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Comparative evaluation of genomic inbreeding parameters in seven commercial and autochthonous pig breeds

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*Single nucleotide polymorphism (**SNP**) genotyping tools, which can analyse thousands of SNPs covering the whole genome, have opened new opportunities to estimate the inbreeding level of animals directly using genome information. One of the most commonly used genomic inbreeding measures considers the proportion of the autosomal genome covered by runs of homozygosity (**ROH**), which are defined as continuous and uninterrupted chromosome portions showing homozygosity at all loci. In this study, we analysed the distribution of ROH in three commercial pig breeds (Italian Large White,* n = *1968; Italian Duroc,* n = *573; and Italian Landrace,* n = *46) and four autochthonous breeds (Apulo-Calabrese,* n = *90; Casertana,* n = *90; Cinta Senese,* n = *38; and Nero Siciliano,* n = *48) raised in Italy, using SNP data generated from Illumina PorcineSNP60 BeadChip. We calculated ROH-based inbreeding coefficients (F_{ROH}) using ROH of different minimum length (1, 2, 4, 8, 16 Mbp) and compared them with several other genomic inbreeding coefficients (including the difference between observed and expected number of homozygous genotypes (F_{HOM})) and correlated all these genomic-based measures with the pedigree inbreeding coefficient (F_{PED}) calculated for the pigs of some of these breeds. Autochthonous breeds had larger mean size of ROH than all three commercial breeds. F_{HOM} was highly correlated (0.671 to 0.985) with F_{ROH} measures in all breeds. Apulo-Calabrese and Casertana had the highest F_{ROH} values considering all ROH minimum lengths (ranging from 0.273 to 0.189 and from 0.226 to 0.152, moving from ROH of minimum size of 1 Mbp (F_{ROH1}) to 16 Mbp (F_{ROH16})), whereas the lowest F_{ROH} values were for Nero Siciliano (from 0.072 to 0.051) and Italian Large White (from 0.117 to 0.042). F_{ROH} decreased as the minimum length of ROH increased for all breeds. Italian Duroc had the highest correlations between all F_{ROH} measures and F_{PED} (from 0.514 to 0.523) and between F_{HOM} and F_{PED} (0.485). Among all analysed breeds, Cinta Senese had the lowest correlation between F_{ROH} and F_{PED}. This might be due to the imperfect measure of F_{PED}, which, mainly in local breeds raised in extensive production systems, cannot consider a higher level of pedigree errors and a potential higher relatedness of the founder population. It appeared that ROH better captured inbreeding information in the analysed breeds and could complement pedigree-based inbreeding coefficients for the management of these genetic resources.*

Keywords: autozygosity, genetic resource, runs of homozygosity, single nucleotide polymorphisms, *Sus scrofa*

Implications

Inbreeding is an essential parameter for the management of livestock populations. Pedigree-based inbreeding (F_{PED}) has several limits which cause biased estimations of the true autozygosity level of an individual animal. This study compared F_{PED} with several genomic inbreeding measures, calculated with a medium-density single nucleotide polymorphism panel, in seven Italian pig breeds (three commercial and four autochthonous breeds). Runs of homozygosity could describe different levels of autozygosity and provided inbreeding genomic coefficients (F_{ROH}; with different runs of homozygosity size) with the highest correlation against F_{PED}. F_{ROH} could complement F_{PED} for routine monitoring of inbreeding, particularly in autochthonous pig breeds.

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Introduction

Conservation and management of animal genetic resources and selection programmes in livestock populations are designed considering inbreeding. Inbreeding is traditionally

calculated using pedigree information which is summarised in an inbreeding coefficient (F_{PED}). F_{PED} can be defined as the probability that, in a diploid organism, the two alleles at a randomly selected locus are identical by descent (**IBD**) with respect to a base population, where all alleles are considered independent (Wright, 1922). This measure is equivalent to the proportion of autozygosity of an individual's genome. In a population, inbreeding is expressed as the average of all F_{PED}'s individual values or as the average of all proportions of autozygosity of the individual's genomes represented in the population. An increased level of inbreeding in a livestock population is related to a small effective population size (Ne) that is usually caused by a low number of animals used in a breeding programme. This, in turn, is determined by a high selection pressure or by the inevitable mating of related animals in small populations (Charlesworth and Willis, 2009). The consequences (defined with the general concept of inbreeding depression) are a reduction of genetic variability and an increased frequency of recessive and deleterious alleles in the population, with negative impacts on the selection potential, reproduction performances, fitness and production efficiencies of the progeny (e.g. Fernández *et al.*, 2002).

Commercial high-throughput single nucleotide polymorphism (**SNP**) genotyping tools in all main livestock species, including the pig (which can interrogate thousands of SNPs covering the whole genome), have opened new opportunities to estimate the inbreeding level directly using whole genome information (Peripolli *et al.*, 2017). Three main approaches have been proposed to estimate the inbreeding level using genomic data: (i) a marker-by-marker evaluation of the level of heterozygosity across the genome, known as multilocus heterozygosity (e.g. Slate *et al.*, 2004); (ii) a method based on identity by state (**IBS**) that summarises SNP-by-SNP this information using a genomic relationship matrix (**GRM**; VanRaden *et al.*, 2011); (iii) methods based on runs of homozygosity (**ROH**) (McQuillan *et al.*, 2008). Among these genomic approaches, ROH methods are considered to estimate more precisely the level of autozygosity of an individual's genome than other methods (Keller *et al.*, 2011; Ceballos *et al.*, 2018). In a diploid organism, ROH are defined as continuous and uninterrupted chromosome portions showing homozygosity at all loci without any heterozygous genotype (Gibson *et al.*, 2006). Runs of homozygosity can be identified using data from SNP chip panels in which the markers are assigned to their corresponding chromosome positions. The ROH length and genome proportion covered by ROH are good indicators of the age, origin and level of autozygosity and thus of the level of inbreeding. Short ROH might originate from remote common ancestors because recombination events over generations (or meiosis) can disrupt long stretches of DNA which, on the other hand, could produce long ROH, indicating an origin of autozygosity from more recent ancestors (Ceballos *et al.*, 2018).

Several studies have been carried out in livestock to analyse the realised autozygosity for different purposes, mainly using ROH approaches (e.g. Purfield *et al.*, 2012; Ferenčaković *et al.*, 2013a and 2013b; Marras *et al.*, 2015; Mastrangelo *et al.*, 2016; Bertolini *et al.*, 2018a). In pigs, ROH were investigated in Chinese and European breeds (including local breeds) to analyse their population structure and to infer their evolutionary or more recent history (e.g. Bosse *et al.*, 2012; Yang *et al.*, 2017). A few other studies used genomic inbreeding measures to evaluate inbreeding depression in closed pig lines (Silió *et al.*, 2013; Gomez-Raya *et al.*, 2015; Saura *et al.*, 2015). Correlation between pedigree and genomic-based inbreeding coefficients were reported for just few pig populations (Gomez-Raya *et al.*, 2015; Saura *et al.*, 2015; Zanella *et al.*, 2016; Joaquim *et al.*, 2019).

