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Article

Spatial Trends of Genetic Variation of Domestic Ruminants in Europe

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Abstract: The introduction of livestock species in Europe has been followed by various genetic events, which created a complex spatial pattern of genetic differentiation. Spatial principal component (sPCA) analysis and spatial metric multidimensional scaling (sMDS) incorporate geography in multivariate analysis. This method was applied to three microsatellite data sets for 45 goat breeds, 46 sheep breeds, and 101 cattle breeds from Europe, Southwest Asia, and India. The first two sPCA coordinates for goat and cattle, and the first sPCA coordinate of sheep, correspond to the coordinates of ordinary PCA

analysis. However, higher sPCA coordinates suggest, for all three species, additional spatial structuring. The goat is the most geographically structured species, followed by cattle. For all three species, the main genetic cline is from southeast to northwest, but other geographic patterns depend on the species. We propose sPCA and sMDS to be useful tools for describing the correlation of genetic variation with geography.

Keywords: cattle; sheep; goat; diversity; spatial structure; PCA; sPCA; Multidimensional scaling; Moran's I

1. Introduction

Livestock breeds have been shaped by centuries of human selection and adaptation to different environments. Various demographic events have created geographic patterns of genetic diversity [1], such as domestication, migration, selection, isolation, and expansion of successful breeds. Several techniques have been developed to analyze spatial patterns of genetic variation among populations [2,3]. One widely used approach is the analysis of spatial auto-correlation [4-6], which is detected if proximate individuals or populations are, for a given variable, more similar or dissimilar than expected for a random distribution.

An alternative method for the detection of spatial patterns is based on multivariate analysis of genetic variation, and in particular, upon the Principal Components Analysis (PCA) [7,8]. The technique, of plotting the values of the synthetic coordinates of a factorial map onto a geographic map, has been pioneered by Cavalli-Sforza for the reconstruction of the early history of human populations [9]. For African cattle, different Principal Components (PC) were proposed to correspond to migrations of taurine and indicine ancestral populations [10]. PCA has several attractive features: (1) It is exploratory, since no genetic model is assumed, such as the Hardy-Weinberg equilibrium or the models that assume the absence of linkage disequilibrium [11]; (2) Different forms of genetic structuring can be revealed, as clines, local contrasts, or relationships of distant populations [12]; (3) Alleles and markers may be classified on the basis of their contributions to the different factors [11]; (4) It is not computer intensive and can be applied to large data sets. The power of PCA with large SNP data sets was demonstrated by Novembre *et al.* [13], who observed a very high correlation between the positions in a PCA plot and human geographic origin.

However, multivariate methods may fail to detect spatial structuring if this is not associated with the most pronounced genetic differentiation. For a more complete characterization of spatial structures, the analysis has to focus on the part of the variance that is spatially structured [14]. This can be accomplished by using spatial information as a component of the optimized criterion. Therefore, Thioulouse *et al.* [15] built on the work of Wartenberg [16] in order to explicitly integrate geography into multivariate factorial methods. Jombart [14,17] specifically developed a spatial Principal Component Analysis (sPCA) suitable for genetic allelic frequencies data. It was shown that sPCA retrieves simple structures as well as more complex patterns of genotypes or populations, and performs, in this respect, better than PCA.

Many European livestock breeds have been analyzed with molecular markers [18]. Most studies used the polymorphic microsatellites, but so far, multivariate analysis has only been carried out for regional panels of breeds [11]. In this paper, we apply sPCA and spatial multidimensional scaling (sMDS) to the analysis of comprehensive microsatellite data sets for goat [19], cattle [20,21], and sheep [22]. We show that spatial methods detect significant geographic trends, which partially depend on the species.

2. Material and Methods

2.1. Spatial "Principal Components Analysis" (sPCA)

We summarize here the description of the sPCA by Jombart [14], from which this presentation is largely borrowed. sPCA analyzes a data matrix **X,** which contains genotypes (or populations) in rows and alleles in columns. Spatial information is stored inside a spatial weighting matrix **L,** which contains positive terms corresponding to some measurement (often binary) of spatial proximity among entities. Most often, these terms can be derived from a connection network, or a neighboring graph, which is created by connecting the neighboring breeds on a map [23]. A Delaunay neighboring graph is suited to evenly distributed entities, but may also connect unrelated peripheral entities. The Gabriel neighboring graph is a subset of the Delaunay graph without peripheral connections. In a further reduced subset, the 1st nearest neighbor graph, each point is connected only to its nearest neighbor. Connection networks can be adapted manually in order to exclude contacts across geographical barriers or to include long-range contacts. **L** is row-standardized (*i.e.*, each of its rows sums to one), and all its diagonal terms are zero. **L** can be used to compute the spatial autocorrelation of a given centered variable **x** (*i.e.*, with mean zero), with n observations, using the Moran's index (I) statistic [24]: $I = \frac{\mathbf{x'Lx}}{\mathbf{x'x}}$, where **x**' denotes the transpose of **x**. In the case of genetic data, **x** contains frequencies of an allele. Moran's I can be used to measure spatial structure among the values of **x**: it is highly positive when values of x observed at neighboring sites tend to be similar, while it is strongly negative when values of **x** observed at neighboring sites tend to be dissimilar. According to Thioulouse *et al.* [15], a positive (resp. negative) autocorrelation refers to a global (resp. local) structure. However, Moran's index measures only spatial structures, and does not take the variability of x into account. The sPCA defines the following function to measure both the spatial structure and variability in **x**: $C(\mathbf{x}) = \mathrm{var}(\mathbf{x}) I(\mathbf{x}) = \frac{1}{n}\mathbf{x'Lx}$

