Estimation of breed composition, breed heterosis and epistatic loss for percent of live spermatozoa in admixed Swiss Fleckvieh bulls

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Introduction

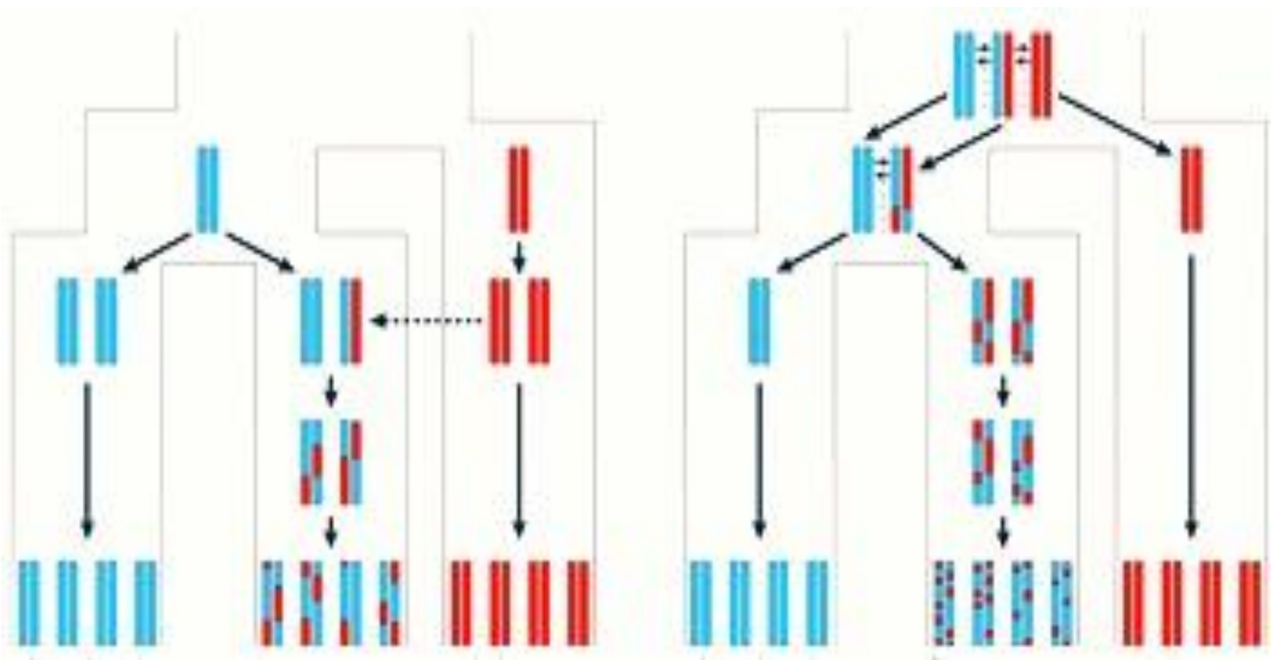
Crossbreeding

- Most common mating in livestock and plant breeding where sire and dams originate from different parental lines
- Optimizes genetic merit of crossbred offspring
  - ✓ Introducing favorable genes
  - ✓ Decreasing inbreeding depression
  - ✓ Benefit from gene interaction of heterosis

Heterosis

- Superiority of a crossbred progeny compared with its mid-parents average for a particular trait due to any non-allelic gene interaction
- Heterosis extent
  - ✓ Difference in frequency of the genetic variants contributed in heterosis
  - ✓ Number of involved parental breeds
  - ✓ Type of crossbreeding (two-way, three-way, backcrossing)

Figure 1 Ancestry pattern along the genome of admixed individuals



Schreiber & Akey, *Nature Review Genetics* (2015)

Table 1 Heterosis as apercentage of full heterosis for different types of crosses