In this study, we analysed ROH and used several approaches to infer the level of autozygosity and calculate genomic inbreeding coefficients in three commercial pig breeds (Italian Large White, Italian Landrace and Italian Duroc) and four autochthonous breeds (Apulo-Calabrese, Casertana, Cinta Senese and Nero Siciliano) raised in Italy and compared these measures with the pedigree inbreeding coefficient.

Material and methods

Animals

Pigs included in this study were from three commercial breeds (Italian Large White, $n = 1968$; Italian Duroc, $n = 573$; Italian Landrace, $n = 46$) and four autochthonous breeds (Apulo-Calabrese, $n = 90$; Casertana, $n = 96$; Cinta Senese, $n = 38$; Nero Siciliano, $n = 48$) for a total of 2859 animals. Pigs of the commercial breeds were from the sib-testing programme of the National Association of Pig Breeders (ANAS) that is running since the 1990s for the Italian heavy pig breeding sector that focuses on the production of Protected Designation of Origin (**PDO**) pork products. The animals of the four autochthonous breeds were from the national conservation programme managed by ANAS. These latter breeds are considered small populations. About 200 to 1000 pigs are registered to their respective herd books (ANAS, 2019). Apulo-Calabrese pigs are raised in the central-south of Italy. Animals of this breed have a black solid coat colour. Casertana pigs are mainly raised in Molise, Campania and Puglia regions (central-south of Italy). Casertana pigs have grey or black coat colour with a typical hairless phenotype. This breed is considered the descendant of the Neapolitan population that, at the beginning of the 19th century, was used for the constitution of the first British breeds. Cinta Senese (Siena Belted) pigs are farmed in the Toscana region. Pigs of this breed have a characteristic black coat colour with a white belt. Nero Siciliano (Sicilian Black) pigs are raised in the Sicily island. The animals have solid black coat colour. Pigs of all these local breeds are mainly raised in extensive or semi-extensive farming systems. More details of the investigated pigs are reported in Supplementary Table S1.

Genotyping data

All pigs were genotyped with the PorcineSNP60 BeadChip array v1 or v2 (Illumina, San Diego, CA, USA). Single nucleotide

polymorphisms were mapped on the Sscrofa11.1 genome version. Only SNPs located in unique positions and mapped on autosomal chromosomes were analysed. PLINK software v1.9 (Chang *et al.*, 2015) was used to calculate minor allele frequency (**MAF**) and call rate of each SNP marker, separately for each breed. Animals were considered in the study when individual call rate was >0.90 of all SNPs, and SNPs were eliminated when call rate was <0.90, MAF was <0.02 and *P*-value in Hardy–Weinberg equilibrium (**HWE**) analysis was <0.0001. Supplementary Table S2 reports a summary of the number of animals and SNPs included in the study after filtering.

Detection of runs of homozygosity

Runs of homozygosity were detected using PLINK software v1.9 (Chang *et al.*, 2015). No pruning was performed based on linkage disequilibrium to avoid biases introduced by this practice (Marras *et al.*, 2015), but a minimum length of 1 Mbp to detect ROH was set to exclude short and common ROH determined by markers in linkage disequilibrium, as previously demonstrated by several studies (e.g. Ferenčaković *et al.*, 2013a and 2013b; Marras *et al.*, 2015). The following parameters were applied, similarly to what was used by other authors (Ferenčaković *et al.*, 2013a; Marras *et al.*, 2015): (i) the minimum number of consecutive homozygous SNPs included in the ROH was 15; (ii) the minimum region length that constituted the ROH was 1 Mbp; (iii) the number of heterozygous SNPs that were allowed in the ROH was 0; (iv) the minimum density of SNP in a genome window was 1 SNP every 100 kbp; (v) the maximum allowed distance between consecutive SNPs was 1000 kbp. According to Fisher (1954), the length of an autozygous chromosome segment is expected to follow an exponential distribution with a mean equal to 100/2g × cM, where g is the number of generations since the common ancestor. Assuming 1 cM = 1 Mbp, an ROH having a length of 1, 2, 4, 8 and 16 Mbp are expected to come from a common ancestor occurring about 50, 25, 12, 6 and 3 generations ago, respectively. Runs of homozygosity were then placed into five classes according to the nomenclature of Kirin *et al.* (2010) and Ferenčaković *et al.* (2013a): 1 to 2, 2 to 4, 4 to 8, 8 to 16 and >16 Mb, identified as ROH1–2, ROH2–4, ROH4–8, ROH8–16 and ROH >16, respectively. For each individual, in each breed, and considering ROH ≥1, ROH ≥2, ROH ≥4, ROH ≥8 and ROH ≥16 (simply indicated as ROH1, ROH2, ROH4, ROH8 and ROH16, respectively, hereafter), the total number of detected ROH (**nROH**), the average length of ROH (**LROH**, in Mbp) and the sum of all ROH segments by animals (**SROH**, in Mbp) were calculated.

Inbreeding parameters and effective population size

Pedigree-based inbreeding (F_{PED}) was estimated according to Wright's coefficient (Wright, 1922). The number of pigs with different pedigree depth information available for the studied breeds is reported in Supplementary Table S2. No pedigree information was available for Apulo-Calabrese and Nero Siciliano pigs and for a few animals of other breeds (Supplementary Table S2). Individual F_{PED} values were used for a correlation with genomic inbreeding parameters (see below) if the individual minimum pedigree depth was ≥10 generations.

F_{ROH} was calculated as the proportion of the genome in ROH overall the length of the autosomal genome: F_{ROH} = L(ROH)/L(Autosomes), where L(ROH) is the sum of all ROH of an animal, and L(Autosomes) is the total length of the autosomal genome covered by analysed SNPs. F_{ROH} was calculated including all ROH classes (≥1 Mbp; F_{ROH1}) or including ROH ≥2 Mbp (F_{ROH2}), ROH ≥4 Mbp (F_{ROH4}), ROH ≥8 Mbp (F_{ROH8}) and ROH ≥16 Mbp (F_{ROH16}), following the mentioned length classification criteria. Mean F_{ROH} values were then calculated for all breeds, considering all different ROH minimum lengths.