$C(\mathbf{x})$ is highly positive when **x** has a large variance, and exhibits a global structure; conversely, $C(\mathbf{x})$ is largely negative when **x** has a high variance and displays a local structure. This function is the criterion used in sPCA, which finds linear combinations of the alleles of **X** decomposing C from its maximum to its minimum value. This is accomplished by the eigenvalue decomposition of the matrix, **X'(L + L')X**. Eigenvalues can be positive or negative for global or local structures, respectively. This also allows the calculation of the contributions of alleles and markers to the eigenvalues. Accordingly, the criterion used in an ordinary PCA is the variance, and the PCA consists of performing the eigenvalue decomposition of the matrix **X'X**.

Statistical tests are proposed by [14] to detect the existence of spatial patterns.

A geographic map, in which component scores each correspond to a different color, may give a synthetic representation of the spatial structures. These plots can show up to three scores at the same time by translating each score into a channel of colors (first, red; second, green; third, blue) [24].

2.2. Spatial Analysis on metric Multidimensional Scaling (Principal Coordinates Analysis)

The use of neighboring relationships can be extended to other types of multivariate analyses [15]. Among them, the Principal Coordinates Analysis or metric Multidimensional Scaling (MDS) [25], is commonly used to infer genetic structuring among genotypes or populations by summarizing a matrix of genetic distances.

Like PCA, MDS produces a set of orthogonal axes, which are ranked according to their eigenvalues. In the case of Euclidean distances, MDS behaves in a Euclidean manner. Running an MDS on the canonical Euclidean distance yields the same results as a PCA would. MDS on non-Euclidean distances generates negative eigenvalues, meaning that some of the dimensions are not in real space. In most cases, this does not affect the representation of objects on the first axes, but this can also be problematic. Functions exist to test whether distances are Euclidean [26]. Although any non-Euclidean distances can be converted into Euclidean ones [27,28], it seems sensible to choose a distance which is not too far from being Euclidean.

Two commonly used genetic distances, the Roger's distance [29], and the pairwise Fst [30], are Euclidean. The Reynold's distance is considered to be either Euclidean [31] or non-Euclidean [32], while its calculation formula also varies, according to the authors [33-35].

Felsenstein [34] defines D_R as:

$$D_R = \sqrt{\frac{\sum_{m=1}^{k}\sum_{i=1}^{n_m}\left(p_{m_i}^{[1]} - p_{m_i}^{[2]}\right)^2}{2\sum_{m=1}^{k}\left(1-\sum_{i=1}^{n_m} p_{m_i}^{[1]} p_{m_i}^{[2]}\right)}}$$

where k is the number of markers, n_m is the number of alleles of the mth marker, and $p_{m_i}^{[j]}$ is the allelic frequency of the i^{th} allele of the m^{th} marker in the j^{th} population. ${D_R}^2$ is the quantity that is expected to rise linearly with cumulated drift. Software either compute ${D_R}^2$ (PHYLIP [34]), or D_R (R package ade4 [36]).

Considering that a squared-root transformation often makes a distance Euclidean [23], and that the numerator of D_R, $\sum_{m=1}^{k}\sum_{i=1}^{n_m}\sqrt{\left(p_{m_i}^{[1]} - p_{m_i}^{[2]}\right)^2}$, is the canonical Euclidean distance, we use D_R instead of ${D_R}^2$, for MDS analysis.

Calculations were carried out using the R software (http://www.R-project.org), especially the *adegenet* package [17], and its *sPCA* function for genetic data handling and sPCA. The *adegenet* package depends on the *ade4* package [36] for multivariate analyses and on the *spdep* package [37] for spatial methods. The spatial structures were found to be statistically significant (p-values < 0.02) according to the permutation test proposed by Jombart [14]. Reynold's distances were processed with the *ade4* package (*is.euclid* and *quasieuclid* functions). The spatial Multidimensional Scaling was run

with the *ade4* package (*multispati* and *dudi.co* function). An R script for the calculation is listed in the supplementary material.

2.3. Data Sets

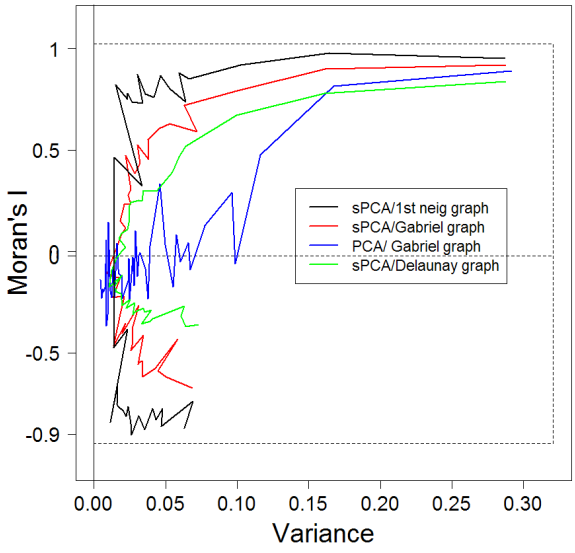
Genotypes of 30 microsatellites in 45 goat breeds [19] and of 31 microsatellites in 46 sheep breeds [22] (after the removal of Merino-derived breeds), were generated during the EU Econogene project (www.econogene.eu). The cattle data set with the genotypes of 19 microsatellites in 101 breeds combined data generated during the EU project, ResGEN 98-118 [20], with data from Southwestern-Asian and Indian [38], Scandinavian [39], Northern Asian [39], Andalusian [40], and Austrian (R. Baumung, unpublished data) breeds. All the genotypes have been standardized with common reference samples. Breed names, countries of origin, codes, and geographical coordinates of breeds are in the supplementary tables S1 through S3 (supplementary section). The locations of the breeds are visualized in Figure S1.

