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Removal of haplotype segments originating from foreign breeds using optimum contribution selection

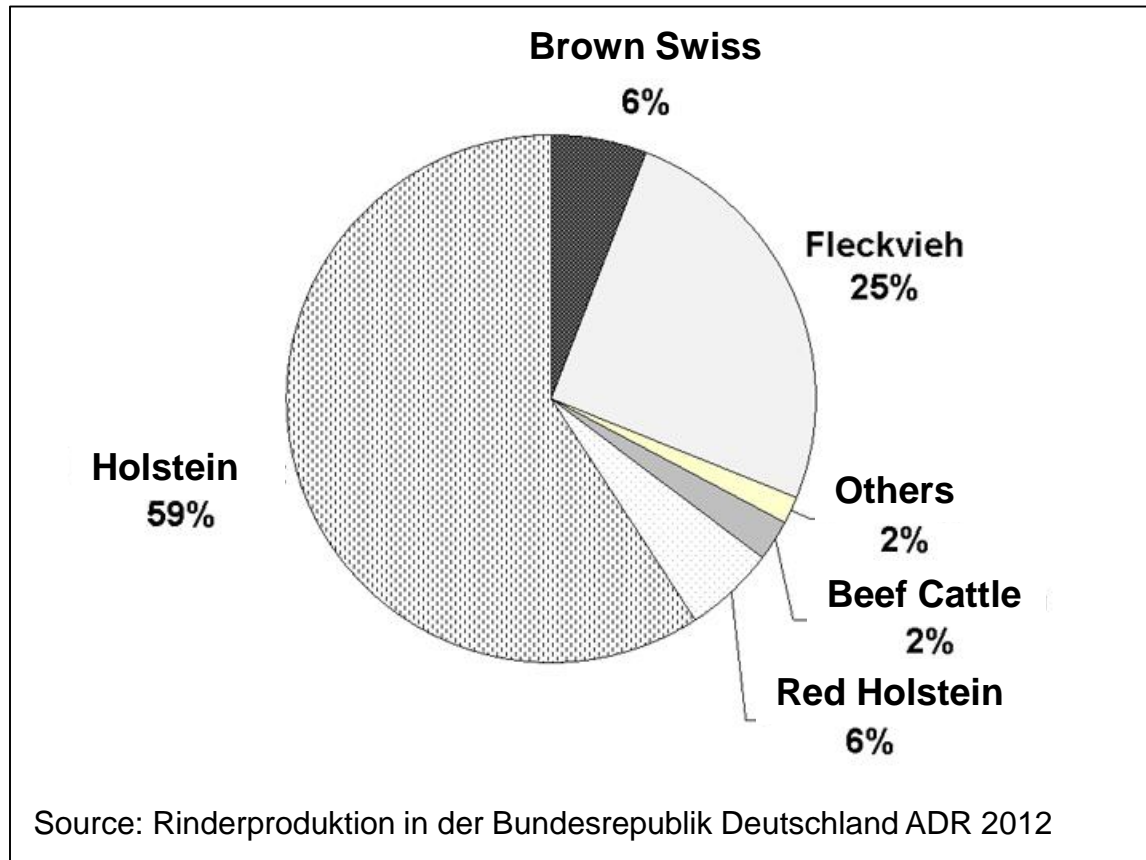
R. Wellmann, Y. Wang, J. Bennewitz

**Farm Animal Genetics and Breeding
Institute of Animal Science
University of Hohenheim**

Outline

- Current situation of local breeds
- Objectives of breeding programs
- Advanced optimum contribution selection
- Results from simulation studies
- Conclusions