Other genomic inbreeding coefficients were calculated: (1) variance-standardised relationship minus 1 (F_{hat1}); (2) excess homozygosity-based inbreeding estimate (F_{hat2}); (3) estimate based on a correlation between uniting gametes (F_{hat3}); (4) values of diagonal elements of GRM (F_{GRM}) (VanRaden *et al.*, 2011); (5) difference between observed and expected number of homozygous genotypes (F_{HOM}). These coefficients were calculated using PLINK software v1.9 (Chang *et al.*, 2015) (i.e. F_{hat1}, F_{hat2}, F_{hat3} and F_{HOM}) and GCTA software v1.92 (Yang *et al.*, 2011) (i.e. F_{GRM}). Spearman's rank correlations (ρ) and Pearson's correlations between all evaluated inbreeding coefficients were calculated.

Effective population size at recent generations was computed using SNP data with the SNeP software (Barbato *et al.*, 2015) using the maximum distance between SNPs to be analysed of 10 Mbp and the binwidth of 100 kbp for the calculation of linkage disequilibrium.

Results

Runs of homozygosity in seven pig breeds

The mean size and mean number of ROH per pig for each breed are reported in Table 1. Among the three commercial breeds, Italian Duroc had the largest mean size of ROH (7696.6 kbp) and the largest mean number of ROH per animal (n = 59.3), whereas Italian Large White had the lowest value of both means (7048.3 kbp and n = 40.2). All four autochthonous breeds had a larger mean size of ROH than all three commercial breeds. Apulo-Calabrese had the largest mean size of ROH (15 634.2 kbp) followed by Casertana (13 711.2 kbp), Cinta Senese (8742.2 kbp) and Nero Siciliano (8094.7 kbp). The mean number of ROH in autochthonous breeds (ranging from 19.8 to 45.6 per animal) was lower than that of two commercial breeds, namely Italian Duroc and Italian Landrace, whereas Italian Large White pigs had, on average, 40.2 ROH. The maximum ROH length was observed in the largest chromosomes and ranged from 84.5 Mbp (on SSC1 in one Casertana pig) to 224.6 Mbp (on SSC1 in one Italian Large White pig; Table 1).

Supplementary Table S3 reports the mean number of ROH of different classes for each pig breed. The largest average number of ROH for Italian Large White, Italian Landrace

Table 1 *Mean size and SD of runs of homozygosity (ROH) per animal (in kbp) and mean number and SD of ROH per animal in the seven investigated pig breeds.*

	ROH length in kbp (SSC)			No. of ROH		
Breeds	Mean ± SD	Min	Max	Mean ± SD	Min	Max
ILW	7048.3 ± 1749.3	1003.4 (SSC7)	224564.4 (SSC1)	40.2 ± 8.8	2	87
ID	7696.6 ± 1673.8	1006.7 (SSC10)	178666.4 (SSC1)	59.3 ± 7.7	21	85
IL	7664.3 ± 1737.1	1322.6 (SSC1)	87133.3 (SSC14)	48.2 ± 9.9	19	75
AC	15634.2 ± 3955.3	1026.2 (SSC8)	186320.8 (SSC13)	42.1 ± 11.7	19	67
CT	13711.2 ± 3917.4	1243.7 (SSC2)	126813.6 (SSC4)	38.5 ± 11.4	8	59
CS	8742.2 ± 2178.0	1241.1 (SSC16)	84512.6 (SSC1)	45.6 ± 13.3	19	75
NS	8094.7 ± 4324.5	1144.6 (SSC7)	155090.2 (SSC1)	19.8 ± 8.3	5	43

Minimum (Min) and maximum (Max) ROH size and Min and Max number of ROH are also reported for each breed. Chromosomes (SSC) where the shortest and longest ROH were identified are reported within parentheses.
ILW = Italian Large White; ID = Italian Duroc; IL = Italian Landrace; AC = Apulo-Calabrese; CT = Casertana; CS = Cinta Senese; NS = Nero Siciliano.

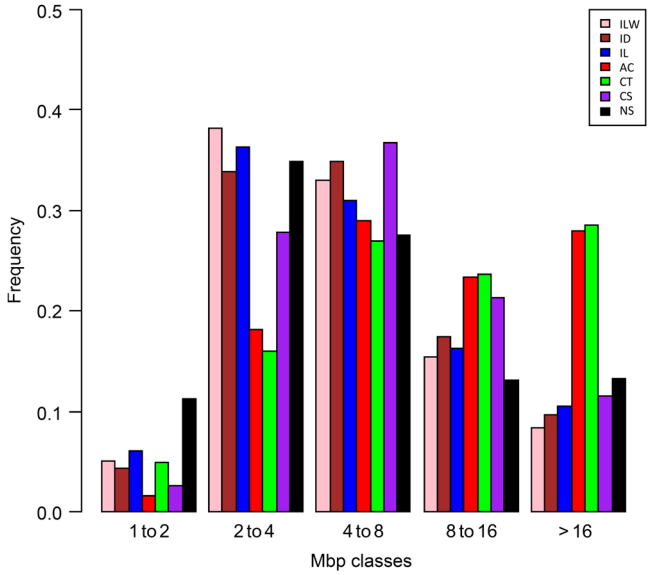

Figure 1 (colour online) Frequency distribution of the number of runs of homozygosity (nROH) of different length classes in the analysed pig breeds. ILW = Italian Large White; ID = Italian Duroc; IL = Italian Landrace; AC = Apulo-Calabrese; CT = Casertana; CS = Cinta Senese; NS = Nero Siciliano.

and Nero Siciliano was in the 2 to 4 Mbp class (ROH2–4, $n = 15.4$, 17.4 and 6.9, respectively). For all other breeds, except Casertana, the largest average number of ROH was in the 4 to 8 Mbp class (ROH4–8), ranging from 12.2 (Apulo-Calabrese) to 20.7 (Italian Duroc). Casertana had the largest average number of ROH in the ≥16 Mbp class (ROH16, $n = 11.0$). In this class, the largest average number was observed in Apulo-Calabrese ($n = 11.7$). The relative frequency distribution of the number of ROH (**nROH**) of the five considered length classes in the seven breeds is reported in Figure 1. Apulo-Calabrese and Casertana showed a high frequency of ROH in the longest length classes (from 4 to ≥16 Mbp) which accounted, in total and on average, for about 80% of all ROH.

Figure 2 shows the plot distribution of the total number of ROH ≥1 Mbp compared to the total length of ROH ≥1 Mbp per animal (SROH). A high correlation between these two parameters was observed for all breeds ($r > 0.9$). Figure 3 reports box plots showing within-breed average SROH1 (considering ROH ≥1 Mbp) and its distribution calculated across all genotyped pigs. Mean SROH ranged from about 179.11 Mbp (Nero Siciliano) to 668.62 Mbp (Apulo-Calabrese) with a large variability and several outlier pigs (Supplementary Table S4). For example, one Apulo-Calabrese pig had about one-half of its autosomal genome covered by ROH. Supplementary Figure S1 reports box plots of the same parameter obtained for SROH2, SROH4, SROH8 and SROH16 Mbp (calculated by adding all ROH ≥2 to 16 Mbp, respectively), and Supplementary Table S4 reports all detailed distribution information, considering all ROH defined with the five considered minimum lengths. Again, in all cases, Apulo-Calabrese showed the highest average SROH values.