3. Results and Discussion

3.1. Comparison of Methods of Analyses

Figure 1 shows, for the goat data set, the spatial Moran's index *I* of successive eigenvalues plotted against the corresponding variances. Eigenvalues of the ordinary PCA (blue line) have higher variances than corresponding sPCA eigenvalues because of the PCA maximization criterion. For the first two eigenvalues, the Moran's *I* components of sPCA are only slightly smaller than the corresponding sPCA values (red line). However, the difference is clearly larger for the subsequent values (0.79 *vs.* 0.48 for the third axis); thus, sPCA detects additional spatially structured components.

Figure 1. Plots of spatial Moran's *I* and variance components of successive eigenvalues of sPCA analysis for goat microsatellite allele frequencies, based on three different graph types, and of PCA analysis of the same data. Note the low Moran's *I* values (according to the Gabriel graph) of the PCA components, which were optimized only with regard to variance. The first eigenvalue is in the top-right corner.



In order to optimize the sPCA, we compared the performance of the Delaunay, Gabriel, and 1st neighbor graphs of the goat breeds (Figure 1 and Figure S2). The shapes of sPCA lines are similar for the first three eigenvalues, showing a slight decrease of *I* values and a larger decrease of the variances. The 1st neighbor graph connects each breed only to its closest neighbor, resulting in high *I* values, but neglects other geographic information. The Delaunay graph connects very distant breeds, such as southern Spanish and Saudian breeds. The Gabriel graph appears to be a good compromise between the 1st neighbor graph and the Delaunay neighbor graph, and is used for subsequent sPCA analyses. However, correlations of the breed scores obtained by the different graph types are close to one (Table S4), so results are robust with respect to the choice of the graph.

A spatial multidimensional scaling was performed based on Reynold's genetic distances, D_R, and the Gabriel neighboring graph. Reynold's distances were empirically checked for euclideanarity and shown to be almost Euclidean.

Figure 2 (top panels) compares the sPCA and PCA of allele frequencies with the decomposition of the spatial multidimensional scaling (sMDS) eigenvalues, which are based on Reynolds' genetic distances. Corresponding values are in Tables S5 and S6. The variance percentage of the first three axes is slightly higher than in the sPCA, at the expense of lower Moran's *I* values. However, breed scores are essentially similar to the sPCA scores, with correlation coefficients of breeds being equal to 0.98 or more, for the first three components (Table S4).

Figure 2. Scatter plots of spatial Moran's *I* and variance components of eigenvalues of PCA or MDS. For each plot, the blue and red lines correspond to the ordinary and spatial analyses, respectively. Top left, bottom left, and right: PCA and sPCA on allele frequencies. Top right: MDS and sMDS on Reynolds' distances.