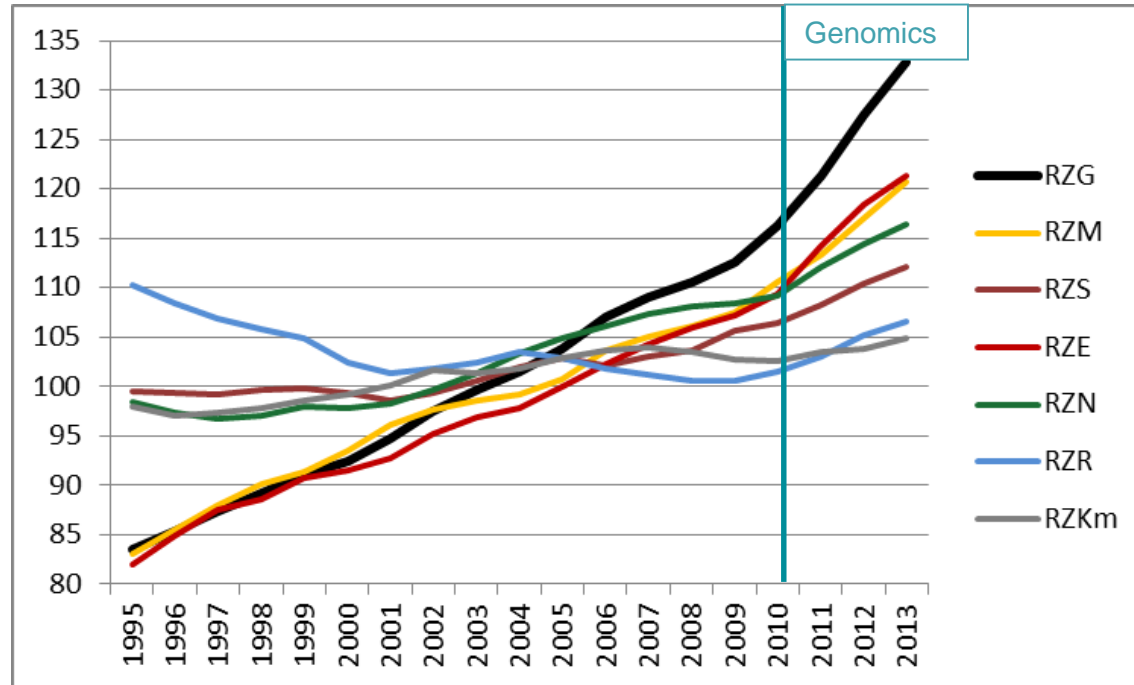
Current situation of local breeds



- Sustained trend towards the use of only a few high-yielding breeds.
- Small population sizes of local breeds.

Current situation of local breeds

ØEBV of used Holstein bulls per year (all inseminations):



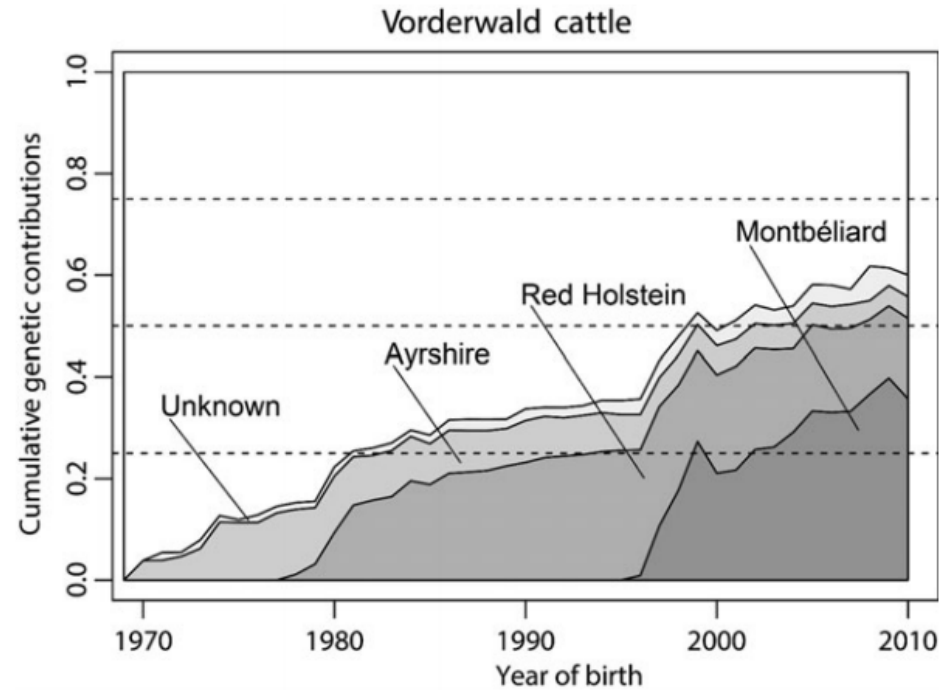
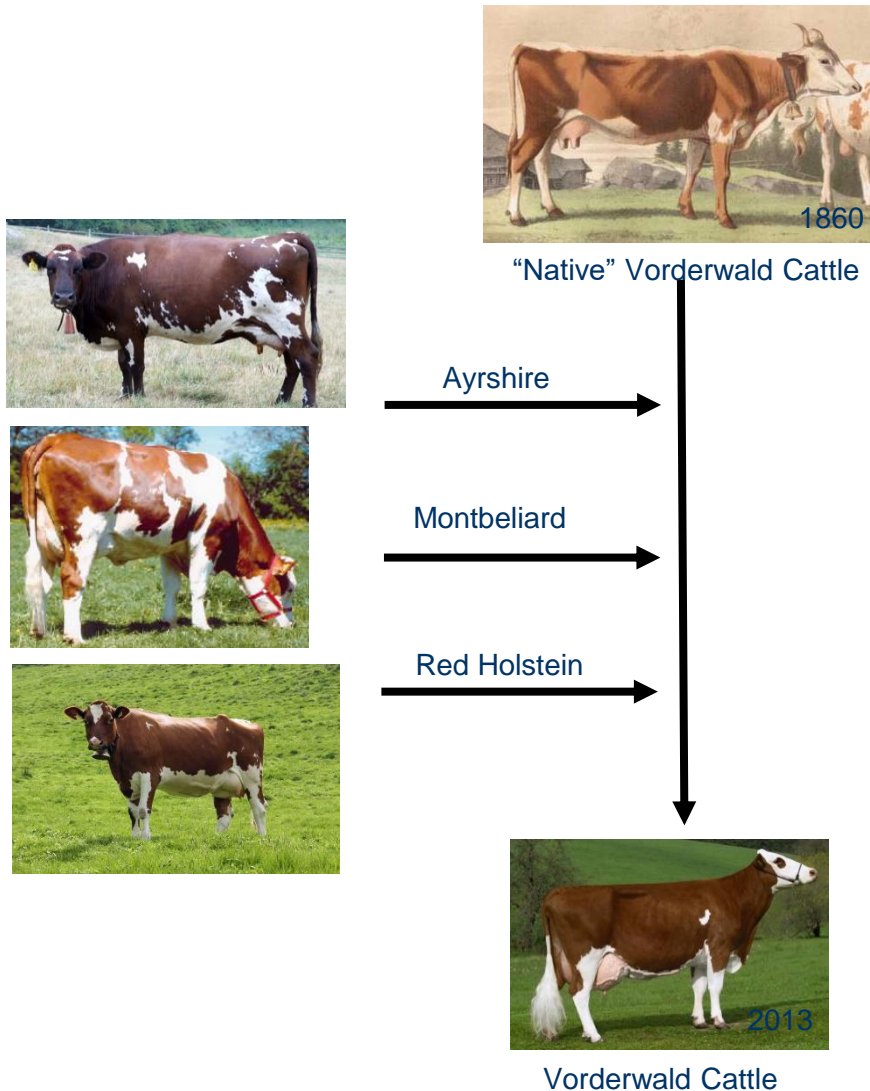
Relative scale with