Inbreeding coefficients, their correlations and relationships with effective population size (Ne)

Table 2 summarises the inbreeding coefficient values obtained for the seven Italian pig breeds. Pedigree information was not available for Apulo-Calabrese and Nero Siciliano; therefore, for these two breeds F_{PED} was not calculated. Average F_{PED} ranged from 0.043 (Italian Large White) to 0.137 (Casertana).

Genomic inbreeding parameters were calculated for all genotyped animals of the seven breeds (Table 2). Nero Siciliano pigs showed the lowest average F_{ROH1} value (0.072), whereas Apulo-Calabrese pigs had the highest average F_{ROH1} value (0.273) followed by Casertana (0.226) and Italian Duroc (0.187). Pigs of these latter breeds had also the maximum individual F_{ROH1} coefficients (0.503, 0.467 and 0.455, respectively).

F_{ROH} decreased as the minimum length of ROH increased for all breeds even if this drop was more evident in commercial breeds than in autochthonous breeds. For Italian Large White, Italian Duroc and Italian Landrace, the average F_{ROH} was reduced about three times from considering ROH ≥1 Mbp to ROH ≥16 Mbp, whereas this reduction

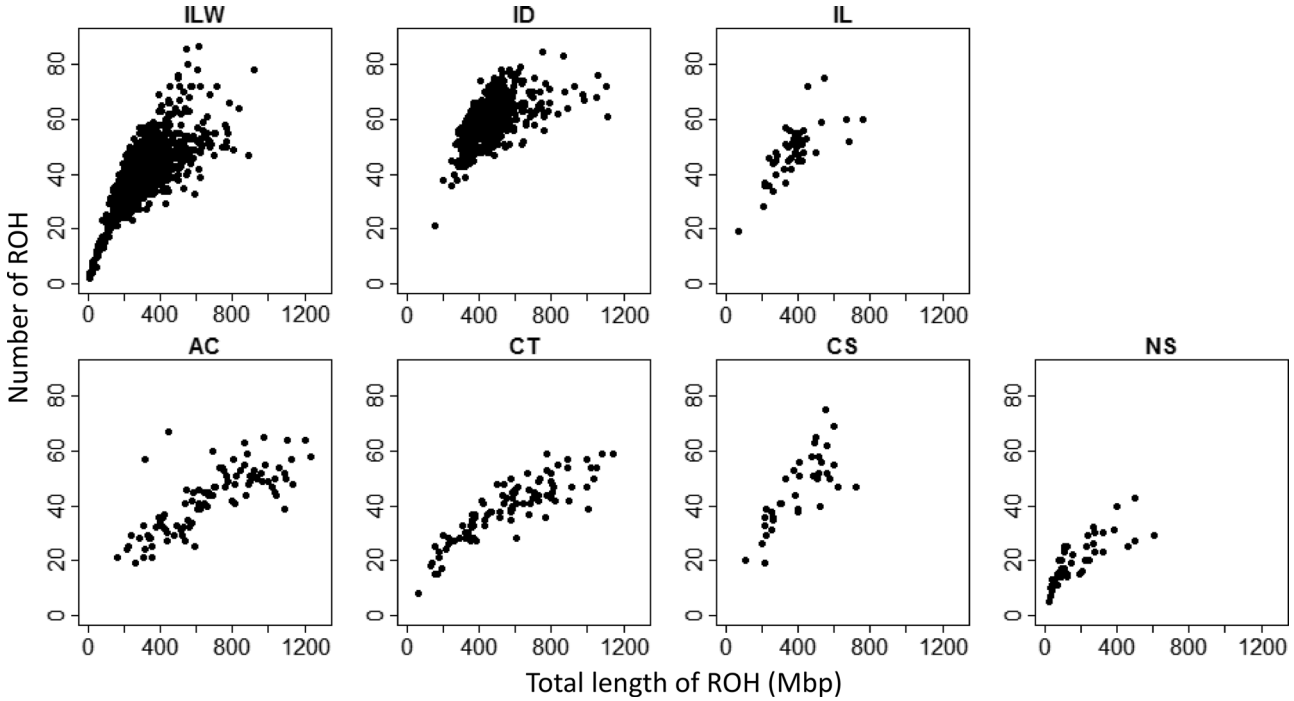

Figure 2 Total number of runs of homozygosity (ROH) ≥1 Mbp plotted with the total length of ROH ≥1 Mbp (SROH) per animal in all investigated breeds. ILW = Italian Large White; ID = Italian Duroc; IL = Italian Landrace; AC = Apulo-Calabrese; CT = Casertana; CS = Cinta Senese; NS = Nero Siciliano.

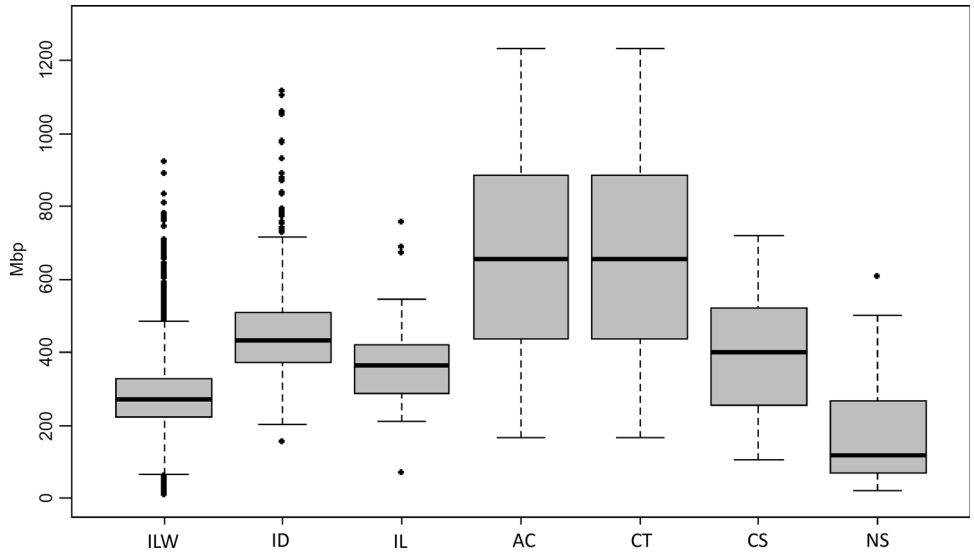

Figure 3 Box plots of within-breed averaged sum of length of runs of homozygosity (ROH) ≥1 Mbp (SROH, in Mbp) calculated across all pigs. ILW = Italian Large White; ID = Italian Duroc; IL = Italian Landrace; AC = Apulo-Calabrese; CT = Casertana; CS = Cinta Senese; NS = Nero Siciliano.

was about 1.2 to 1.5 times for Apulo-Calabrese, Casertana and Nero Siciliano and 2.2 times for Cinta Senese. Standard deviations of all F_{ROH} measures were similar to that obtained from pedigree data.