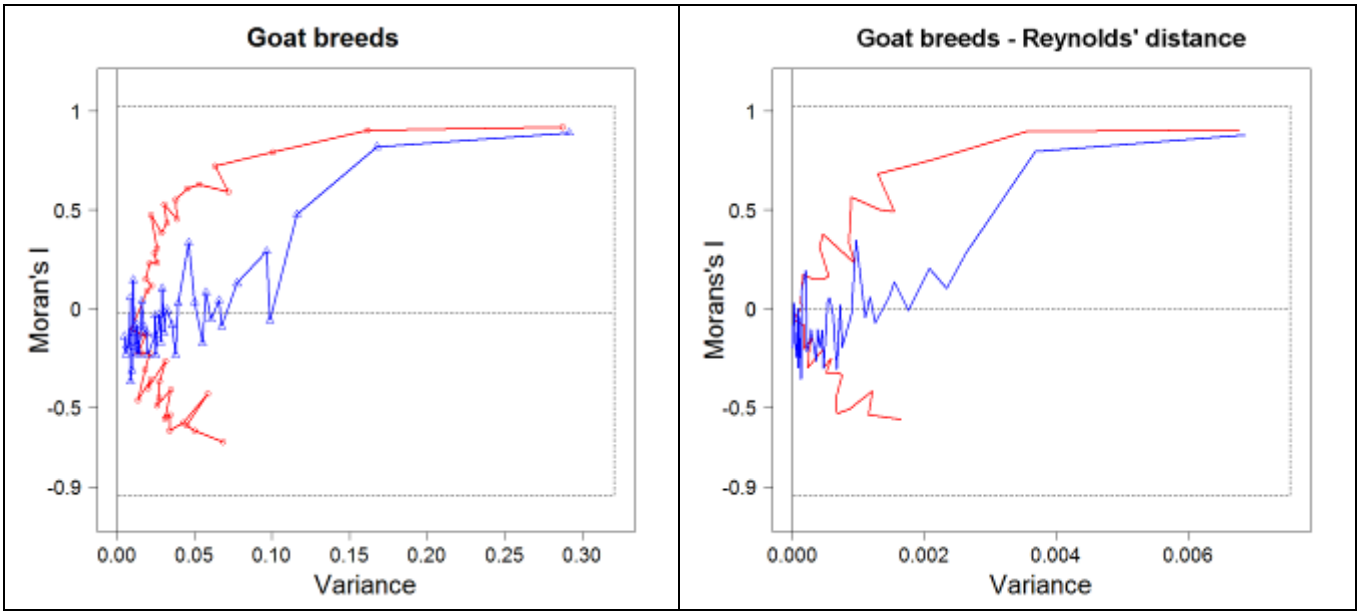
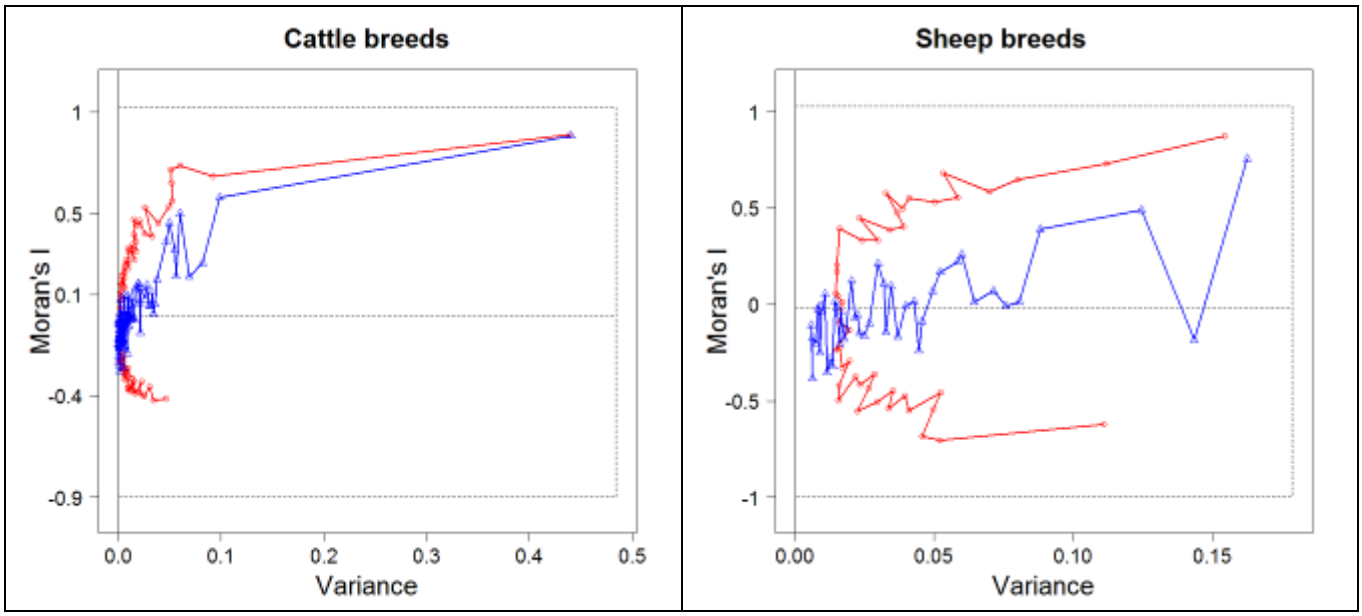