Ø 100 and $s=12$

Rensing, VIT Verden, 2016

- ➔ Genomic Selection doubles genetic progress in large breeds.
- ➔ Small breeds become less competitive.

Current situation of local breeds



➔ Progressive replacement of the genetic background with genetic material from high-yielding breeds

Hartwig et al. (2014)

Current situation of local breeds

	daily gain at station	YD milk
N	846	2634
Year of birth	1973-2011	1986-2011

$$y = \sum_m b_m c_m + X\beta + Zu + e$$

c_m : Vector with genetic contributions from breed m

	daily gain ¹		YD milk ²	
	\hat{b}_m	p-value	\hat{b}_m	p-value
Unknown	119	0.202	858	<0.001
Ayrshire	-19	0.854	281	0.522
Montbéliard	138	0.014	1179	<0.001
Red Holstein	91	0.272	1193	<0.001
Others	-27	0.793	1120	<0.001

→ Introggression with foreign breeds contributed considerably to the genetic gain in Vorderwald cattle

1: Hartwig et al. (2014) 2: Hartwig et al. (2015)

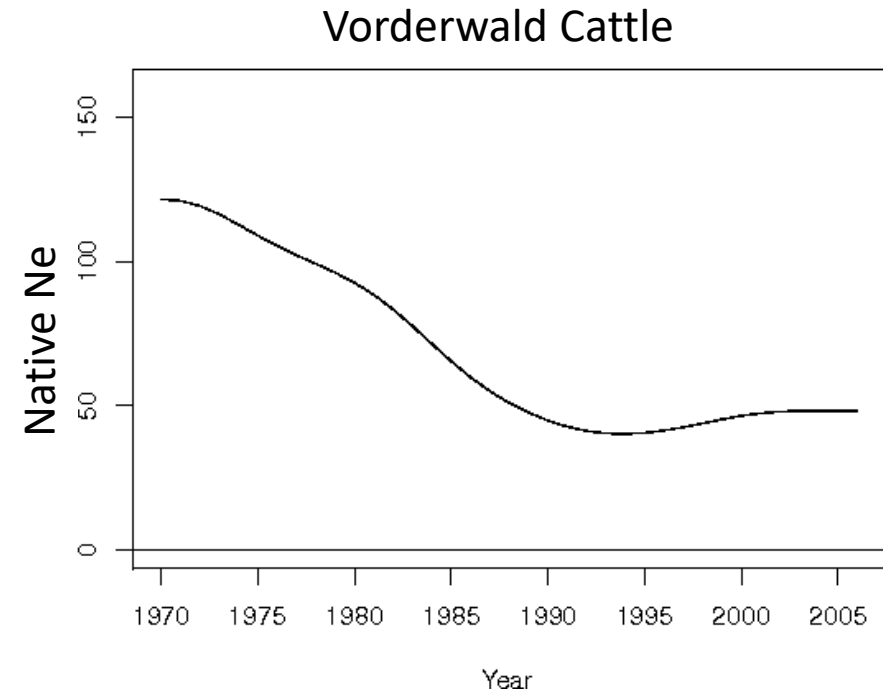


Current situation of local breeds

Native Effective Size

Size of an idealized hypothetical population, whose genetic diversity decreases at the same rate as the diversity at native alleles decreases in the breed of interest.

Wellmann et al. (2012)

