Insights in two actual projects - Swiss goats and Alpine cattle

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Goat project: Runs of homozygosity based on sequence data

In collaboration with Institute of Genetics, Vetsuisse Faculty, University of Bern

Goals

- Define appropriate parameters for ROH derivation using whole genome-sequence data from local goat breeds.

- Derive genomic regions, that are highly homozygous in these breeds.
  → Selection signatures?

- What genes do we find in such regions?

Material

- SNP data extracted from sequence data of 226 goats:

  - Applied criteria: «pass» SNP, autosomal SNP, call rate 90%, polymorphic SNP

  → 31'313'770 variants and 226 goats pass filters and QC.

breed	name	# of animals
APZ	Appenzell goat	24
BEZ	Bezoar goat	9
BST	Grisons striped goat	24
CAG	Capra Grigia	12
GFG	Chamois colored	19
NER	Nera Verzasca goat	24
PFA	Peacock goat	24
SAN	Saanen goat	19
STG	Booted goat	24
TOG	Toggenburg goat	24
VAG	Valais goat	23
		226

Material

VAG (Foto: SZZV)

TOG (Foto: SZZV)

APZ (Foto: SZZV)

BST (Foto: SZZV)

CAG (Foto: ProSpecieRara)

GFG (Foto: SZZV)

NER (Foto: SZZV)

PFA (Foto: SZZV)

SAN (Foto: SZZV)

STG (Foto: ProSpecieRara)

breed	category	# of herd-book animals 2017	Risk status FAO
APZ		1'263	At risk
BST		2'834	At risk
CAG		426	At risk
GFG	main	9'328	Not at risk
NER		814	At risk
PFA		1'193	At risk
SAN	main	6'146	Not at risk
STG		493	At risk
TOG	main	3'412	At risk
VAG		1'894	At risk

Methods

▸ Determine runs of homozygosity (ROH) using PLINK1.9 option: --homozyg.

▸ Parameter setting:

   ▸ Meyermans et al. 2019: «PLINK's minimal density requirement is crucial for medium density genotypes and if set too low, genome coverage of the ROH analysis is limited.»

   ▸ For sequence data setting of --homozyg-density is not crucial, but the setting of --homozyg-window-het (number of heterozygous SNP per window), especially for low coverage data (Ceballos et al. 2018), to account for possible calling errors that may break a long ROH wrongly.

   ▸ Depending on goal of the study: setting of --homozyg-kb (the minimum length of an ROH).

Methods

Length in Mb	Length in Morgan	Number of generations
16	0.16	3
8	0.08	6
4	0.04	13
2	0.02	25
1	0.01	50
0.3	0.003	167
0.1	0.001	500

▸ Parameter setting PLINK1.9:

--homozyg-snp 100
--homozyg-kb (100, 300, 1000)
--homozyg-density 50
--homozyg-window-snp 50
--homozyg-window-het 1 to 5 (preliminary work→ 3)
--homozyg-window-missing 5
--homozyg-window-threshold 0.05
--homozyg-gap 1000

▸ Genomic inbreeding (FROH) is defined as the length of the autosomal genome present in ROH, divided by the overall length of the autosomal genome covered by SNP.

FROH

breed	# of animals	Based on 50k from sequences			Based on sequences		
		avg. NSEG	avg. KB	FROH_50k_1Mb (%)	avg. NSEG	avg. KB	FROH_seq_1Mb (%)
APZ	24	49.08	305284.13	12.44	125.17	307384.96	12.46
BEZ	9	42.44	287160.08	11.70	80.67	154950.58	6.28
BST	24	23.29	167401.52	6.82	61.04	162505.80	6.59
CAG	12	11.17	83022.04	3.38	35.25	88837.36	3.60
GFG	19	22.58	138731.48	5.65	60.84	141078.64	5.72
NER	24	18.92	145791.00	5.94	60.75	157509.97	6.39
PFA	24	14.17	107481.98	4.38	43.25	111072.20	4.50
SAN	19	34.21	217682.87	8.87	93.32	204216.00	8.28
STG	24	30.50	249440.00	10.16	86.50	240990.29	9.77
TOG	24	49.21	286342.92	11.66	130.25	302886.71	12.28
VAG	23	48.09	284925.35	11.61	123.17	302527.43	12.27