Figure 2. *Cont.*



3.2. sPCA of Goat Allele Frequencies

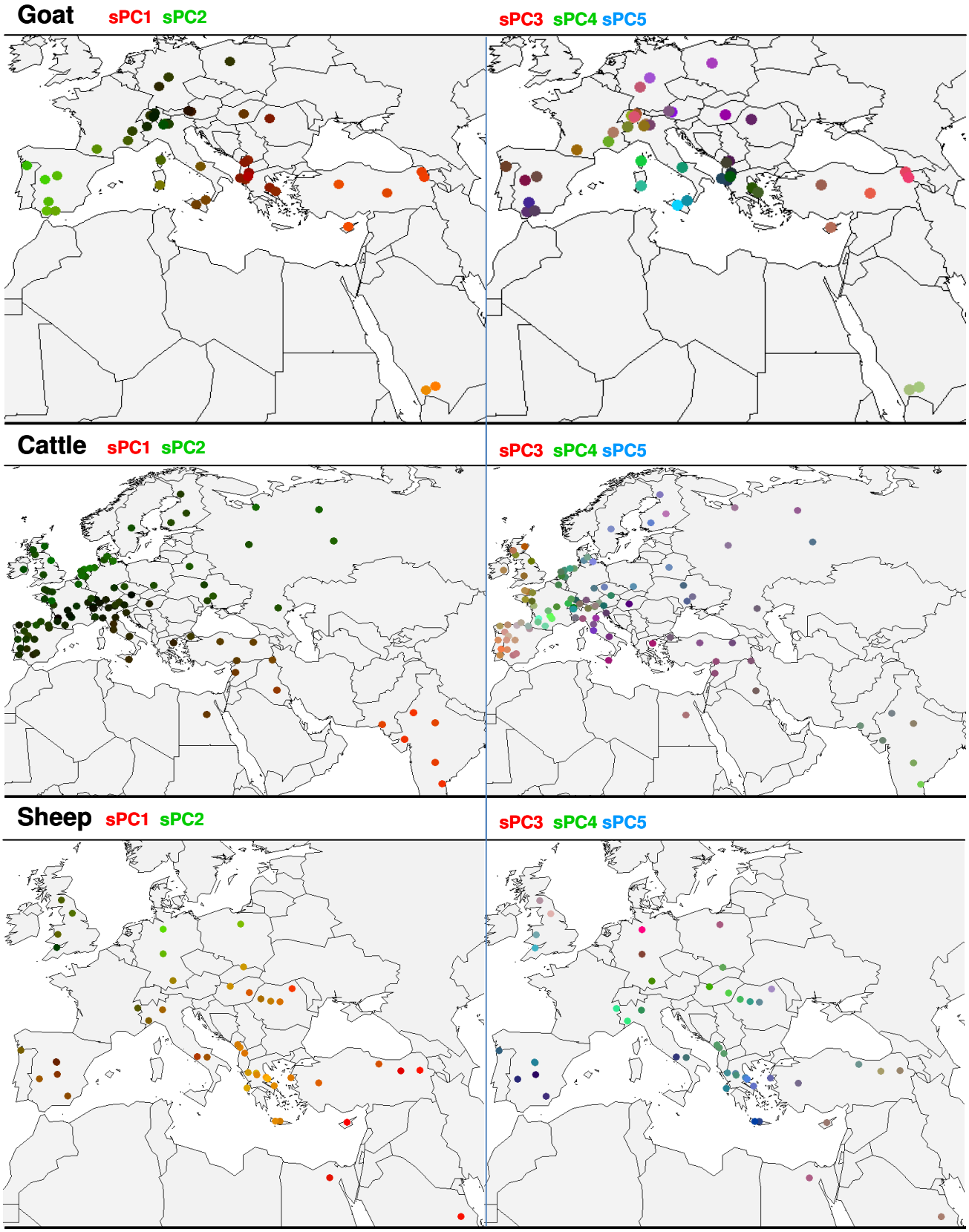
The variances of the first five goat sPCA components of Figure 2 (top left) represent 42% of the total variance, (Table S5). For the first and second factors, breed scores of sPCA and PCA correlate well (coefficients of 0.997 and 0.982, respectively).

Figure 3 (top) shows a color representation of the first five spatial Principal Components) (sPC's) Separate sPC's are plotted in Figure S3. The first two sPCs correspond to the first two coordinates of ordinary PCA analysis; sPC1 reveals the southeast to northwest gradient [18] from the Asian site of domestication to Europe [33], and sPC2 shows an east-west gradient. However, subsequent sPCA coordinates are not detected by PCA. The third sPC shows a north-south contrast. The fourth sPC with high Moran *I* values has a clearly lower variance than the first three sPC's. It shows a contrast of Italian and French *vs.* Iberian, central European, and eastern European breeds. Likewise, sPC5 separates northern Mediterranean breeds from both northern and southern breeds. Combining the information of five sPC's suggest regional clusters of breeds in Southwest Asia, Italy with Corsica, Albania and Greece, and the Iberian peninsula and Germany with Austria and Eastern Europe (Figure 3). This is essentially in agreement with model-based clustering and distance analysis of the same data [19].

A strong geographic clustering was also apparent from Y-chromosomal variation [41,42], thus contradicting the original notion of a weak geographic structure for goats [43]. However, this was based on the worldwide dispersal of the mitochondrial haplotype A, which is now explained by the domestication of mainly haplotype A carrying animals [44]. Apparently, microsatellites are more sensitive to the recent demographic history of a species than to mitochondrial DNA, and reveal a geographic clustering that reflects the isolation by distance.

Figure S7 illustrates the contribution of each marker to the construction of the first three axes. For instance, *SRCRSP8* and *TGL53* contribute relatively much to sPC1, while *ILSTS087* and *ILSTS029* are the most important for sPC2.

Figure 3. sPCA of goat, sheep, and cattle breeds. Coordinates have been displayed with the color as indicated, and the intensity of the color is proportional to the sPC values.



3.3. sPCA of Cattle Allelic Frequencies

For cattle, the first five components of sPCA represent 41% of the total variance (Figure 2, Table S7). Again, the two components of sPCA and PCA have similar variances and Moran's *I*. However, sPCA detects additional geographical structuring. The first sPC (Figures 3, S4) shows a strong structuring along a southeast to northwest cline, and corresponds to a gradient from Indian zebu to European taurine cattle [38,45]. The second sPC separates northern from southern European breeds. These results agree with archeological data [46], which reveal that farmers spread from the Fertile Crescent to Northwestern Europe, following two main colonization routes, along the river Danube and along the Mediterranean coasts. A north-south contrast was also apparent from previous microsatellite data [47], AFLP genotypes [21], and Y-chromosomal variation [48]. The third sPC is not detected by ordinary PCA and mainly emphasizes breeds near the Atlantic coast. In combination with sPC4 and sPC5, this generates a pattern that differentiates mainly Central-European breeds from the surrounding Atlantic, Mediterranean, and Nordic breeds. The first five sPC's together show a pronounced geographic structure of the genetic variation in European and Southwest-Asian cattle.