The average F_{hat1} values ranged from −0.168 (Cinta Senese) to 0.088 (Apulo Calabrese), with large within- and among-breeds variability. Similar large variability was evident for F_{hat2} and F_{hat3} (average values from −0.024 in Cinta Senese to 0.172 in Apulo-Calabrese for both parameters) that had also large standard deviations (Table 2). F_{GRM} is equivalent to F_{hat1}, even if scaled in a different way, and had the same standard deviation reported for F_{hat1}. Average F_{HOM} was negative for Cinta Senese (−0.034) and Italian Landrace (−0.003), whereas it was positive in all other breeds. Apulo-Calabrese showed the largest standard deviation and the largest absolute range.

Spearman's rank correlation coefficients (ρ) between F_{PED} and all genomic inbreeding measures are reported in Table 3. Pearson's correlation coefficients have been also calculated for comparison with results reported in other

Table 2 *Average inbreeding coefficient values ± SD and their minimum and maximum values (within parentheses) in the seven pig breeds*

Inbreeding measures	ILW	ID	IL	AC	CT	CS	NS
F_{PED}	0.043 ± 0.044 (0.000 to 0.376)	0.062 ± 0.071 (0.000 to 0.353)	0.072 ± 0.051 (0.000 to 0.210)	_	0.137 ± 0.104 (0.000 to 0.344)	0.136 ± 0.063 (0.085 to 0.225)	_
F_{ROH1}	0.117 ± 0.044 (0.004 to 0.376)	0.187 ± 0.051 (0.062 to 0.455)	0.153 ± 0.051 (0.029 to 0.308)	0.273 ± 0.110 (0.068 to 0.503)	0.226 ± 0.107 (0.024 to 0.467)	0.164 ± 0.063 (0.044 to 0.294)	0.072 ± 0.059 (0.009 to 0.247)
F_{ROH2}	0.116 ± 0.044 (0.003 to 0.374)	0.185 ± 0.052 (0.062 to 0.455)	0.150 ± 0.051 (0.028 to 0.308)	0.272 ± 0.110 (0.067 to 0.502)	0.225 ± 0.107 (0.023 to 0.464)	0.163 ± 0.062 (0.044 to 0.294)	0.072 ± 0.059 (0.008 to 0.246)
F_{ROH4}	0.097 ± 0.043 (0.002 to 0.358)	0.160 ± 0.052 (0.050 to 0.439)	0.129 ± 0.052 (0.015 to 0.289)	0.263 ± 0.109 (0.062 to 0.491)	0.217 ± 0.106 (0.020 to 0.460)	0.147 ± 0.060 (0.030 to 0.275)	0.063 ± 0.059 (0.004 to 0.241)
F_{ROH8}	0.067 ± 0.039 (0.003 to 0.325)	0.113 ± 0.051 (0.027 to 0.403)	0.095 ± 0.047 (0.003 to 0.255)	0.234 ± 0.106 (0.039 to 0.460)	0.192 ± 0.103 (0.010 to 0.429)	0.109 ± 0.056 (0.021 to 0.247)	0.052 ± 0.055 (0.004 to 0.234)
F_{ROH16}	0.042 ± 0.034 (0.007 to 0.270)	0.066 ± 0.046 (0.007 to 0.355)	0.061 ± 0.039 (0.008 to 0.192)	0.189 ± 0.096 (0.017 to 0.411)	0.152 ± 0.092 (0.009 to 0.353)	0.068 ± 0.046 (0.007 to 0.214)	0.055 ± 0.049 (0.009 to 0.205)
F_{hat1}	−0.032 ± 0.325 (−0.319 to 3.273)	0.024 ± 0.206 (−0.262 to 2.267)	−0.085 ± 0.449 (−0.341 to 2.339)	0.088 ± 0.798 (−0.437 to 4.748)	−0.072 ± 0.234 (−0.381 to 0.719)	−0.168 ± 0.213 (−0.431 to 0.531)	−0.084 ± 0.175 (−0.362 to 0.426)
F_{hat2}	0.022 ± 0.164 (−0.966 to 0.340)	0.024 ± 0.104 (−0.485 to 0.403)	0.008 ± 0.211 (−0.867 to 0.260)	0.172 ± 0.293 (−1.026 to 0.583)	0.085 ± 0.190 (−0.393 to 0.460)	−0.024 ± 0.226 (−0.726 to 0.293)	0.015 ± 0.127 (−0.297 to 0.206)
F_{hat3}	0.022 ± 0.118 (−0.086 to 1.561)	0.024 ± 0.098 (−0.106 to 0.955)	0.009 ± 0.136 (−0.079 to 0.783)	0.172 ± 0.304 (−0.033 to 2.027)	0.085 ± 0.107 (−0.089 to 0.346)	−0.024 ± 0.033 (−0.089 to 0.050)	0.016 ± 0.066 (−0.084 to 0.188)
F_{GRM}	0.968 ± 0.325 (0.681 to 4.274)	1.024 ± 0.206 (0.738 to 3.267)	0.915 ± 0.449 (0.659 to 3.339)	1.088 ± 0.798 (0.563 to 5.748)	0.928 ± 0.234 (0.619 to 1.719)	0.832 ± 0.213 (0.569 to 1.531)	0.916 ± 0.175 (0.638 to 1.426)
F_{HOM}	0.018 ± 0.062 (−0.247 to 0.396)	0.022 ± 0.076 (−0.108 to 0.389)	−0.003 ± 0.071 (−0.206 to 0.170)	0.140 ± 0.176 (−0.191 to 0.499)	0.119 ± 0.152 (−0.214 to 0.444)	−0.034 ± 0.136 (−0.355 to 0.182)	0.021 ± 0.085 (−0.145 to 0.200)

ILW = Italian Large White; ID = Italian Duroc; IL = Italian Landrace; AC = Apulo-Calabrese; CT = Casertana; CS = Cinta Senese; NS = Nero Siciliano; F_{PED} = pedigree inbreeding coefficient; F_{ROH1} = inbreeding coefficient based on runs of homozygosity (ROH) of a minimum size of 1 Mbp; F_{ROH2} = inbreeding coefficient based on ROH of a minimum size of 2 Mbp; F_{ROH4} = inbreeding coefficient based on ROH of a minimum size of 4 Mbp; F_{ROH8} = inbreeding coefficient based on ROH of a minimum size of 8 Mbp; F_{ROH16} = inbreeding coefficient based on ROH of a minimum size of 16 Mbp; F_{hat1} = inbreeding coefficient based on variance-standardized relationship minus 1; F_{hat2} = inbreeding coefficient based on excess of homozygosity; F_{hat3} = inbreeding coefficient based on a correlation between uniting gametes; F_{HOM} = inbreeding coefficient based on the number of homozygous genotypes; F_{GRM} = values of diagonal elements of the genomic relationship matrix.

