

Prediction of global and local Simmental and Red Holstein Friesian admixture levels in Swiss Fleckvieh cattle

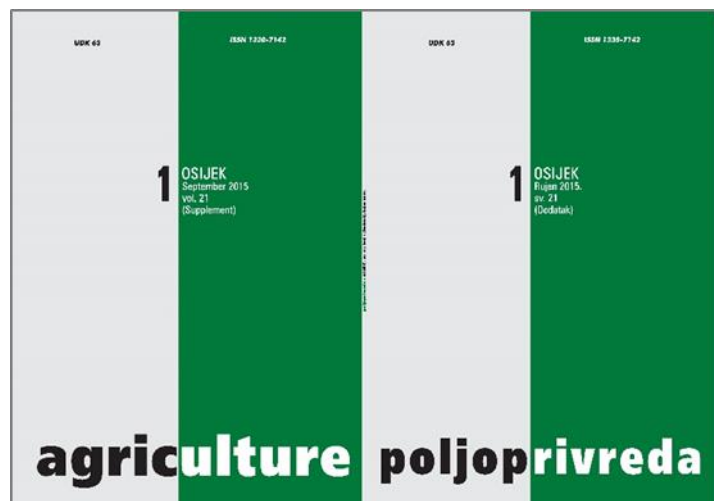
Khayatzadeh, N., Mészáros, G., Gredler, B., Schnyder, U., Curik, I., Sölkner, J.

Poljoprivreda/Agriculture

ISSN: 1848-8080 (Online)

ISSN: 1330-7142 (Print)

<http://dx.doi.org/10.18047/poljo.21.1.sup.14>



Poljoprivredni fakultet u Osijeku, Poljoprivredni institut Osijek

Faculty of Agriculture in Osijek, Agricultural Institute Osijek

PREDICTION OF GLOBAL AND LOCAL SIMMENTAL AND RED HOLSTEIN FRISIAN ADMIXTURE LEVELS IN SWISS FLECKVIEH CATTLE

Khayatzadeh, N.⁽¹⁾, Mészáros, G.⁽¹⁾, Gredler, B.⁽²⁾, Schnyder, U.⁽²⁾, Curik, I.⁽³⁾, Sölkner, J.⁽¹⁾

Original scientific paper

SUMMARY

In this study we estimated levels of local ancestry for individuals of the Swiss Fleckvieh dairy cattle population. It is a composite breed descending from two pure breeds, Simmental (SIM) and Red Holstein Friesian (RHF). Illumina BovineSNP50 Beadchip genotyping data for a total of 500 pure and admixed animals were used for the analysis. The global ancestries estimated by Hidden Markov model were 0.68 and 0.32 for RHF and SIM respectively. Local ancestry levels investigated along chromosomes 2, 3 and 13 indicated that there were some regions across the chromosomes exhibiting substantial fluctuations in admixture. On chromosome 2, in the range of 28 to 31, 41 to 46 and 54 to 56 Mb RHF ancestry is substantially higher than average (0.77-0.78). These regions on chromosome 2 are wide, indicating recent admixture. Along the segments on chromosome 2, many QTLs related to dairy, conformation, reproduction, health and carcass traits were found. We observed sharper excess in favour of SIM on chromosome 3, whereas different regions with excess of RHF and SIM were found out on Chromosome 13. At the first part of chromosome 13, an excess of RHF was observed. Moreover, in regions between 40 and 57 Mb excess of SIM, referred to recent admixture was detected. In respect of RHF chromosome segments in admixed animals, dairy, reproduction and health QTLs were found. In positions where more Simmental segments were detected, QTLs related to meat and carcass traits as well as udder health traits were found. In conclusion, the authors believe that estimation of local admixture levels in crossbred populations can add information to the composite breeds history of selection.

Key-words: cattle, admixture, SNP, global ancestry, local ancestry, QTL

INTRODUCTION

Crossbreeding is a mating system that is widely used in dairy cattle to improve milk production as well as health, reproduction and survival traits. Since differences between breeds are larger than the differences within breeds, extra benefits can be achieved from heterosis due to crossbreeding (Swalve, 2007).

The amount of heterosis depends on the difference in allele frequencies between pure ancestral populations and it will be maximized when one allele is fixed in one pure population and the alternative allele is fixed in the other population (Caraviello, 2004).