The first component has a large contribution of *HEL13* (14%, Figure S3), which has zebu-specific alleles [49]. The third component is dominated by the microsatellite *ETH10* (13%), which is linked to the *Silver* gene [50] and to another QTL affecting a growth trait, possibly the *myf* 5 gene [51].

3.4. sPCA of Sheep Allelic Frequencies

The first five sheep sPCs (Figures 2, 3, Figure S5, and Table S8) represent only 33.8% of the total variation. However, sheep shares, with cattle and goat, the southwest to northwest cline represented by sPC1. This is also the only component that corresponds to a PCA component. The second and third sPCs differentiate mainly in the north-south direction, and sPC4 and sPC5 highlight central European breeds. As for cattle and goat, the subsequent sPCs represent less than 3% of the variation with the exception of sPC45 (Figure 2), which has an appreciable variance (6.5% of the total variance) and a strongly negative auto-correlation -0.62. This clear local structure corresponds to the genetic contrast between the German breeds DEGGH and DERHO, and to a lesser extent, to the difference between the English breeds UKEXH and UKSDL (Figure S6). Since these breeds also have low allelic richness and expected heterozygosity [22] (see Figure S6), this can be explained by genetic drift in relatively small and isolated populations.

The relatively strong north-south contrast of the first three components may be explained by the effect of climate, but also to the contrasts of the English and Merino-types of breeds, which both have been used frequently for crossbreeding. Relatively weak geographic structuring was also indicated by model-based clustering and may be caused by a higher level of crossbreeding. Presumably, this reflects a more economically oriented style of husbandry for sheep than for goats [18], but may have eroded geographic structures of older origin.

4. Conclusion

We conclude that the sPCA allows for a more sensitive detection of geographic structuring than ordinary PCA would, and provides both quantitative and qualitative comparisons of species inhabiting the same region. Geographic trends are strong for goat, intermediate for cattle, and relatively weak for sheep. Our analysis reveals for all three ruminant livestock species a major cline from the southeast to the northwest. In addition, the analysis shows the differences between the species' genetic patterns in Europe: for goats, a genetic compartmentalization of Central European and Mediterranean regions; for cattle, a contrast between the central continent and the peripheral isles or peninsulas; and for sheep, the most clear north-south contrast, and a local structure mainly due to genetic drift.

For goat and cattle (not shown), we found a good agreement of sPCA and sMDS. Although slightly lower Moran *I* values show that sMDS is slightly less sensitive for the detection of geographic structure, sMDS extends the spatial analysis to distance data sets, provided that distances are Euclidean or almost Euclidean, which seems to be the case for the Reynold's distance. These may be particularly useful for meta-analysis of data sets with overlapping marker panels, for which it has been shown that the Reynolds' distance is relatively insensitive to the category or panel of markers (unpublished results; [21]).

Differential contributions of markers to the coordinates may be suggestive of the effects of selection. An interesting perspective is the localization of functional traits by spatial analysis of high-density genotyping data [52,53].

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References

1. Novembre, J.; Di Rienzo, A. Spatial patterns of variation due to natural selection in humans. *Nat. Rev. Genet.* **2009**, *10*, 745-755.
2. Diniz-Filho, J.A.F.; Nabout, J.C.; Telles, M.P.d.C.; Soares, T.N.; Rangel, T.F.L.V.B. A review of techniques for spatial modeling in geographical, conservation and landscape genetics. *Genet. Mol. Biol.* **2009**, *32*, 203-211.
3. Manel, S.; Schwartz, M.K.; Luikart, G.; Taberlet, P. Landscape genetics: combining landscape ecology and population genetics. *Trends Ecol. Evol.* **2003**, *18*, 189-197.
4. Sokal, R.R.; Wartenberg, D.E. A test of spatial autocorrelation analysis using an isolation-by-distance model. *Genetics* **1983**, *105*, 219-237.
5. Bertorelle, G.; Barbujani, G. Analysis of DNA diversity by spatial autocorrelation. *Genetics* **1995**, *140*, 811-819.
6. Smouse, P.E.; Peakall, R. Spatial autocorrelation analysis of individual multiallele and multilocus genetic structure. *Heredity* **1999**, *82*, 561-573.

