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Haplotype richness drop: a new method for mapping selection signatures

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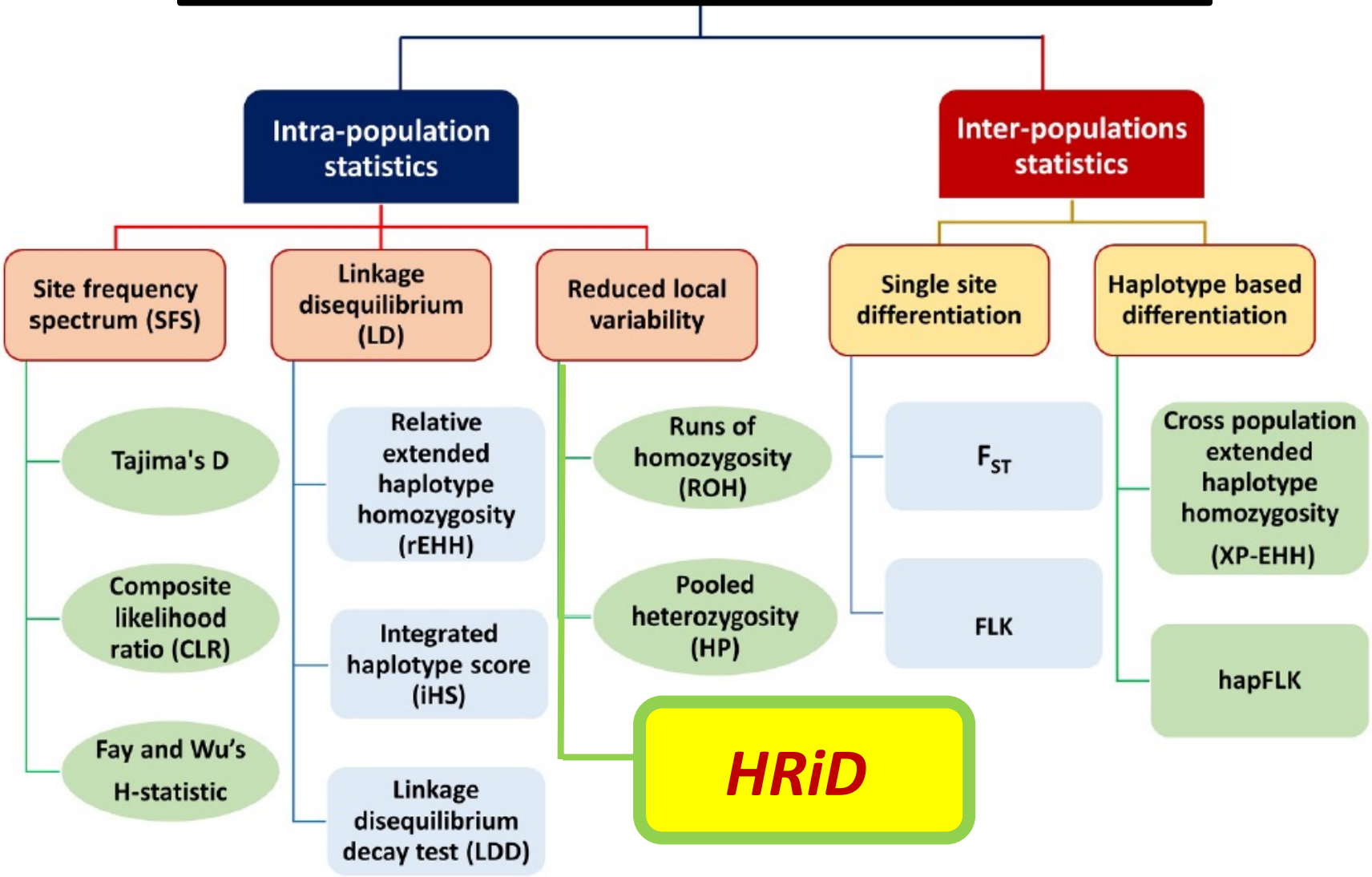
Detection (mapping) of selection signatures is an important aspect of the population genomics