With recombination, taking place at each generation, the genome of admixed animals is a mosaic of segments originating from different ancestral popula-

tions. In a recently admixed population, the fraction of ancestry (termed global ancestry) from each pure population varies substantially across individuals. However, the proportion of ancestries along the chromosomes (termed local ancestry) of an individual varies as well, and the wideness of the mosaic segments can also lead us to infer the age of the admixture (Sankararaman et al., 2008; Padhukasahasram, 2014; Zhang and Stram, 2014).

(1) M.Sc. Negar Khayatzadeh, Dr. Gábor Mészáros, Prof. Dr. Johann Sölkner (johann.soelkner@boku.ac.at) - BOKU, Department of Sustainable Agricultural Systems, Division of Livestock Sciences (NUWI), Augasse 2-6, 1090 Vienna, Austria, (2) Birgit Gredler, Urs Schnyder - Qualitas AG, Chamerstrasse 56, Ch-6300, Zug, Switzerland, (3) Prof. Dr. Ino Curik - Department of Animal Science, Faculty of Agriculture, University of Zagreb, Svetošimunska cesta 25, 10000 Zagreb, Croatia

Pedigree information is conventionally used to estimate global ancestry and assumes equal contributions of all ancestors of a generation (Sölkner et al., 2010). Admixture analysis based on the single nucleotide polymorphism (SNP) chip data is expected to replace pedigrees with high accuracy (0.97) or pedigree analysis in case of non-pedigreed populations (Frkonja et al., 2012).

The estimation of genetic ancestry in human populations is widely used to control population stratification in association studies (Kang et al., 2009; Zhang and Stram, 2014) and admixture mapping (Seldin, 2007; Chen et al., 2014). Admixture estimation based on molecular data has also been performed in livestock. Bray et al. (2014) investigated the historic population processes using microsatellite markers in a Lincoln Red breed. Some studies have also used SNP chip data to detect the levels of the admixture in sheep and cattle populations (Sölkner et al., 2010; Frkonja, et al., 2012, García-Ruiz et al., 2015).

In this study, we estimated the local admixture with LAMP program for Swiss Fleckvieh admixed animals, using SNP chip data to consider the trends of the admixture at local levels across three autosomal chromosomes (2, 3 and 13). Our aim was to monitor which chromosome segments on these three chromosomes show deviations from global admixture, higher/lower proportions of the ancestral Simmental (SIM) and Red Holstein Friesian (RHF) populations. Such deviating regions were then inspected for genes and QTL to infer causes of selective pressure in the recently admixed population.

MATERIAL AND METHODS

Swiss Fleckvieh is a composite breed of Simmental and Red Holstein Friesian that has been established over the last forty years with the emphasis on high milk production derived from the Holstein Friesian as well as on additional traits like beef value, fitness traits and longevity of Simmental breed. The genotype data from the Illumina Bovine SNP50 beadChip were available for 100 pure RHF, 100 pure SIM and 300 Swiss Fleckvieh bulls. The quality control of the data was performed with PLINK 1.07 (Purcell et al., 2007). Dataset was controlled to exclude SNPs with call rate of <95% that were monomorphic (based on minor allele frequency) and with $p\text{-value} < 1.0 \times 10^{-6}$ deviating from Hardy Weinberg Equilibrium (HWE). The animal samples with more than 5% missing genotypes and SNPs with more than 5% missing data were removed from the dataset. SNPs located on sex chromosomes were also not used in the analysis. There were 39,525 SNPs and 485 animals left after pruning and filtering.

We performed unsupervised global ancestry estimation with the full SNP set applying Hidden Markov Models (HMM) using ADMIXTURE (Alexander et al., 2009) with the number of ancestral populations fixed at 2. Global estimates were used as a reference metric to scale the local ancestry estimates.

Estimation of local ancestry can also be performed based on HMM for every single SNP on each chromosome separately. In this study we used LAMP software calculating local ancestry based on HMM. We ran LAMP in the LAMPANC mode and used the allele frequencies of the Red Holstein Friesian and Simmental as information of ancestral populations. The following configuration parameters were used: admixture proportions (α) = 0.68, 0.32 based on the results from ADMIXTURE, number of generations since admixture (g) = 7, recombination rate (r) = $1e-8$, fraction of overlap between adjacent windows (offset) = 0.2. LAMP relies on a predefined set of ancestry informative markers that are in low linkage disequilibrium ($r^2 < 0.1$ for each pair of selected SNPs). We did not include LD in this research.