7. Pearson, K. On lines and planes of closest fit to systems of points in space. *Philos. Mag.* **1901**, *2*, 559-572.
8. Patterson, N.; Price, A.L.; Reich, D. Population structure and eigenanalysis. *PLoS Genet.* **2006**, *2*, 2074-2093.
9. Cavalli-Sforza, L.L. Population structure and human evolution. *Proc. R. Soc. B* **1966**, *164*, 362-379.
10. Hanotte, O.; Bradley, D.G.; Ochieng, J.W.; Verjee, Y.; Hill, E.W.; Rege, J.E.O. African pastoralism: Genetic imprints of origins and migrations. *Science* **2002**, *296*, 336-339.
11. Moazami-Goudarzi, K.; Laloe, D. Is a multivariate consensus representation of genetic relationships among populations always meaningful? *Genetics* **2002**, *162*, 473-484.
12. Jombart, T.; Pontier, D.; Dufour, A.B. Genetic markers in the playground of multivariate analysis. *Heredity* **2009**, *102*, 330-341.
13. Novembre, J.; Johnson, T.; Bryc, K.; Kutalik, Z.; Boyko, A.R.; Auton, A.; Indap, A.; King, K.S.; Bergmann, S.; Nelson, M.R.; Stephens, M.; Bustamante, C.D. Genes mirror geography within Europe. *Nature* **2008**, *456*, 98-101.
14. Jombart, T.; Devillard, S.; Dufour, A.B.; Pontier, D. Revealing cryptic spatial patterns in genetic variability by a new multivariate method. *Heredity* **2008**, *101*, 92-103.
15. Thioulouse, J.; Chessel, D.; Champely, S. Multivariate analysis of spatial patterns: a unified approach to local and global structures. *Environ. Ecol. Stat.* **1995**, *2*, 1-14.
16. Wartenberg, D. Spatial autocorrelation as a criterion for retaining factors in ordinations of geographic data. *Math. Geol.* **1985**, *17*, 665-682.
17. Jombart, T. Adegenet: a R package for the multivariate analysis of genetic markers. *Bioinformatics* **2008**, *24*, 1403-1405.
18. Groeneveld, L.F.; Lenstra, J.A.; Eding, H.; Toro, M.A.; Scherf, B.; Pilling, D.; Negrini, R.; Finlay, E.K.; Jianlin, H.; Groeneveld, E.; Weigend, S. GLOBALDIV Consortium. Genetic diversity in farm animals - a review. *Anim. Genet.* **2010**, *41*, 6-31.
19. Canon, J.; Garcia, D.; Garcia-Atance, M.A.; Obexer-Ruff, G.; Lenstra, J.A.; Ajmone-Marsan, P.; Dunner, S. ECONOGENE Consortium. Geographical partitioning of goat diversity in Europe and the Middle East. *Anim. Genet.* **2006**, *37*, 327-334.
20. Lenstra, J.A. European Cattle Genetic Diversity Consortium. Marker-assisted conservation of European cattle breeds: an evaluation. *Anim. Genet.* **2006**, *37*, 475-481.
21. Negrini, R.; Nijman, I.J.; Milanesi, E.; Moazami-Goudarzi, K.; Williams, J.L.; Erhardt, G.; Dunner, S.; Rodellar, C.; Valentini, A.; Bradley, D.G.; Olsaker, I.; Kantanen, J.; Ajmone-Marsan, P.; Lenstra, J.A. European Cattle Genetic Diversity Consortium. Differentiation of european cattle by AFLP fingerprinting. *Anim. Genet.* **2007**, *38*, 60-66.
22. Peter, C.; Bruford, M.; Perez, T.; Dalamitra, S.; Hewitt, G.; Erhardt, G. ECONOGENE Consortium. Genetic diversity and subdivision of 57 European and Middle-Eastern sheep breeds. *Anim. Genet.* **2007**, *38*, 37-44.
23. Legendre, P.; Legendre, L. *Numerical Ecology*, 2nd English ed.; Elsevier Science BV: Amsterdam, The Netherlands, 1998.
24. Piazza, A.; Menozzi, P.; Cavallisforza, L.L. Synthetic gene-frequency maps of man and selective effects of climate. *Proc. Natl. Acad. Sci. USA.* **1981**, *78*, 2638-2642.

25. Gower, J. Some distance properties of latent root and vector methods used in multivariate analysis. *Biometrika* **1966**, *53*, 325-338.
26. Gower, J.C.; Legendre, P. Metric and Euclidean properties of dissimilarity coefficients. *J. Classif.* **1986**, *3*, 5-48.
27. Lingoes, J. Some boundary conditions for a monotone analysis of symmetric matrices. *Psychometrika* **1971**, *36*, 195-203.
28. Cailliez, F. The analytic solution of the additive constant. *Psychometrika* **1983**, *48*, 305-310.
29. Baker, A.J.; Moeed, A. Rapid genetic differentiation and founder effect in colonizing populations of common mynas (acridotheres-tristis). *Evolution* **1987**, *41*, 525-538.
30. Zhivotovsky, L.A.; Rosenberg, N.A.; Feldman, M.W. Features of evolution and expansion of modern humans, inferred from genomewide microsatellite markers. *Am. J. Hum. Genet.* **2003**, *72*, 1171-1186.
31. Fullaondo, A.; Vicario, A.; Aguirre, A.; Barrena, I.; Salazar, A. Quantitative analysis of two-dimensional gel electrophoresis protein patterns: a method for studying genetic relationships among Globodera pallida populations. *Heredity* **2001**, *87*, 266-272.
32. Reif, J.C.; Melchinger, A.E.; Frisch, M. Genetical and mathematical properties of similarity and dissimilarity coefficients applied in plant breeding and seed bank management. *Crop Sci.* **2005**, *45*, 1-7.
33. Reynolds, J.; Weir, B.S.; Cockerham, C.C. Estimation of the Coancestry Coefficient: Basis for a Short-Term Genetic Distance. *Genetics* **1983**, *105*, 767-779.
34. Felsenstein, J. PHYLIP—Phylogeny Inference Package (Version 3.2). *Cladistics* **1989**, *5*, 164-166.
35. Weir, B.S. *Genetic Data Analysis*; Sinauer Associates: Sunderland, MA, USA, 1990.
36. Chessel, D.; Dufour, A.B.; Thioulouse, J. The ade4 package. I. One-table methods. *R News* **2004**, *4*, 5-10.
37. Bivand, R. Implementing Spatial Data Analysis Software Tools in R. *Geogr. Anal.* **2006**, *38*, 23-40.
38. Loftus, R.T.; Ertugrul, O.; Harba, A.H.; El-Barody, M.A.A.; Machugh, D.E.; Park, S.D.E.; Bradley, D.G. A microsatellite survey of cattle from a center of origin: the Near East. *Mol. Ecol.* **1999**, *8*, 2015-2022.
39. Li, M.H.;Tapio, I.; Vilkki, J.; Ivanova, Z.; Kiselyova, T.; Marzanov, N.; Cinkulov, M.; Stojanovic, S.; Ammosov, I.; Popov, R.; Kantanen, J. The genetic structure of cattle populations (Bos taurus) in northern Eurasia and the neighboring Near Eastern regions: implications for breeding strategies and conservation. *Mol. Ecol.* **2007**, *16*, 3839-3853.
40. Luque, A.; Valera, M.; Azor, P.J.; Goyache, F.; Rodero, E.; Molina, A. La raza bovina autóctona española Pajuna: Situación actual y programa de recuperación. *Anim. Genet. Resour. Inf.* **2006**, *39*, 1-14.
41. Lenstra, J.A. ECONOGENE Consortium. Evolutionary and demographic history of sheep and goats suggested by nuclear, mtDNA and Y chromosome markers. In *Proceedings of the International Workshop on the Role of Biotechnology for the Characterization and Conservation of Crop, Forestry, Animal and Fishery Genetic Resources*, Torino, Italy, 5–7 March 2005; pp. 97-100.