Saravanan et al. (2020) Livestock Science

The goal of this research

To present new approach - **Haplotype Richness Drop (HRiD)** for mapping selection signals within populations

- complementation to other intra-population statistical approaches

- ✓ **Motivation**
- ✓ **Background and basic idea**
- ✓ **Empirical evaluation and comparison with other approaches**
- ✓ **Drawbacks**
- ✓ **Possibilities and future work**

extreme Runs Of Homozygosity islands

Across the genome distributions of ROH are not uniform !

Positive selection signals

Humans: Nothnagel et al., 2010; Pemberton et al., 2012

Domestic animals: Boyko et al. 2010; Curik et al., 2014

Population under selection: # alleles ↘

- favouring fixation of selected alleles (haplotypes)

Partially inbred HWE population: # alleles =

- increase of homozygosity across all genotypes

Homozygotes: $Q_{ii} = f\,p_i + (1-f)\,p_i^2$

Heterozygotes: $Q_{ij} = 2p_ip_j - 2\,f\,p_ip_j$, *where* $i<j$

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ORIGINAL RESEARCH
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Identification of Selection Signals on the X-Chromosome in East Adriatic Sheep: A New Complementary Approach

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Background and basic idea

Directional selection (fixation) vs. non-selected population (drift)

Drop (↘) in the number (#) of alleles (haplotypes) is an indication of the positive selection signal

The effective number of alleles is a measure of allelic richness,

"**the number of alleles that would result in the same expected heterozygosity (homozygosity) at the same frequencies as in a population in which not all allele frequencies are the same**" (originally defined by *Kimura and Crow, 1964*).

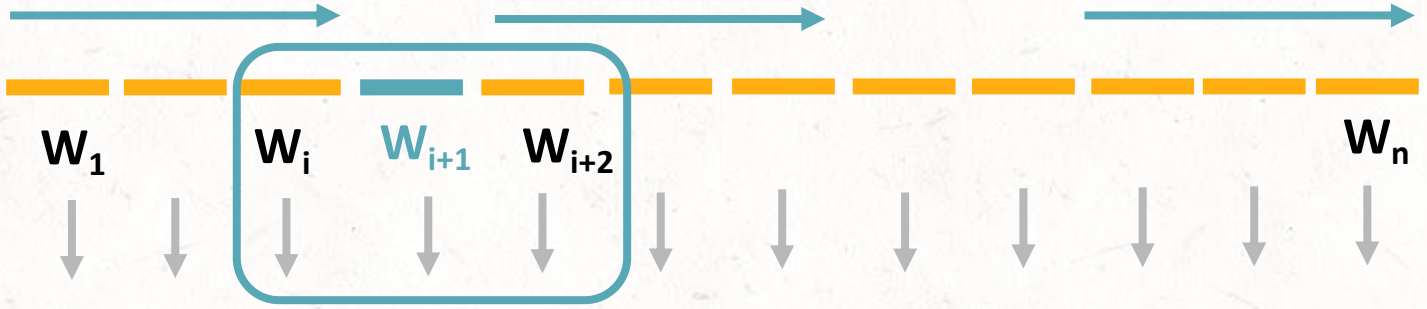
Effective number of alleles (haplotypes) = $1 / \Sigma p_i^2$

For example, a population with five alleles with frequencies $p_1 = 0.68$, $p_2 = 0.17$, $p_3 = 0.05$, $p_4 = 0.05$ and $p_5 = 0.05$ has the same effective number of alleles (2) as a population with two alleles with the same frequencies ($p_1 = 0.5$ and $p_2 = 0.5$).