Table 3 *Spearman's rank correlation coefficients between F_{PED} and all genomic inbreeding derived measures in Italian Large White (ILW), Italian Duroc (ID), Italian Landrace (IL) and Cinta Senese (CS).*

Inbreeding measures	ILW	ID	IL	CS
F_{ROH1}	0.376***	0.514***	0.494***	0.208
F_{ROH2}	0.377***	0.517***	0.498***	0.203
F_{ROH4}	0.393***	0.523***	0.508***	0.182
F_{ROH8}	0.399***	0.518***	0.473**	0.134
F_{ROH16}	0.373***	0.516***	0.388**	0.084
F_{hat1}/F_{GRM}	0.155***	0.133**	−0.514***	−0.197
F_{hat2}	0.348***	0.407***	0.641***	0.244
F_{hat3}	0.079**	0.371***	0.021	0.260
F_{HOM}	0.303***	0.485***	0.477***	0.181

Correlations were not reported for Casertana due to the limited pedigree depth of the animals.
F_{ROH1} = inbreeding coefficient based on runs of homozygosity (ROH) of a minimum size of 1 Mbp; F_{ROH2} = inbreeding coefficient based on ROH of a minimum size of 2 Mbp; F_{ROH4} = inbreeding coefficient based on ROH of a minimum size of 4 Mbp; F_{ROH8} = inbreeding coefficient based on ROH of a minimum size of 8 Mbp; F_{ROH16} = inbreeding coefficient based on ROH of a minimum size of 16 Mbp; F_{hat1} = inbreeding coefficient based on variance-standardized relationship minus 1; F_{hat2} = inbreeding coefficient based on excess of homozygosity; F_{hat3} = inbreeding coefficient based on a correlation between uniting gametes; F_{HOM} = inbreeding coefficient based on the number of homozygous genotypes; F_{GRM} = values of diagonal elements.
$^{**}P < 0.01$, $^{***}P < 0.001$.

studies and are reported in Supplementary Table S5. Figure 4 shows the regression plots of several genomic inbreeding parameters on F_{PED}.

Italian Duroc had the highest ρ values between all F_{ROH} measures and F_{PED} (ρ ranged from 0.514 for F_{ROH1} to 0.523 for F_{ROH4}) and between F_{HOM} and F_{PED} ($\rho = 0.485$). Italian Landrace had, however, the highest ρ value between a genomic inbreeding measure and F_{PED} observed in this study (i.e. F_{hat2}, $\rho = 0.641$). For this breed, ρ values between all F_{ROH} measures and F_{PED} were lower but close to that reported in Italian Duroc, with the lowest value for F_{ROH16} ($\rho = 0.388$) and the highest value again for F_{ROH4} ($\rho = 0.508$). The lower value obtained with F_{ROH16} is in agreement with the distribution of all ROH in this breed (Figure 1). A potential bias on this correlation, however, might have been also introduced by the lower number of analysed animals of this breed compared to that of other commercial breeds. For Italian Large White, ρ between all F_{ROH} measures and F_{PED} were lower than that of the other two commercial breeds (from 0.373 to 0.399). The same was also for F_{hat2} and F_{HOM}. In Cinta Senese, correlations derived by the mentioned genomic inbreeding measures and F_{PED} were always lower than that of the three commercial breeds. F_{hat1}/F_{GRM} and F_{hat3} had, in general, low or very low correlations with F_{PED} in all breeds and with values that could not provide a general trend (Table 3). Similar results were observed using the Pearson's correlation coefficients, for which Italian Landrace reported the highest values with all F_{ROH} measures, F_{HOM} and F_{hat2} (Supplementary Table S5).

Correlations were also calculated for all pairs of genomic inbreeding parameters (Supplementary Table S6). The highest values were obtained, in general, for F_{HOM} against all F_{ROH} measures, with a decreasing trend from F_{ROH1} to F_{ROH16} in all compared breeds (values ranged from 0.985 in Casertana for F_{ROH1} to 0.614 in Cinta Senese for F_{ROH16}). Other highly correlated pairs included F_{hat2} against all F_{ROH} measures (ranging from 0.918 in Casertana for F_{ROH1} to 0.335 in Italian Large White for F_{ROH16}).

Estimated effective population size (Ne; Supplementary Table S7), which indirectly provides information on the level of genetic diversity within a population, matched to some extent the level of inbreeding reported in the analysed breeds (Table 2). The lowest and highest Ne values (from 25 to 3 generations ago) were observed in Casertana and Italian Large White, respectively (Supplementary Table S7). Among the autochthonous breeds, only Nero Siciliano had Ne values higher than that of one commercial breed, that is Italian Landrace, which had in turn the lowest Ne values among the commercial breeds.

Discussion

The inbreeding level of a population is an important parameter to monitor its genetic diversity and an essential information for its management. A high level of inbreeding causes inbreeding depression and should be avoided in livestock breeds (e.g. Fernández *et al.*, 2002). Breeding nuclei and autochthonous breeds are genetically considered small populations as their Ne is usually <100. Inbreeding is traditionally measured using pedigree information. However, the pedigree-based inbreeding coefficient (F_{PED}) has some limits: (i) it does not account for the true relatedness of founder animals of the base population (as it assumes that all animals of the base population are unrelated, which could not be true); (ii) it needs complete pedigree registration for both paternal and maternal lineages to fully account for the relationships of the animals between and within lineages; (iii) it assumes that all pedigree registrations are correct, which is difficult to verify, especially in extensive production systems, where mating events cannot be precisely recorded (e.g. a high misidentification rate has been reported even in cattle populations in which recording systems are expected to be more precise than in other livestock species; e.g. Russo *et al.*, 2012); (iv) it does not take into account the stochasticity of recombination events occurring during meiosis through the generations; (v) it does not consider the potential biases derived by the selection on some genomic regions.