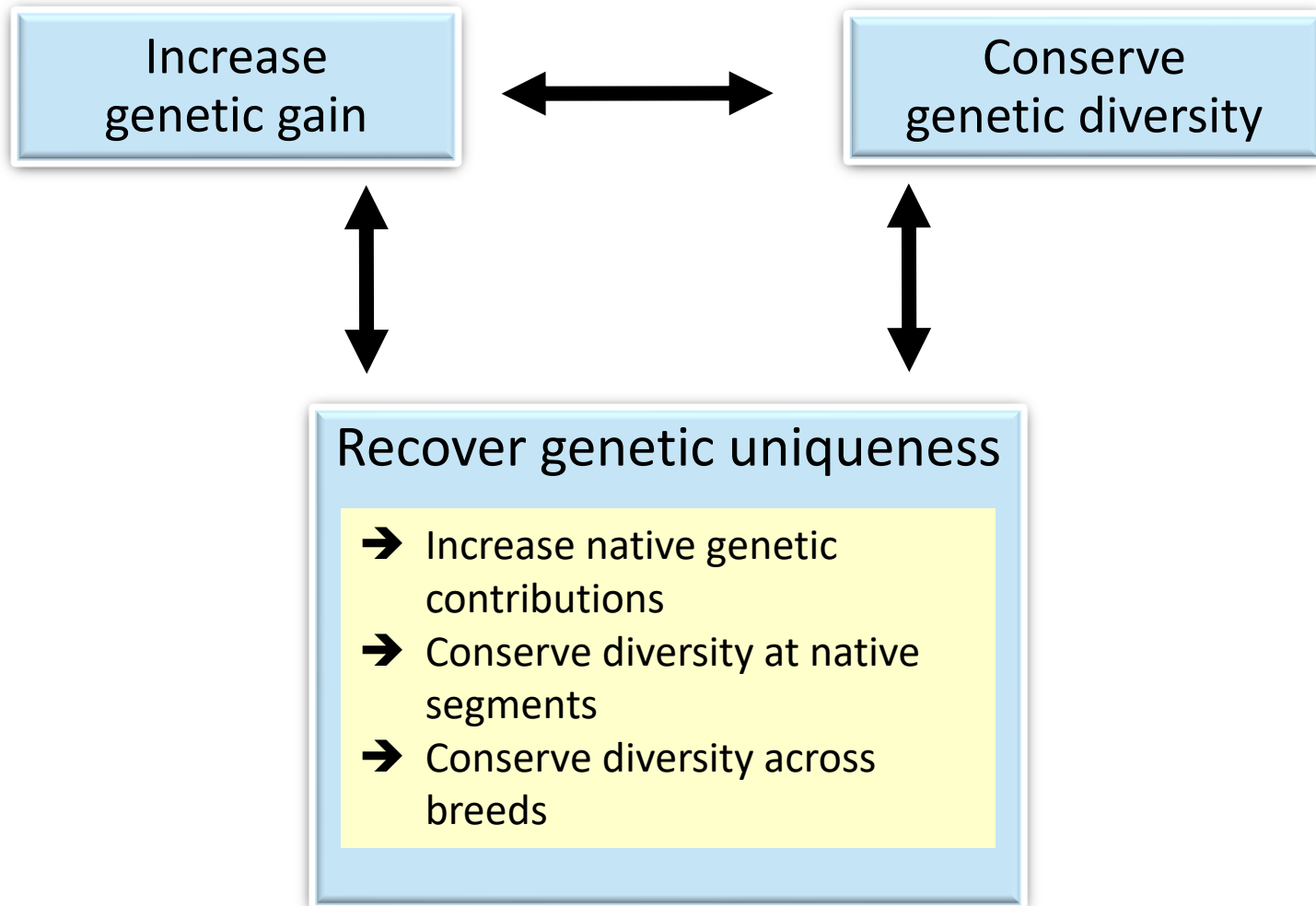


$N_e = 105$, but native $N_e \approx 50$

Hartwig et al. (2013)

→ Diversity at native alleles decreased faster than the overall genetic diversity

Objectives of breeding programs



Pedigree-based native kinship

A new method for estimating the kinship at native alleles from pedigree data $f_{PED|N}$ was developed in Wellmann et al. (2012) and applied to OCS:

Wellmann et al. *Genetics Selection Evolution* 2012, **44**:34
<http://www.gsejournal.org/content/44/1/34>

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Optimum contribution selection for conserved populations with historic migration

Robin Wellmann^{*}, Sonja Hartwig and Jörn Bennewitz

Abstract