Haplotype richness Drop - HRiD

Sliding windows W_i where i = 1, …, n

1



h_{wi} – effective number of haplotypes in defined window

$$\text{HRiD score } w_i = \frac{h_{wi} + h_{wi+2}}{2\,h_{wi+1}}$$

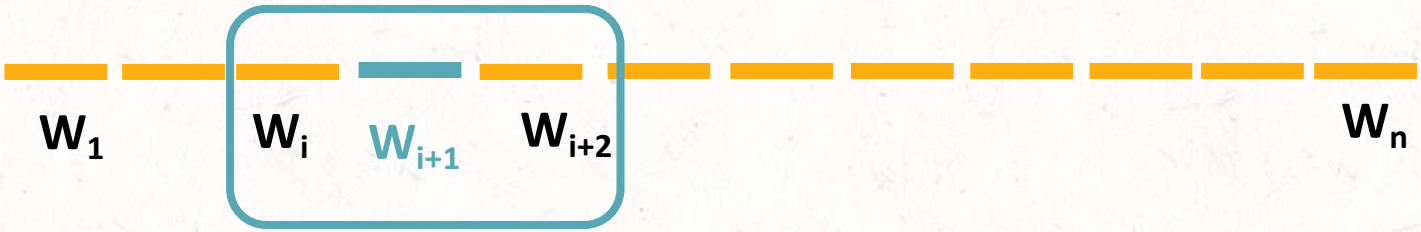
2

$$\text{HRiD score } w_i = \frac{h_{w2} + h_{w3}}{2\,h_{w1}}$$

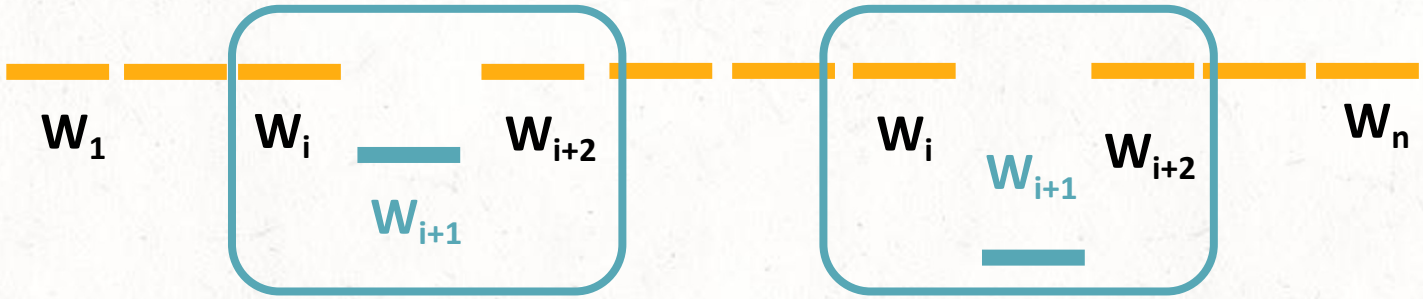
$$\text{HRiD score } w_i = \frac{h_{wn-1} + h_{wn-2}}{2\,h_{wn}}$$

