROH} = 0.131$

0.315

RZooROH

All individuals

Conclusion & Future Work

- **New approach** was presented **to analyse the estimation of regional inbreeding patterns** shown to be influenced by chromosome position and sex
- The approach presented improves our understanding of the estimation of regional and chromosomal inbreeding with particular attention to the **specific patterns observed for the X chromosome**
- Regions with high differences in inbreeding were observed, both **overall** and between the **sexes** (biological specificity?)

- To include more species
 - To include more case studies per species
 - To evaluate the genetic map
- **To investigate inbreeding depression using the same approach**



Thank you for your attention!

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