Type of cross	Heterosis %
F1 (S × T)	100
F2 (S × T) × (S × T)	50
Back cross S × (S × T) or T × (S × T)	50
Second generation of a rotational cross S × (T × (S × T))	75
Third generation of a rotational cross T × (S × (T × (S × T)))	62.5
Rotational cross after many generation	66.6
Second generation of a synthetic line (= F2) (S × T) × (S × T)	50
Third generation of a synthetic line (= F3) (S × T) × (S × T) ×	50
(S × T)	50
Synthetic two-breed line after many generations	66.6
Synthetic three-breed line after many generations	

Recombination loss

- Unfavorable gene effects in crossbred offsprings due to breakdown of preantal epistatic gene complex
- Measure of deviation from linear association of heterosis
- Average fraction of indepenenlty segrgating gametes which are expected to be non-parental (Disckerson , 1965)
- Kinghorn (1982) defined the epistatic loss term (e_x)as the probability two random chosen non-allelic genes (derived from either one or both parents) originate from different breeds

Aim of study

Estimation of average breed effect , heterosis and epistatic loss on percentage of live sperm in Swiss Fleckvieh admixed bulls, using genomic information

Materials and methods

Red Holstein Frisian

Swiss Simmental

- High milk production
- Functional and fitness

Swiss Fleckvieh

Phenotypic records

Table 2 overall phenotypic data information

Breed	Holstein Frisian, Simmental, admixed Swiss Fleckvieh
Trait	Live sperm (%)
No. of records	68,475
No. of bulls	1298
AI Station	Mülligen, Switzerland,
Dates	2000-2015

- ✓ Remove bulls with less than 10 records
- ✓ Remove ejaculates with < 3 days interval
- ✓ Discard ejaculates beyont the range of ± 3 standar deviation

43,782 recordsfor 1296 bulls

Genotypic records

- Genotypes from Swissherdbook cooperative Zollikofen from different Illumina® chip (50K,150K and HD)

- Imputed genotypes with 44,999 subset, using ***F-impute*** software (Sargolzaei, 2014) Standard quality control hasd been pweformed
- After applying standard quality control **38,299 SNP for 147 HF, 207 SI and 815 SWF (1169 bulls)** (PLINK2)

Statistical analysis (lme4, CRAN package)

$$y_{ijklmn} = \mu + \alpha_i + age_j + cont_k + elps_l + assist_m + bp_{ijklmn} + \varepsilon_{ijklmn}$$
$$y_{ijklmn} = \mu + \alpha_i + age_j + cont_k + elps_l + assist_m + bp_{ijklmn} + bhet_{ijklmn} + \varepsilon_{ijklmn}$$
$$y_{ijklmn} = \mu + \alpha_i + age_j + cont_k + elps_l + assist_m + bp_{ijklmn} + epstloss_{ijklmn} + \varepsilon_{ijklmn}$$
$$y_{ijklmn} = \mu + \alpha_i + age_j + cont_k + elps_l + assist_m + bp_{ijklmn} + bhet_{ijklmn} + epstloss_{ijklmn} + \varepsilon_{ijklmn}$$

$\boldsymbol{y_{ijklmn}}$ observation for each bull

$\boldsymbol{\mu}$ overall mean

$\boldsymbol{\alpha_i}$ random permanent effect of each bull

$\boldsymbol{age_j}$, $\boldsymbol{cont_k}$, $\boldsymbol{elps_l}$ and $\boldsymbol{assist_m}$ fixed effects of age, contemporary group, ejaculate interval and sperm collector respectively

$\boldsymbol{bp_{ijklmn}}$ regression coefficient for breed percent (HF proportion) averaged across incorporated SNP

$\boldsymbol{bhet_{ijklmn}}$ regression coefficient for breed heterosis averaged across SNP

$\boldsymbol{epstloss_{ijklmn}}$ regression coefficient for epistatic loss (Kinghorn, 1982)

$\boldsymbol{\varepsilon_{ijklmn}}$ random error associated with each observation (SAS, proc mixed)