No selection: HRiD ≈ 1

$$\text{HRiD score } w_i = \frac{h_{wi} + h_{wi+2}}{2\, h_{wi+1}}$$



Directional positive selection: HRiD > 1



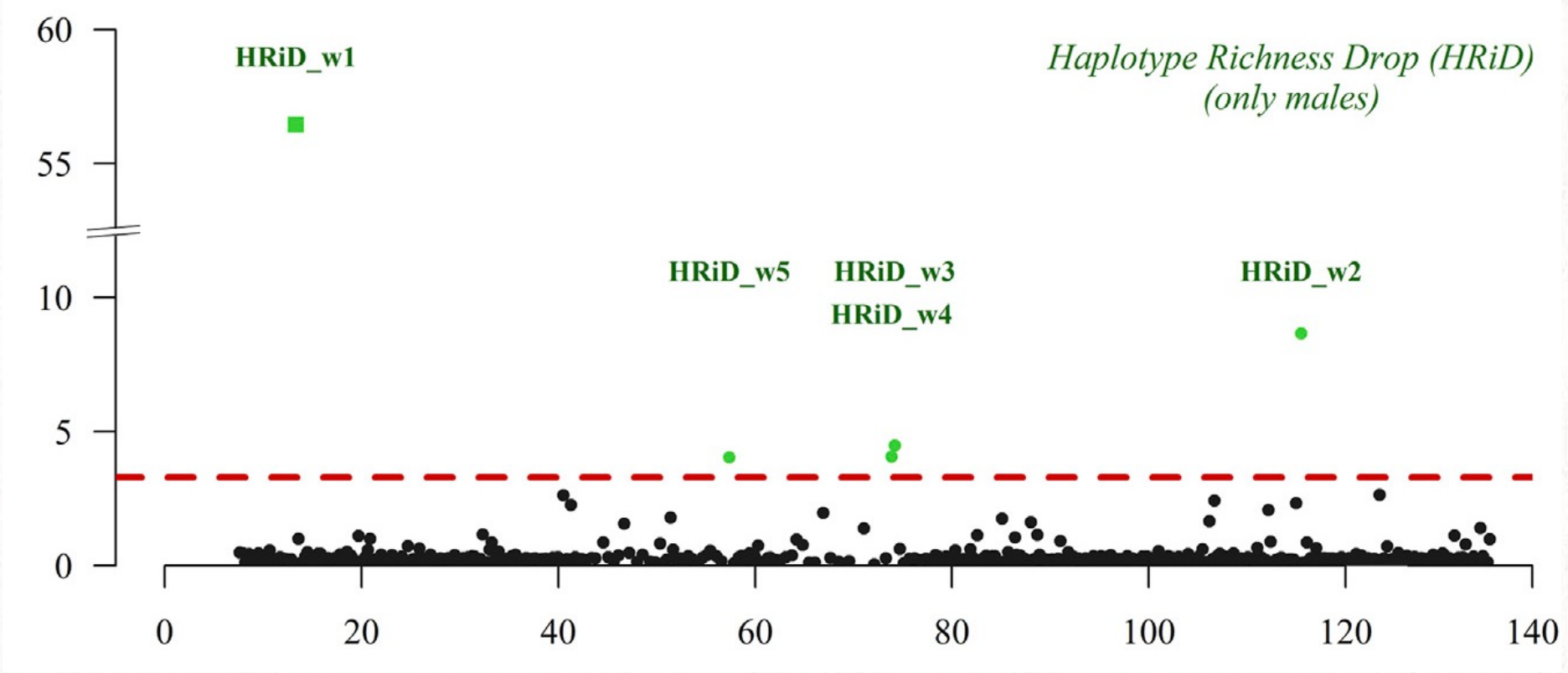