FROH

▸ Correlation (FROH_50k_1Mb, FROH_seq_1Mb) with BEZ: 0.95

▸ Correlation (FROH_50k_1Mb, FROH_seq_1Mb) without BEZ: 0.98
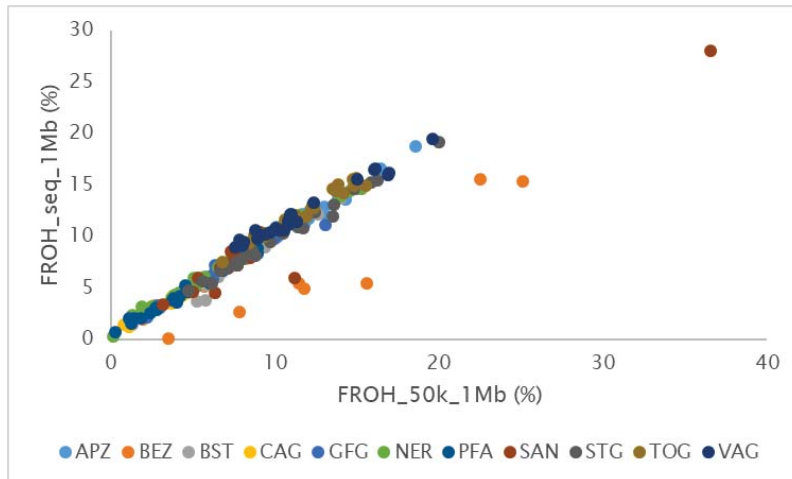
FROH

| # of animals	breed	avg. NSEG	avg.KB	avg. KBAVG	avg. FROH (%)_300kb	avg. NSEG	avg. KB	avg. KBAVG	avg. FROH (%)_100kb
24	APZ	308.83	404781.60	1309.35	16.41	1307.08	557677.40	427.01	22.61
9	BEZ	372.33	301773.50	765.30	12.24	1828.89	526792.60	288.87	21.36
24	BST	171.00	217042.50	1241.72	8.80	1110.88	359535.20	324.16	14.58
12	CAG	161.25	148033.60	903.29	6.00	1296.83	321208.50	248.03	13.03
19	GFG	192.95	206769.10	1050.78	8.38	1256.11	367609.40	292.08	14.91
24	NER	219.33	235040.10	1021.93	9.53	1366.25	411150.80	301.14	16.67
24	PFA	170.46	171514.40	979.56	6.96	1303.54	344489.70	264.85	13.97
19	SAN	295.89	310710.60	1032.27	12.60	1380.95	477264.40	343.19	19.35
24	STG	215.04	304596.70	1389.14	12.35	1276.46	465782.60	366.29	18.89
24	TOG	341.63	414345.90	1210.10	16.80	1352.21	570155.30	421.76	23.12
23	VAG	307.52	398796.00	1288.29	16.17	1363.44	561123.80	412.06	22.75

Homozygous regions

▶ Detection of homozygous regions depends on minimum length of ROH segments:
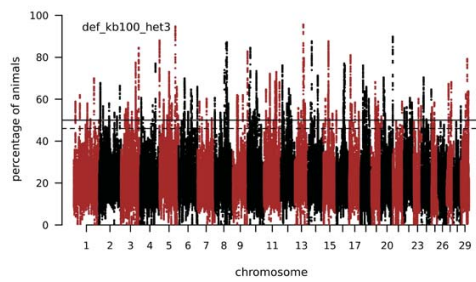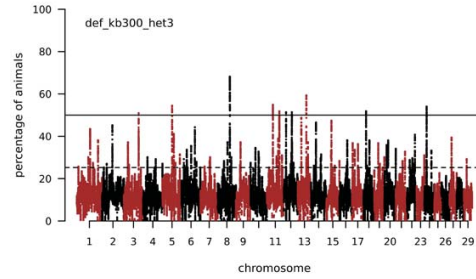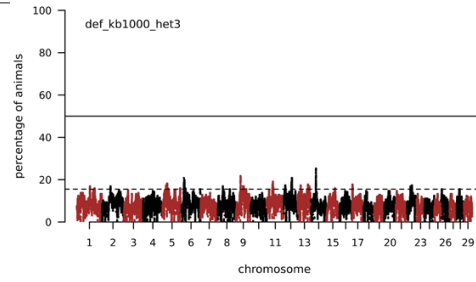
Homozygous regions