Furthermore, LAMP estimates the locus-specific ancestry for each individual with respect to pure breeds. Under the assumption of a dihybrid population model, marker specific ancestries were estimated across 3 autosomal chromosomes (2, 3 and 13) for each animal separately. The genome wide mean estimations were used as reference line for local ancestry detection. For 300 admixed animals, we computed the average locus-specific ancestry level. We then calculated r ancestry by subtracting the genome wide ancestry from the average locus specific ancestry for each of the two ancestry components (Tang et al., 2007).

RESULTS AND DISCUSSION

At first individual admixture proportions of Swiss Fleckvieh animals based on both pedigree and 39,525 SNPs information were estimated. Figure 1 presents individual admixture levels of admixed animals based on pedigree and SNP information. Animals were ordered from the highest to lowest RHF proportions based on pedigree. Global admixture based on pedigree and using 39,525 SNPs indicated the high correlation between estimations (0.97) as, also, inferred by Frkonja et al. (2012) for the same dataset. The average admixture level based on pedigree was 0.69 RHF (with 0.20 standard deviation) whereas based on SNP data it was 0.68 RHF (with 0.19 standard deviation).

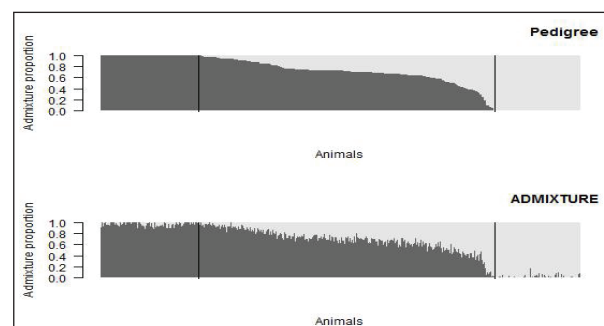


Figure 1. Genetic contributions derived from pedigree and from SNP information (39,525) using ADMIXTURE (RHF = 1, SIM = 0)

Figure 2 displays average ancestry across chromosomes 2, 3 and 13 derived from LAMP program for admixed animals, keeping the same order as in Figure 1, i.e. sorting animals from high to low RHF levels based

on pedigree information. The average ancestry regards to RHF across chromosomes 2, 3 and 13 was estimated 0.73, 0.70 and 0.65 respectively.

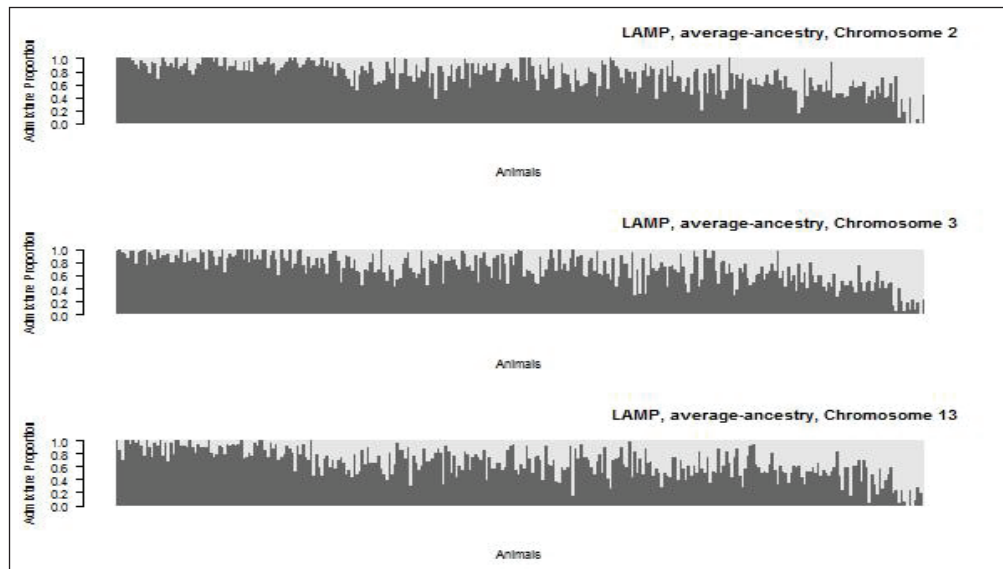


Figure 2. Average ancestry estimates across chromosomes 2, 3 and 13 (RHF=dark grey, SIM= light grey)