Statistical evaluation

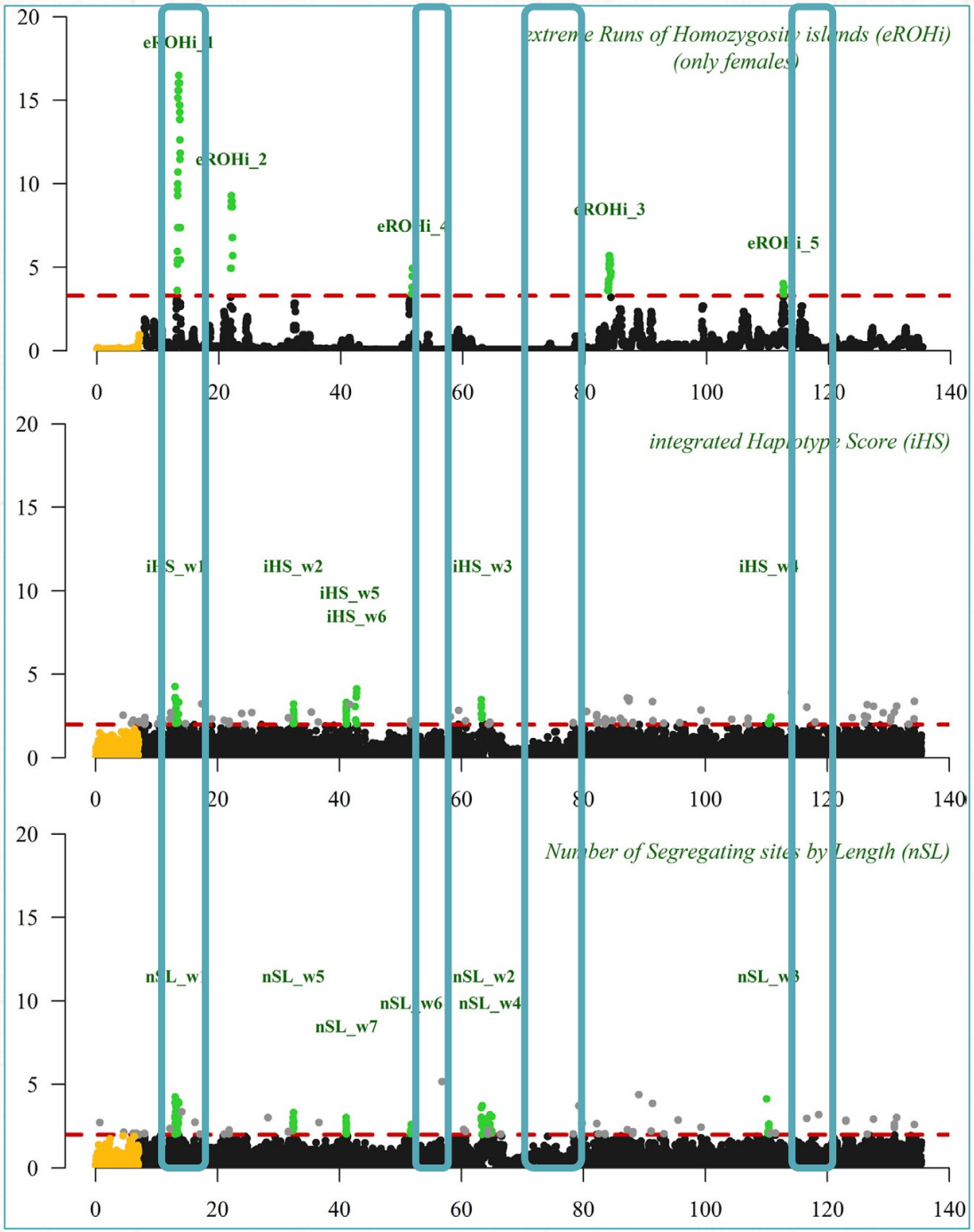
- standardisation (normalisation) and through the one-sided distribution (all windows) conversion to the – log (P values)