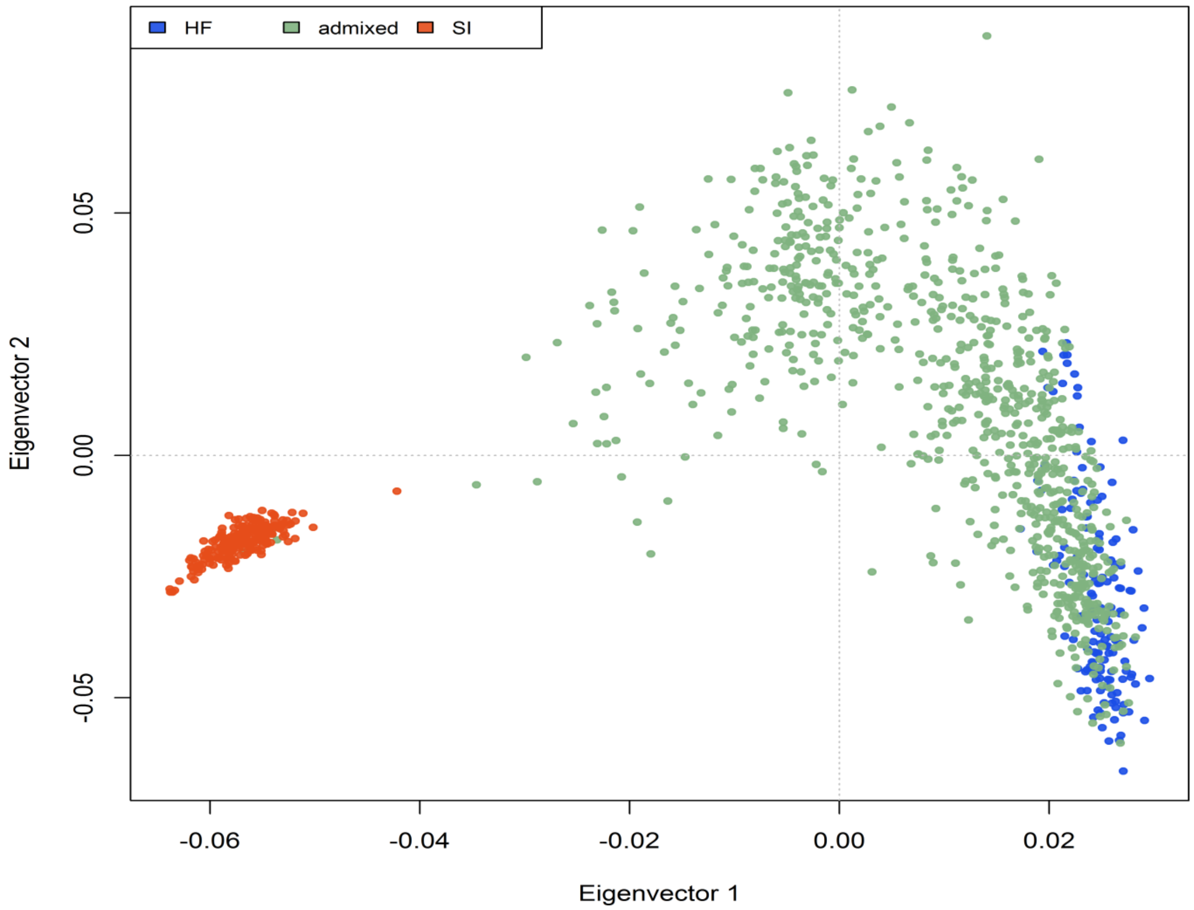
Regression coefficinets

- **Breed percent** the average of HF proportion for all incorporated SNP extracted from LAMP (Sankararaman *et al*. 2008)
- **Breed heterosis**
  - ✓ 0 if both allele originated from the same origin
  - ✓ 1 if alleles had different ancestry origin
  - ✓ taking the average of breed heterosis for all incorporated SNP
- **Epistatic loss**
  - ✓ Sampling randomly 100,000 two SNP across the whole genome
  - ✓ randomly chosen one alllele from each SNP
  - ✓ 0 if both non parental alleles had different ancestry origin
  - ✓ 1 if they had same origin