Background: In recent decades, local varieties of domesticated animal species have been frequently crossed with economically superior breeds which has resulted in considerable genetic contributions from migrants. Optimum contribution selection by maximizing gene diversity while constraining breeding values of the offspring or *vice versa* could eventually lead to the extinction of local breeds with historic migration because maximization of gene diversity or breeding values would be achieved by maximization of migrant contributions. Therefore, other objective functions are needed for these breeds.

Advanced optimum contribution selection

Goal: Compute the optimum number of matings per selection candidate

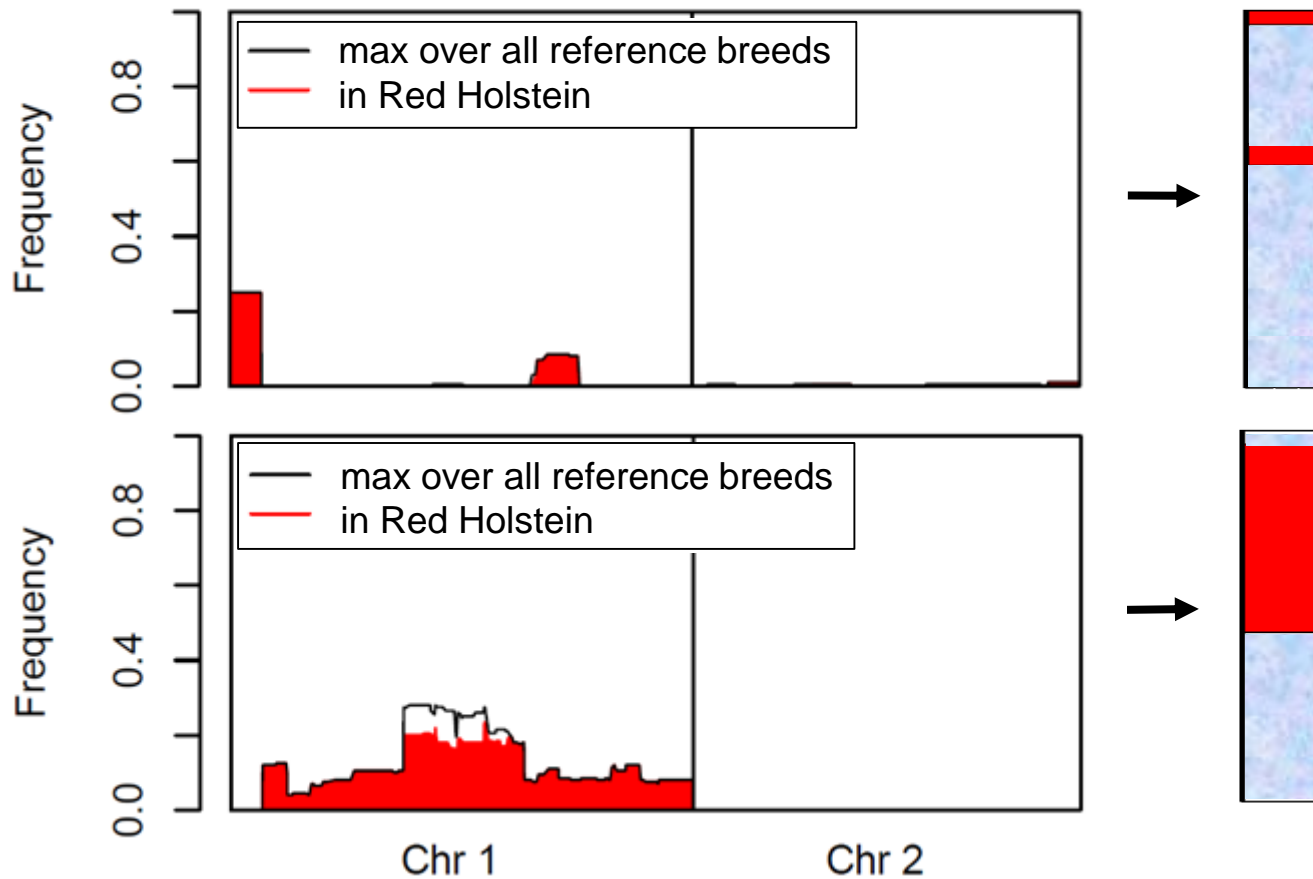
- in this next generation, or
- until the next evaluation time (year)