In this study, we used genomic information obtained from a medium-density SNP chip to calculate genomic inbreeding parameters and compared these measures with pedigree-based information in several Italian pig breeds, divided into two main groups. One group included Italian Large White, Italian Duroc and Italian Landrace. These pigs belong to breeding nuclei that are under the heavy pig national

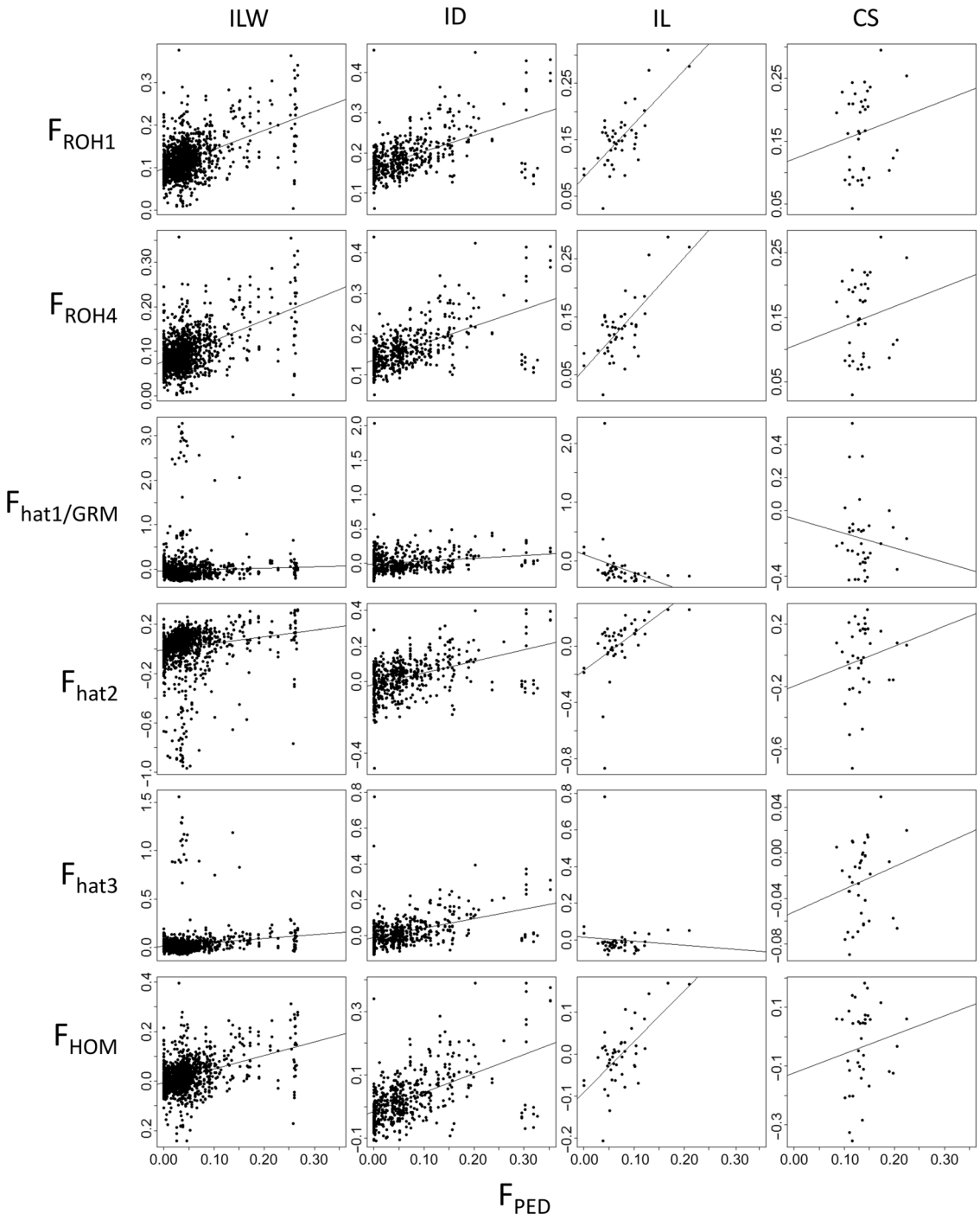

Figure 4 Plots of regression of several genomic inbreeding parameters. On *y*-axis: inbreeding coefficient based on runs of homozygosity (ROH) of a minimum size of 1 Mbp (F_{ROH1}), inbreeding coefficient based on ROH of a minimum size of 4 Mbp (F_{ROH4}), inbreeding coefficient based on variance-standardized relationship minus 1 (F_{hat1}) that is equivalent to the values of diagonal elements of the genomic relatedness matrix (F_{GRM}), inbreeding coefficient based on excess of homozygosity (F_{hat2}), inbreeding coefficient based on an estimate based on correlation between uniting gametes (F_{hat3}) and inbreeding coefficient based on the number of homozygous genotypes (F_{HOM}); on *x*-axis: pedigree inbreeding coefficient (F_{PED}) for three commercial breeds (ILW = Italian Large White; ID = Italian Duroc; IL = Italian Landrace) and one autochthonous breed (CS = Cinta Senese) for which the minimum pedigree depth of genotyped pigs was ≥10 (see Supplementary Table S2). Plots for inbreeding coefficient based on ROH of minimum size of 2, 8 or 16 Mbp (F_{ROH2}, F_{ROH8} and F_{ROH16}) were not reported as they were similar to F_{ROH1} and F_{ROH4} plots.

selection programme, which has substantially shaped the genome of these breeds over the last three decades (Schiavo *et al.*, 2016; Bertolini *et al.*, 2018b). Other four breeds (Apulo-Calabrese, Casertana, Cinta Senese and Nero Siciliano) are autochthonous pig genetic resources under conservation programmes, which have as one of the main objectives the control of the level of inbreeding in these small populations (ANAS, 2019).

The proportion of ROH covering the autosomal genome (F_{ROH}) and LROH are considered good estimators of the level

and origin of autozygosity (e.g. Purfield *et al.*, 2012; Ferenčaković *et al.*, 2013a and 2013b; Ceballos *et al.*, 2018). In all pig breeds analysed in this study, the frequency of short ROH (1 to 2 Mbp) was low (Figure 1), compared to that reported in cattle breeds using a genotyping tool of similar SNP density (Marras *et al.*, 2015). Only in Nero Siciliano this class of short ROH accounted for about 12% of all ROH. Other ROH classes (ROH2–4 and ROH4–8 Mbp) were more frequent and, on average, covered the largest fraction of all ROH segments in both commercial and autochthonous pig breeds. This indicates that they might have originated, at least in part, from more recent common ancestors than that suggested for Nero Siciliano. Nero Siciliano is considered the most heterozygous local pig population raised in Italy, probably due to several gene flows and admixture with other pig populations (Muñoz *et al.*, 2018). This is also reflected by the estimated Ne (Supplementary Table S7). This breed had the highest Ne values among the analysed autochthonous breeds. It is, however, important to note that the Ne trends may be partially a consequence of the relatively small sample size for a few breeds (i.e. Italian Landrace, Cinta Senese and Nero Siciliano), in addition to several other factors that might have contributed to define the structure of all investigated breeds (e.g. bottleneck, genetic drift and artificial selection). Apulo-Calabrese and Casertana had the highest SROH values (considering all five ROH minimum lengths; Supplementary Table S4) and the highest mean LROH (Table 1), which, again, provided a general picture of a high level of autozygosity.