Figure 3 shows the average excess or deficiency of local ancestry from genome wide ancestry at each SNP location on chromosomes 2, 3 and 13 for all 300 admixed animals. The graphs indicate that some SNPs

have different amount of proportion of each breed across these chromosomes. Deviations on most locations are in accordance with genome wide ancestry. However, some regions exhibit extreme fluctuations.

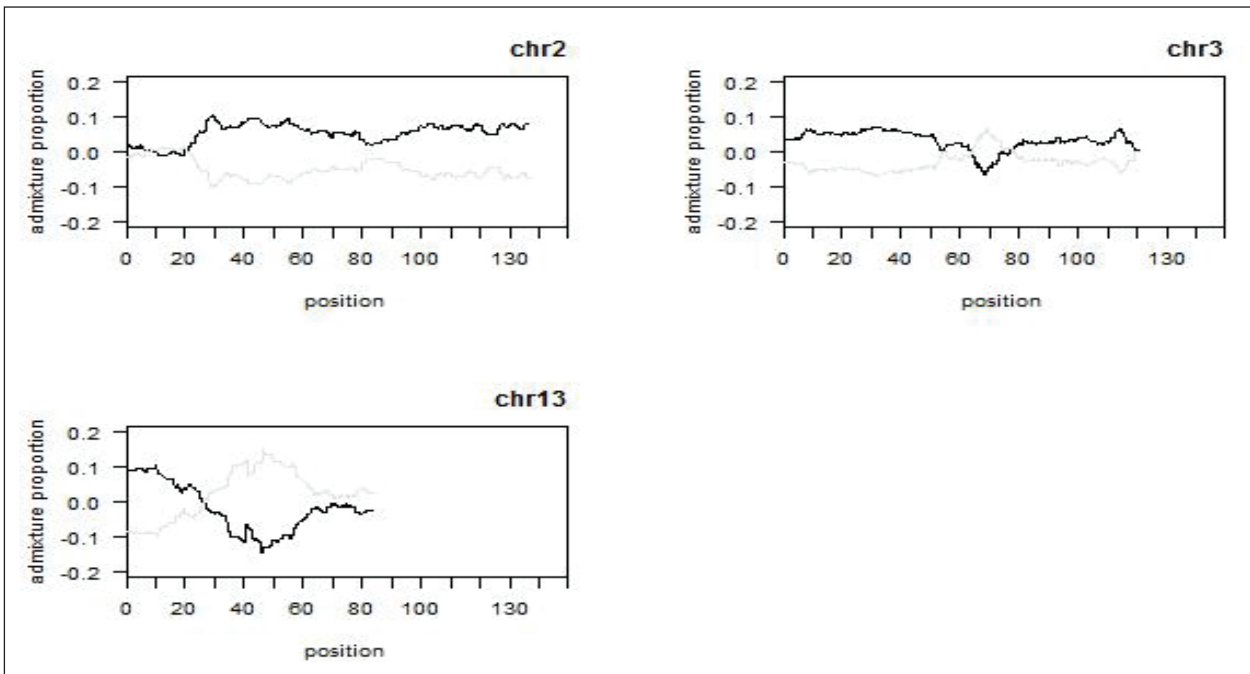


Figure 3. Genome wide variation of ancestry in Swiss Fleckvieh, the Y-axis shows the delta ancestries at the corresponding SNP for 300 admixed animals (RHF=dark grey, SIM= light grey lines)

Based on the results in Figure 3, we observed some excess and deficiency of local ancestry from global ancestry estimation, not probable only by chance, and indicated that the genomes of the admixed animals in these parts have higher proportions of one breed and long range of LD. The genomes of admixed animals contain wide segments of each ancestral breed (graphs not shown), indicating recent admixture. Therefore, extreme deviations from genome wide admixture may have been caused by recent selection.