Parameters to be improved:	pedigree-based	segment-based
↑ average breeding value	BV	
↑ average native contribution	NC_{PED}	NC_{SEG}
↓ average kinship	f_{PED}	f_{SEG}
↓ average native kinship	$f_{PED N}$	$f_{SEG N}$

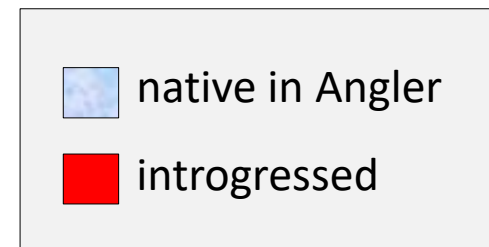
→ One of these parameters can be optimized, the others could be constrained with **R package optiSel**

Segment-based native contribution

Frequencies of haplotype segments in other breeds



Maternal and paternal haplotype of an Angler cow



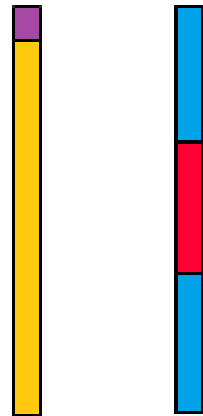
$$NC_{SEG}(i) = 0.71$$

IBD Segments

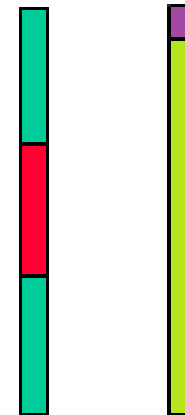
An IBD segment (Run Of Homozygosity) with respect to two haplotypes is a segment in which both haplotypes are identical.

- at least L contiguous markers must be shared,
- a minimum length is specified.

Individual i



Individual k



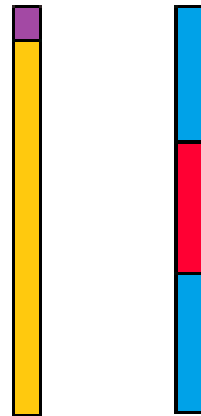
Segment-based kinship

Segment-based kinship of two individuals:

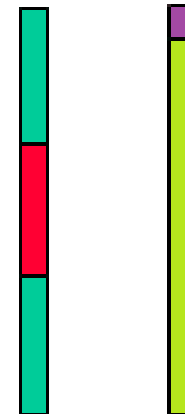
Probability that two alleles, taken at random from both individuals belong to identical segments.

de Cara et al. (2013)