Several studies have suggested that the identification of ROH might be affected by the density of the used SNP genotyping platform and by the parameters used to call ROH (e.g. Ferenčaković *et al.*, 2013a and 2013b; Marras *et al.*, 2015). However, there is no general agreement on the use of different parameters to call ROH (Peripolli *et al.*, 2017). We set parameters frequently used by other studies (e.g. Ferenčaković *et al.*, 2013a; Marras *et al.*, 2015) and evaluated a few other options. For example, we did not allow any heterozygous SNPs in ROH, but when we tested the inclusion of one or two heterozygous markers, correlations calculated for all corresponding F_{ROH} measures (obtained with different number of heterozygous SNPs, from 0 to 2) were >0.99. Therefore, for the main purpose of this study, the number of up to two heterozygous SNPs allowed was not relevant. Moreover, the minimum length that constituted ROH was considered as defining different length thresholds (1, 2, 4, 8 and 16 Mbp). These five levels gave the opportunity to test different measures of F_{ROH} and compare them with F_{PED} and other genomic inbreeding coefficients.

Apulo-Calabrese and Casertana had the highest F_{ROH} values considering all ROH minimum lengths (ranging from 0.273 to 0.189 and from 0.226 to 0.152, moving from F_{ROH1} to F_{ROH16} and for the two breeds, respectively). The high mean F_{ROH} values in Casertana are in agreement with the high mean values of F_{PED} in this breed (Table 2). The Apulo-Calabrese population has generally a high level of inbreeding, as reported in its herd book (ANAS, 2019). Even if comparisons with other studies that analysed F_{ROH} are difficult due to the different parameters used to call ROH, it seems that the values observed in autochthonous Italian breeds are similar or lower than that reported in other European local breeds (e.g. Yang *et al.*, 2017). For example, Gomez-Raya *et al.* (2015) analysed a close Iberian population and reported F_{ROH} values ranging from about 0.20 to 0.45. Other studies are needed to obtain a more complete comparative analysis among European local pig breeds.

Italian Duroc had the highest F_{ROH} values (from 0.187 to 0.066, considering the different ROH minimum lengths) among the three commercial breeds. This high F_{ROH} level compared to the F_{PED} mean value of this breed might be due to the captured IBD states of the base population that could not be detected with pedigree information. The lowest F_{ROH} values were for Nero Siciliano (from 0.072 to 0.051) and for Italian Large White (from 0.117 to 0.042), reflecting the pictures observed with ROH length distribution in these breeds.

Correlations between F_{ROH} and F_{PED} did not change substantially whether or not short ROH were considered. This is mainly due to the lowest frequency of the shortest ROH class (ROH1–2) in all breeds (Figure 1). The highest correlation between F_{ROH} and F_{PED} was obtained for F_{ROH4} in Italian Duroc. In Italian Landrace, the highest correlation between ROH inbreeding measures and F_{PED} was again for F_{ROH4}, whereas the highest within-breed value in Italian Large White pigs was observed using F_{ROH8}. Again, this is in line with the general distribution of all ROH length classes in the three commercial breeds (Figure 1). Runs of homozygosity with a low length might also not represent a true identity by descent homozygous regions in these breeds. Among all analysed breeds, Cinta Senese had the lowest correlation between F_{ROH} and F_{PED}. This might be due to the imperfect measure of F_{PED}, which, mainly in local breeds raised in extensive production systems, cannot consider a higher level of pedigree errors and a potential higher relatedness of the founder population (in particular if the population experienced bottlenecks), in addition to all other factors which might reduce the precision of F_{PED} to estimate the level of autozygosity. Lower correlations in extensively managed breeds compared to commercial and intensively managed populations (which might have also experienced bottlenecks) have been also reported in other livestock species (Purfield *et al.*, 2017; Peripolli *et al.*, 2018).

Correlations between F_{ROH} and F_{PED} in the three commercial pig breeds were much higher than that reported by other studies in similar pig breeds using the same genome SNP density. For example, Joaquim *et al.* (2019) showed a very low Pearson's correlation (0.04) between F_{ROH} and F_{PED} in a Landrace population. Similar very low correlations between F_{ROH} and F_{PED} values were calculated in two other commercial pig populations of Landrace and Large White (Zanella *et al.*, 2016). However, Saura *et al.* (2015) reported Pearson's correlations between F_{ROH} and F_{PED} in Iberian pigs (0.631 using all ROH lengths and 0.603 using only long ROH, i.e. >5 Mbp) that were close to what we reported in the three commercial pig breeds (Supplementary Table S5).

Among the other genomic inbreeding measures, only two (F_{hat2} and F_{HOM}) were consistent with the moderate correlations obtained between F_{ROH} and F_{PED}. F_{GRM} could not provide a reliable measure of genomic inbreeding, compared to what we observed for F_{ROH} (and defined based on a correlation with F_{PED}). This is in line with what was reported by Marras *et al.* (2015) in several cattle breeds for which F_{GRM} had also a low correlation with F_{ROH}. We observed the same low correlation between F_{GRM} and all F_{ROH} minimum length classes (Supplementary Table S6).

Summing up all results, it appeared that ROH better captured inbreeding information in all analysed pig breeds and could complement pedigree-based inbreeding for the management of these genetic resources.

Conclusion

This study provided a first comparative analysis of several inbreeding measures, pedigree and genomic based, to describe autozygosity in seven pig breeds that are managed for different purposes. Runs of homozygosity analyses showed that these breeds have different distribution and structure of autozygous regions. Other studies will be carried out to identify ROH islands which could mark selection sweeps in the genome of these breeds. All calculated F_{ROH} parameters (and in part also F_{hat2} and F_{HOM}) are useful to monitor inbreeding in both commercial and autochthonous breeds and might be considered for routine applications.

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Declaration of interest

The authors declare that they do not have competing interests.

Ethics statement

No ethical approval was required since only genotyping data were used in the study, and data were provided by the research programme INNOVAGEN (Italian Ministry of Agriculture, Food and Forestry).

Software and data repository resources

None of the data were deposited in an official repository.

Supplementary material

To view supplementary material for this article, please visit https://doi.org/10.1017/S1751731111900332X

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