On chromosome 2 some excesses of RHF have been indicated in 28 to 31 Mb (0.77-0.78), 41 to 46 Mb (0.77) and 54 to 56 (0.77) Mb positions, proportions that deviate by 0.10 or more from estimates of global admixture (0.68). The fact that the chromosome segments deviating from expectation are wide indicates recent admixture and not enough time for selection to sharpen the signal.

We used *CattleQTLdb* website to examine whether such regions harbour QTL. The results are summarized

in Table 1. On chromosome 2 we found QTLs associated to dairy, conformation, reproduction, health and carcass traits. On chromosome 3, we have searched for QTLs in the region of 67 to 72 Mb. In this region only one QTL associated with fertility was detected.

The SNP pattern on chromosome 13 indicates excess of RHF ancestry around Mb 0-15 and SIM ancestry around Mb 40-60. The most important reason for the excess of RHF segments in the first part of the chromosome may be selection for calving ease, as this used to be one of the most important problems in the Simmental breed. A QTL for calving ease was detected in this region in previous studies (Table 1). On the other hand, selection for udder health (somatic cell score, mastitis), female fertility and meat/carcass traits certainly preferred SIM segments in the middle of chromosome 13, see Table 1 for information about respective QTL.

Table 1. The segment of chromosome 2, 3 and 13 QTLs are located in these area (Cattle QTL database).

Chr	Position (bp)	Breed	Trait / Type
2	27034490-29073969		Age at puberty/Reproduction
2	30080851-32170510	Holstein-Friesian	Lean meat yield, subcutaneous fat/ Meat and carcass
2	30080851-32170510	Holstein-Friesian	Post-partum interval to commencement of luteal activity/ Reproduction and fertility
2	30080851-32170510	Holstein-Friesian	Viral diarrhea susceptibility/Health
2	44067070-44085642	Holstein-Friesian	Milk yield, milk fat and protein yield/Milk
2	45093319-45313175	Holstein-Friesian	Milk fat and protein/Milk
2	45093319-45313175	Holstein-Friesian	Fertilization rate/Reproduction
2	46834289-46834365	Holstein-Friesian	Milk yield, milk fat and protein yield/Milk
2	46834289-46834365	Holstein-Friesian	Udder height, udder cleft/Udder morphology
2	46834289-46834365	Holstein-Friesian	Bovine tuberculosis susceptibility/Health
3	71791844-71793206	Brahman	Interval to 1 st estrus after calving, age at puberty/Reproduction
13	9258332-10558420	Holstein-Friesian	Milk kappa-casein and alpha-casein percentage/Milk
13	9258332-10558420	Holstein-Friesian	Gestation length/Gestation and fertility
13	9258332-10558420		Subcutaneous fat/Meat and carcass
13	10665897-11438802	Holstein-Friesian	Calving ease (direct and maternal)/Parturition
13	10665897-11438802	Holstein-Friesian	Gestation length/Gestation
13	10665897-11438802	Holstein-Friesian	Somatic cell count and mastitis/Health
13	10665897-11438802	Holstein-Friesian	Milk yield, milk fat and protein percentage/Milk
13	46178647-52998234	Norwegian red	Clinical mastitis/Health
13	46834289-46834365	Ayrshire,Norwegian	non return rate/ interval to first estrus after calving/Reproduction
13	51062875-56847265		Somatic cell count ,mastitis/Health
13	53561417-56839719		Body weight, conformation traits
13	57016938-57993671	Gelbvieh	Yield grade/Meat and carcass

CONCLUSION

This study considered three sample chromosomes of the bovine genome to explore the variability of levels of admixture along the genome of Swiss Fleckvieh cat-

tle, a composite of Simmental and Red Holstein Friesian. Substantial deviations (>0.1) from global admixture were observed for several regions, implying the possibility of strong recent selection in the crossbred popu-

lation. The signals found are wide, which is consistent with the small number of generations (~10) since the start of crossbreeding in this population and not enough generations having passed for narrowing the signatures of selection.

ACKNOWLEDGEMENT

We would like to thank the Swissherdbook cooperative Zollikofen for providing genotypes for the analysis.