Results

Population structure

Figure 2 PCA results for HF and SI pure ancestral population and admixed bulls



Ancestry proportion

Pedigree

HF 0.85 : SI0.15

ADMIXTURE (Alexander *et al.* 2009)

HF 0.82 : 0.18 (0.16 SD)

Pearson correlation : **0.97**

Comapring models

- Fixed effects showed significant differences between models, except sperm collector

Table 3 Model Adequacy comparing between models

Models	1 (bp)	2(bp+bhet)	3(bp+epst)	4(bp+bhet+epst)
1 (bp)		33	30	31
2(bp+bhet)			3	2
3(bp+epst)				1

- Bp, bhet and epst denote for breed percent, breed heterosis and epistatic loss
- AIC is the Akaike information criteria and ΔAIC is the difference
- ΔAIC < 2 no significant difference between models
  3 < ΔAIC < 7 considerably less support
  ΔAIC > 7 no likely

Comparing the model based ΔAIC (Akaike information criteria)

- **model 1 with 2,3 and 4** model 1 is not likely, breed heterosis has significant effect in the model
- **model2 and 3** model 3 with less support
- **model 2 and 4** no significant difference
- **model 3 and 4** no significant difference

- The classical model with breed percent and breed heterosis was most probable model
- Considering epistatic loss did not have significant influence

Table 4 Regression coefficients (±standard error) for percent of live spermatozoa with different models

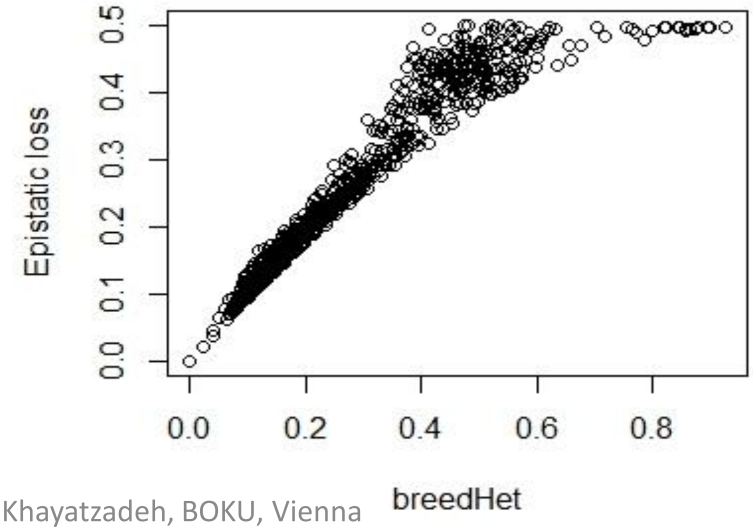
Models	Breed percent	Breed heterosis	Epistatic loss
1	0.65 (0.19)***		
2	0.41(0.19)***	2.00(0.34)***	
3	0.37 (0.20)***		2.03(0.41)***
4	0.43(0.20)***	2.5(1.39)***	-0.65(1.68)n.s

Epistatic loss (Kinghorn, 1982)

**** $p < 0.0001$, *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$, $^{n.s}$ $p > 0.1$

Discussion

- The classical model with breed percent and breed heterosis was most probable and considering epistatic loss did not have significant influence in the model
- Separation of the effects is not completely possible due to high correlation between breed heterosis and epistatic loss
- Confounding the effect of breed heterosis and epistatic loss was also reported by Fries *et al.* (2002)



Conclusions

- Crossbred populations provide unique opportunity to study non-additive genetic effects of heterosis and epistatic loss
- Usually higher heterosis is expected for traits with low heritability such as reproduction traits
- Heterosis effect on percentage of live sperm in admixed Swiss Fleckvieh bulls was expected to be 2.00 (±0.34) % more in compare with the mean of purebred HF and SI
- Including epistatic loss showed 0.65 % decrease in percentage of live sperm
- Due to high correlation between these two effects, the estimates of heterosis and epistatic loss were confounded

Thank you!