Individual i



Individual k



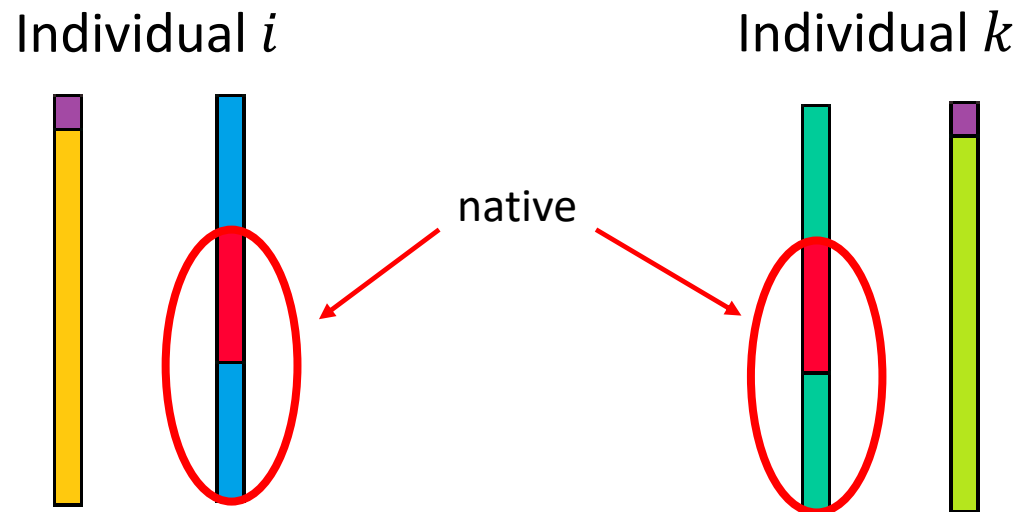
Segment-based kinship at this chromosome:

$$f_{SEG}(i, k) = \frac{(0+0.05+0.30+0)}{4}$$

Segment-based native kinship

Segment-based native kinship of two individuals:

Conditional probability that two alleles, taken at random from both individuals belong to identical segments, given that they are native.



Segment-based native kinship at this chromosome:

$$f_{SEG|N}(i, k) = 0.5$$

Segment-based kinship

Segment-based kinships f_{SEG} within and between breeds

	Angler	Fleckvieh	Holstein	Red Holstein
Angler	0.056	0.006	0.046	0.049
Fleckvieh	0.006	0.073	0.007	0.007
Holstein	0.046	0.007	0.101	0.096
Red Holstein	0.049	0.007	0.096	0.119

$L = 20$

Angler: $f_{SEG|N} = 0.073$

- Angler cattle have low kinship due to historic introgression with Red Holstein
- Native Kinship in Angler cattle is similar to kinships in other breeds like Fleckvieh

Advanced OCS with pedigree data

- 1 generation of selection
- 199 male candidates
- females: equal contributions
- f_{PED} constrained such that $N_e = 50$.

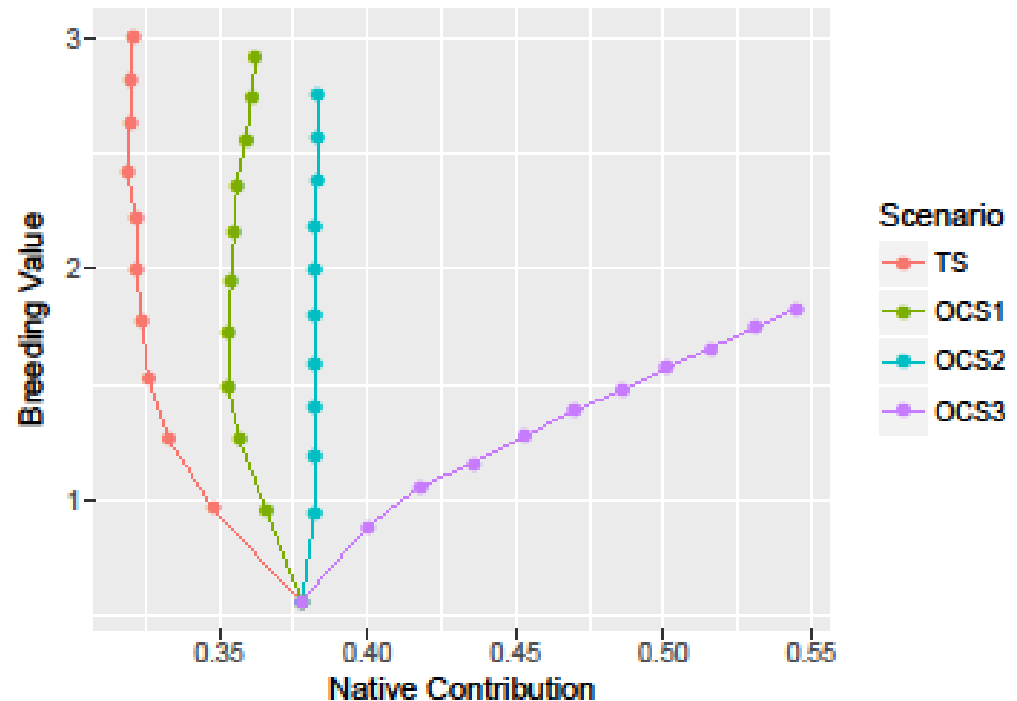
optim.	Angler				
	f_{PED}	$f_{PED N}$	NC	BV	sel.
-	0.022	0.049	0.28	0.00	-
$f_{PED N}$	0.020	0.040	0.22	-0.13	43%
NC	0.030	0.083	0.43	-0.50	11%
BV	0.030	0.082	0.26	1.02	9%

Wang et al. (2017)

- ➔ If one parameter is optimized, then the others usually become worse.
- ➔ A breeding program should account for all of them simultaneously.
- ➔ Many breeding animals needed if the aim is to minimize native kinship.