REFERENCES

- Alexander, D.H., Novembre, J., Lange, K. (2009): Fast model-based estimation of ancestry in unrelated individuals. *Genome Research*, 19: 1655-1664. doi: <http://dx.doi.org/10.1101/gr.094052.109>
- Caraviello, D.Z. (2004): Crossbreeding in dairy cattle. *Reproduction and Genetics*, 610: 1-5.
- Chen, M., Yang, C., Li, C., Hou, L., Chen, X., Zhao, H. (2014): Admixture mapping analysis in the context of GWAS with GAW18 data. *BMC Proceedings*, 8(Suppl 1): S3. doi: <http://dx.doi.org/10.1186/1753-6561-8-S1-S3>
- Bray, T.C., Hall, S.J.G., Bruford, M.W. (2014): Admixture analysis in relation to pedigree studies of introgression in a minority British cattle breed: the Lincoln Red. *Journal of Animal Breeding and Genetics*, 13(1): 19–26. doi: <http://dx.doi.org/10.1111/jbg.12047>
- Frkonja, A., Gredler, B., Schnyder, U., Curik, I., Sölkner, J. (2012): Prediction of breed composition in an admixed cattle population. *Animal Genetics*, 43(6): 696-703. doi: <http://dx.doi.org/10.1111/j.1365-2052.2012.02345.x>
- García-Ruiz, A., Ruiz-López, F.J., Van Tassell, C.P., Montaldo, H.H., Huson, H.J. (2015): Genetic differentiation of Mexican Holstein cattle and its relationship with Canadian and U.S. Holsteins. *Frontiers in Genetics*, 6(7): 1-7. doi: <http://dx.doi.org/10.3389/fgene.2015.00007>
- Kang, S.J., Larkin, E.K., Song, Y., Barnholtz-Sloan, J., Baechle, D., Feng, T., Zhu, X. (2009): Assessing the impact of global versus local ancestry in association studies. *BMC Proceedings*. 3(Suppl 7): SI07.
- Padhukasahasram, B. (2014): Inferring ancestry from population genomic data and its applications. *Frontiers in Genetics*, 5(204): 1-5. doi: <http://dx.doi.org/10.3389/fgene.2014.00204>
- Purcell, S., Neale, B., Todd-Brown, K., Thomas, L., Ferreira, M., Bender, D., Maller, J., Sklar, P., de Bakker, P., Daly, M.J., Sham, P.C. (2007): PLINK: a toolset for whole-genome association and population-based linkage analysis. *American Journal of Human Genetics*, 81(3): 559–575.
- Sankararaman, S., Sridhar, S., Kimmel, G., Halperin, E. (2008): Estimating local ancestry in admixed populations. *The American Journal of Human Genetics*, 82: 290-303. doi: <http://dx.doi.org/10.1016/j.ajhg.2007.09.022>
- Seldin, M.F. (2007): Admixture mapping as a tool in gene discovery. *Current Opinion in Genetics & Development*, 17(3): 177-181. doi: <http://dx.doi.org/10.1016/j.gde.2007.03.002>
- Sölkner, J., Frkonja, A., Raadsma, H.W., Jonas, E., Thaller, G., Gootwine, E., Seroussi, E., Fuerst, C., Egger-Danner, C., Gredler, B. (2010): Estimation of individual levels of admixture in crossbred populations from SNP chip data: Example with sheep and cattle populations. *Interbull Bulletin*, 42: 62-66.
- Swalve, H.H. (2007): Crossbreeding in dairy cattle: International trends and results from crossbreeding data in Germany. *Lohman Information*, 42: 38-46.
- Tang, H., Choudhry, Sh., Mei, R., Morgan, M., Rodriguez-Cintron, W., Burchard, E.G., J. Risch, N. (2007): Recent genetic selection in the ancestral admixture of Puerto Ricans. *The American Journal of Human Genetics*, 81: 626-633. doi: <http://dx.doi.org/10.1086/520769>
- Zhang, J., Stram, D.O. (2014): The role of local ancestry adjustment in association studies using admixed populations. *Genetic Epidemiology*, 38(6): 502-515. doi: <http://dx.doi.org/10.1002/gepi.21835>
- Natioal Animal Genome Research, 1998-2015, Home page address: <http://www.animalgenome.org> (April, 2015).

(Received on 20 May 2015; accepted on 30 July 2015)