Empirical evaluation & comparison with other apporaches

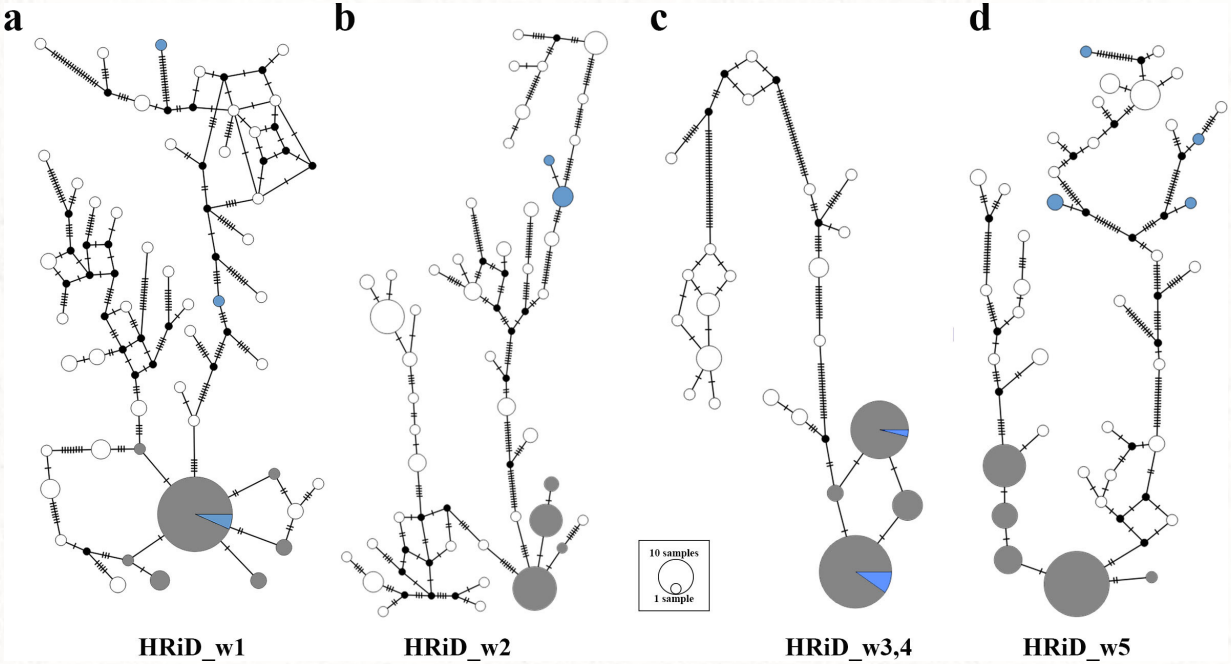
Identification of Selection Signals on the **X Chromosome** in East Adriatic Sheep (**100 males**)

– log (P values)




extreme Runs of Homozygosity islands (eROHi)
(only females)
eROHi_1
eROHi_2
eROHi_3
eROHi_4
eROHi_5
integrated Haplotype Score (iHS)
iHS_w1
iHS_w2
iHS_w3
iHS_w4
iHS_w5
iHS_w6
Number of Segregating sites by Length (nSL)
nSL_w1
nSL_w2
nSL_w3
nSL_w4
nSL_w5
nSL_w6
nSL_w7
0
5
10
15
20
0
20
40
60
80
100
120
140

Signal name	Position (Mb)	n_a	h_w	HRiD	-log(P)	Candidate genes
HRiD_w1	13.04-13.62	42	5.4	9.6	56.5	TMEM27, CDC42, CA5B, ZRSR2, AP1S2, GRPR
HRiD_w2	115.30-115.73	36	13.3	4.2	8.7	AMOT, LHFPL1
HRiD_w3	73.90-74.54	13	4.3	3.2	4.5	DACH2
HRiD_w4	73.57-74.20	10	1.9	3.1	4.1	CHM, DACH2
HRiD_w5	56.64-58.09	33	6.9	3.1	4.0	AR, OPHN1, YIPF6



Drawbacks

Sensitivity to the size of window !?

The size of the window = 70 SNPs with a slider of 35 SNPs (≈ 500 Kb & 250 Kb) to allow direct comparison of signals with those obtained by other methods.