Advanced OCS with marker data

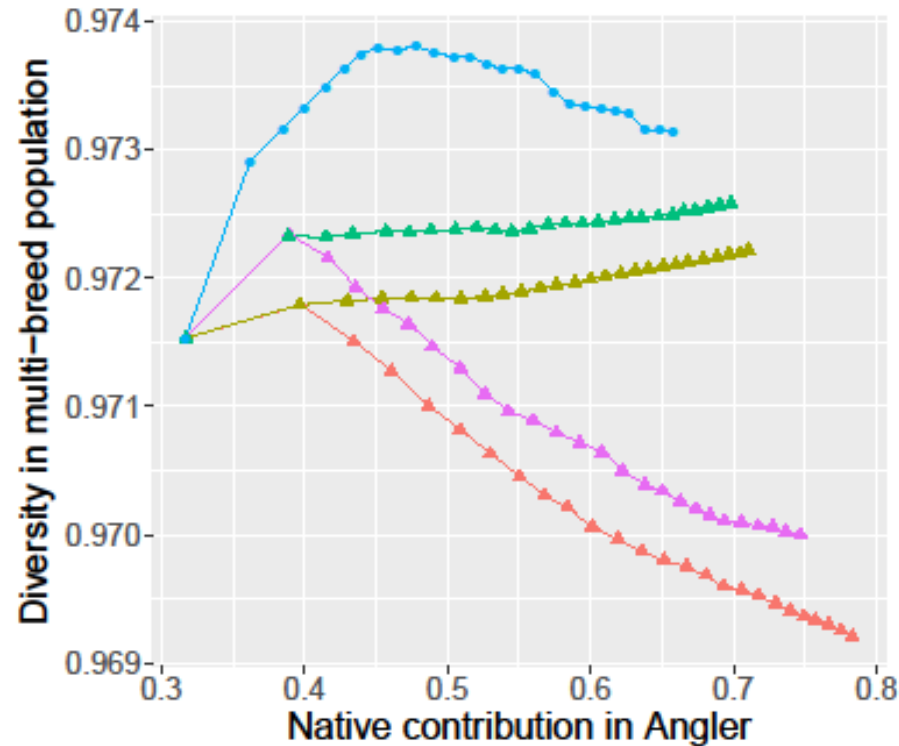
- 1500 QTN with effects from gamma-distribution, $\alpha = 0.4$
- 10 generations of selection
- 500 male candidates / gen.
- Females: equal contributions
- f_{SEG} constrained such that $N_e = 100$.
- Objective: maximize BV
- Different constraints on NC



- ➔ Truncation selection (TS) reduces the native contribution.
- ➔ If the native contribution is forced to increase (OCS3), then genetic gain is considerably smaller.

Recovering the native background

- 25 generations of selection
- 400 individuals
- Both sexes were optimized
- female contributions were constrained
- $N_e \geq 100$.



Objective

- max. multi-breed diversity
- max. native contribution

Constraints

- kin
- kin, acrossKin
- kin, acrossKin, nativeKin
- kin, nativeCont
- kin, nativeKin

- ➔ Maximizing native contributions decreases the diversity across breeds due to the loss of other rare alleles.
- ➔ **Recommendation:** Maximize the native contribution, but constrain the kinship across breeds and the increase in kinship at native alleles

Conclusions

For many breeds with historic introgression,

- the original genetic background vanishes,
- the diversity at native alleles decreased faster than the overall genetic diversity (native $N_e < N_e$).
- native contributions and total merit are negatively correlated.

→ Efforts should be made to de-extinct these breeds

For recovering the native background:

- Maximize the native contribution or a selection index with an appropriate weight given to the native contribution.
- Constrain the increase in native kinship such that native $N_e \geq 75$.
- Constrain the increase in kinship across breeds.

→ R package optiSel available for advanced OCS

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Recovering the native background



Thank you for your attention!