42. Pereira, F.; Queiros, S.; Gusmao, L.; Nijman, I.J.; Cuppen, E.; Lenstra, J.A.; Davis, S.J.M.; Nejmeddine, F.; Amorim, A. ECONOGENE Consortium. Tracing the History of Goat Pastoralism: New Clues from Mitochondrial and Y Chromosome DNA in North Africa. *Mol. Biol. Evol.* **2009**, *26*, 2765-2773.
43. Luikart, G.; Gielly, L.; Excoffier, L.; Vigne, J.D.; Bouvet, J.; Taberlet, P. Multiple maternal origins and weak phylogeographic structure in domestic goats. *Proc. Natl. Acad. Sci. USA* **2001**, *98*, 5927-5932.
44. Naderi, S.; Rezaei, H.R.; Taberlet, P.; Zundel, S.; Rafat, S.A.; Naghash, H.R.; El-Barody, M.A.A.; Ertugrul, O.; Pompanon, F. Large-scale mitochondrial DNA analysis of the domestic goat reveals six haplogroups with high diversity. *PLoS ONE* **2007**, *2*, e1012.
45. Kumar, P.; Freeman, A.R.; Loftus, R.T.; Gaillard, C.; Fuller, D.Q.; Bradley, D.G. Admixture analysis of South Asian cattle. *Heredity* **2003**, *91*, 43-50.
46. Payne , W.J.A.; Hodges, J. *Tropical Cattle. Origins, Breeds and Breeding Policies*; Blackwell Science: London, UK, 1997.
47. Cymbron, T.; Freeman, A.R.; Malheiro, M.I.; Vigne, J.D.; Bradley, D.G. Microsatellite diversity suggests different histories for Mediterranean and Northern European cattle populations. *Proc. R. Soc. B* **2005**, *272*, 1837-1843.
48. Gotherstrom, A.; Anderung, C.; Hellborg, L.; Elburg, R.; Smith, C.; Bradley, D.G.; Ellegren, H. Cattle domestication in the Near East was followed by hybridization with aurochs bulls in Europe. *Proc. R. Soc.* B **2005**, *272*, 2345-2350.
49. Ibeagha-Awemu, E.M.; Jann, O.C.; Weimann, C.; Erhardt, G. Genetic diversity, introgression and relationships among West/Central African cattle breeds. *Genet. Sel. Evol.* **2004**, *36*, 673-690.
50. Gutierrez-Gil, B.; Wiener, P.; Williams, J.L. Genetic effects on coat colour in cattle: dilution of eumelanin and phaeomelanin pigments in an F2-Backcross Charolais x Holstein population. *BMC Genet.* **2007**, *8*, 56.
51. Li, C.; Basarab, J.; Snelling, W.M.; Benkel, B.; Murdoch, B.; Hansen, C.; Moore, S.S. Assessment of positional candidate genes myf5 and igf1 for growth on bovine chromosome 5 in commercial lines of Bos taurus. *J. Anim. Sci.* **2004**, *82*, 1-7.
52. Pariset, L.; Joost, S.; Marsan, P.A.; Valentini, A.; Ec Landscape genomics and biased FST approaches reveal single nucleotide polymorphisms under selection in goat breeds of North-East Mediterranean. *BMC Genet.* **2009**, *10*, 7.
53. Manel, S.; Segelbacher, G. Perspectives and challenges in landscape genetics. *Mol. Ecol.* **2009**, *18*, 1821-1822.