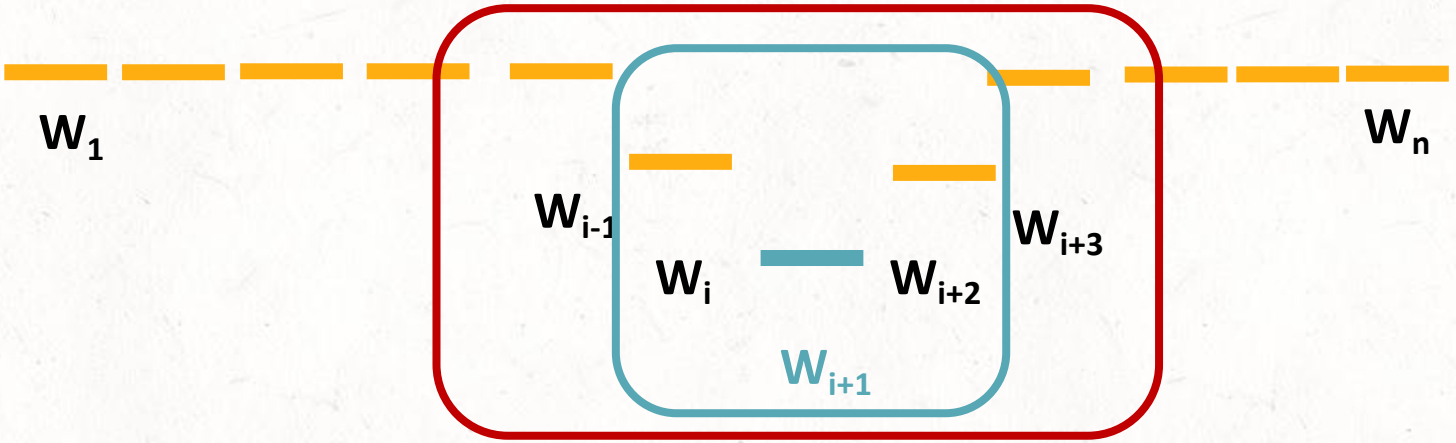
$$\text{HRiD score } w_i = \frac{h_{wi} + h_{wi+2}}{2\, h_{wi+1}}$$

Directional positive selection: HRiD > 1

Window size ?

$$\text{HRiD score } w_i = \frac{h_{wi} + h_{wi+2}}{2\, h_{wi+1}}$$

Directional positive selection: HRiD > 1

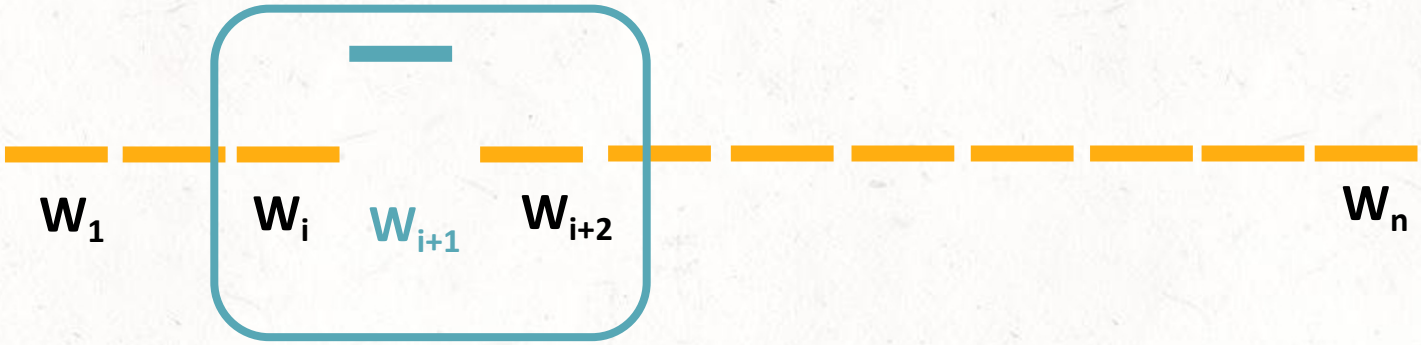


$$\text{HRiD score 1 } w_i = \frac{h_{wi} + h_{wi+2}}{2\, h_{wi+1}}$$

$$\text{HRiD score 2 } w_i = \frac{H_{wi-1} + h_{wi+3}}{2\, h_{wi+1}}$$

Possibilities and future work

- ✓ Balancing selection (overdominance): HRiD < 1



Two-sided statistical evaluation ?

- ✓ Phased diploid genomic information
- ✓ Computer simulations required
- ✓ Basic R script available, while implementation of extended version to Ghap (Yuri Utsonomiya) is discussed

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SirjeIN

any questions ? glad to answer

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LazAg

Thanks for your attention!