APZ: Zoom in
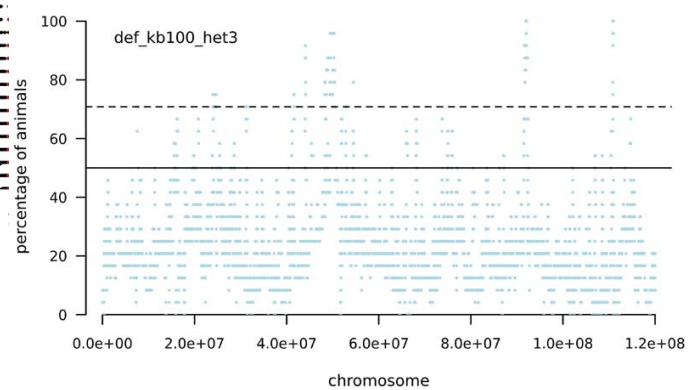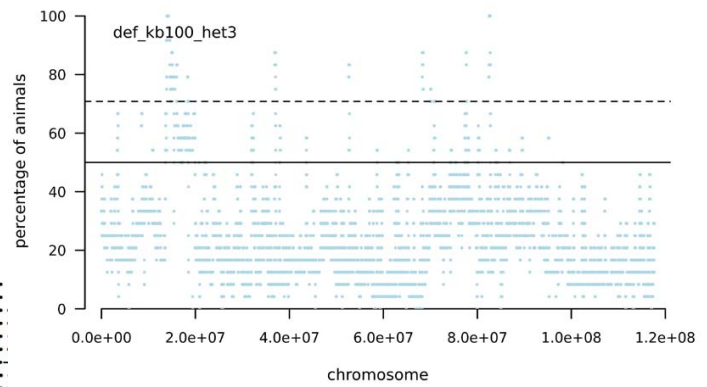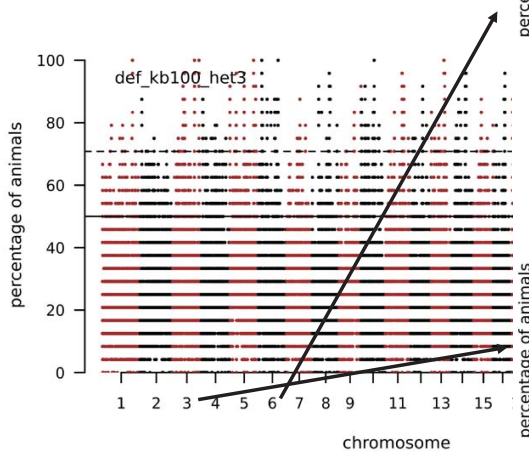
Outlook

- Work in progress:

  - Look deeper into regions where all animals of a breed are homozygous:
    - Is there something of interest? Do we find candidate genes?
    - Are there structural variants?
    - Can we link candidate genes and potential variants with specific properties of the Swiss goat populations?

  - Publication of the results

Conclusion

- SNP chip data is dense enough to determine genomic inbreeding for diversity studies and conservation issues.

- But if the interest is on enriched homozygous regions, sequence data can help to go into more detail.

Cattle project: Genetic diversity of alpine cattle

In collaboration with national and international organisations and institutes.

Genetic diversity of alpine cattle breeds

Background

▸ Signer-Hasler et al. (2017) investigated population structure of nine Swiss cattle breeds.

▸ Variability in the Evolèner breed is high and breeders wish to better understand its background.

▸ Eringer and Evolèner breeds are closely related with the breeds from Aosta valley (Valdostana castagna and Valdostana pezzata nera).

▸ Küttel et al. (2019) reported a complex structural variant responsible for the specific white spotting pattern of Pinzgau and Tux-Zillertal cattle. The variant segregates in Evolèner and the Eringer breed.
   → Historical relationships between these breeds.

▸ High density (or 50k) SNP-data is available for several alpine cattle breeds

Genetic diversity of alpine cattle breeds

Goals

▸ Collect genotypes from different alpine cattle breeds.

▸ Analysis of genetic diversity within and between populations.

▸ Derivation of actual and historical admixture.

Genetic diversity of alpine cattle breeds

Breeds and number of genotypes

Country	Breed	# Genotypes	Institution
CH	Simmental	150	Swissherdbook
CH	Original Brown	150	Braunvieh Schweiz
CH	Eringer*	250	UniBE, HAFL
CH	Evolèner*	250	UniBE, HAFL, Swissherdbook
AUT	Pinzgauer	220	Boku Vienna
AUT	Tyrolean Grey	220	Boku Vienna
AUT	Tux-Zillertaler	63	ÖnGENE
AUT	Ennstaler Bergschecken	25	ÖnGENE
AUT	Pustertaler Sprinzen	25	ÖnGENE
SVN	Cika	26	Biotechnical faculty, Ljubljana
IT	Valdostana- Castana	24	ANABORAVA
IT	Valdostana- Black	25	ANABORAVA
IT	Valdostana- Red	47	University of Milano
GER	Hinterwälder	12	University Hohenheim
GER	Vorderwälder	58	University Hohenheim
GER	Murnau-Werdenfelser	96	LMU München
FR	Abondance	42	INRA
FR	Tarentaise	40	INRA
	Total	**1723**	

20

* 250 genotypes will be randomly chosen to avoid overrepresentation of these Swiss breeds

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Genetic diversity of alpine cattle breeds

Outlook

▸ Funding request submitted to OFAG by end of June 2020
▸ Data set is complete since end of July
▸ Analysis starts asap

▸ We would very much appreciate to submit a contribution from this study for EAAP 2021 in Davos!

Thanks for your attention