10

Landscape Genomics in Livestock

Lorraine Pariset[1], Stephane Joost[2],
Maria Gargani[1] and Alessio Valentini[1]
[1]*Department for Innovation in Biological, Agro-Food and Forest Systems (DIBAF), University of Tuscia, Viterbo*
[2]*Laboratory of Geographic Information Systems (LASIG), School of Architecture Civil and Environmental Engineering (ENAC) Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne*
[1]*Italy*
[2]*Switzerland*

1. Introduction

Landscape genomics correlates genetic variation patterns with geographic variables to investigate how geographical and environmental characteristics affect the genetic structure of populations (Luikart et al., 2003; Joost et al., 2007; Holderegger & Wagner, 2008; Pariset et al., 2009; Shwartz et al., 2009). A field combining molecular markers, genetics and landscape structure was first described by Manel et al. (2003) and its definition evolved and changed in the following years (Storfer et al., 2007; Holderegger & Wagner, 2006).

Landscape genomics requires the recording of the exact location of the sampling and the assessment of a number of molecular markers on a representative number of individuals in a population, obtaining the allelic frequency at these loci (Joost et al., 2008). Markers can vary from mtDNA to Y chromosome, microsatellites, Single Nucleotide Polymorphisms (SNP) (Manel et al., 2003; Wang, 2011). The nature of the markers used for the analysis can affect the detection of geographical structuring of populations, as suggested by Naderi et al. (2007). The simultaneous use of both nuclear and single parent transmitted markers (mitochondrial and Y chromosome) is likely to provide more significant results respect to the use of either marker alone (Hewitt, 2004; Gonçalves et al., 2010; Wang et al., 2011; Pariset et al., 2011).

Recently, the availability of high density SNP devices for a few species has given new possibilities of analysis. High throughput genomics is providing new DNA sequences suitable for gene discovery and for the study of genetic variation at different levels. Most important, the quick expansion of molecular genetic technologies not only is providing a huge amount of genomic data and suitable markers: it is offering data at affordable and constantly declining costs. Therefore the genomic information available for most species, including livestock, is rapidly increasing (Luikart et al., 2003; Marnis et al., 2007; Segelbacher et al., 2010; Helyar et al., 2010) making possible the setup of high throughput SNP devices for livestock (Box 7).

Box 1. Molecular Markers for livestock landscape genomics

To analyse the interaction between geographic variables and genetic patterns, landscape genomics requires a high number of molecular markers for providing enough power of resolution. The main marker systems utilized in livestock studies are AFLPs, microsatellites or STR, SNPs and CNV.

AFLP

The AFLP technique consists of two steps: a DNA digestion and a PCR amplification. Specifically, the fragments obtained from digestion are linked to adapters and amplified using specific primers (complementary to the adapters). This technology generates a mixture of fragments that are separated and identified by polyacrylamide gel electrophoresis or by sequencing devices. These markers are assumed to be dominant and neutral (Vos et al., 1995) and were widely applied to livestock (Negrini et al., 2007; Ajmone-Marsan et al., 2008, 2011), but they can be used to find genes under selection with a population genomics method (Luikart et al., 2003). The advantage of AFLPs is that they allow analyzing several loci in a single experiment and that they can be applied to species of which genome sequences are unknown. However, their mostly dominant behaviour makes it difficult to assess allelic frequencies when Hardy Weinberg equilibrium is not assured. They also require substantial hand work.

Microsatellites

Microsatellites are codominant markers located in the nuclear DNA. They are short tandem repeats of two to eight or more nucleotides which occur as interspersed repetitive elements in all eukaryotic genomes (Tautz & Renz, 1984). The microsatellite polymorphism consists in the number variation of the tandem repeated units; the alleles at the same locus differ in their length. After PCR amplification performed using primers flanking the repeated motif, the different alleles are analyzed by gel electrophoresis or by automated sequencers. The microsatellites are not very suitable for massively parallel analysis because traditional multiplexing cannot be expanded to more than a few loci (far less than 20); too many DNA amplifications are required and microsatellite are now being replaced by more efficient systems. However, recently a STR profiling method was developed using the Roche Genome Sequencer FLX to sequence multiple microsatellite loci (Fordyce et al., 2011).

Mithocondrial DNA

Mitochondrial DNA (mtDNA) is a uniparental marker as its inheritance is clonal (maternal) and it is not subject to recombination (Galtier et al., 2009). mtDNA is present in hundreds of copies per cell and evolves 10 times faster than nuclear DNA. The evolution of mitochondrial genes varies from region to region: the ribosomal DNA genes are highly conserved; the region known as non-coding control region (containing the displacement loop or D-loop and the origin of replication) is much more variable since it is deemed to be not being subject to selective pressure. Mitochondrial markers are amplified by PCR and then sequenced or, today more rarely, assessed by restriction enzymes. Sequencing can be performed by Sanger or by parallel devices (Galtier et al., 2009). The multiplicity of copy number of mtDNA in a cell makes it suitable for the analysis of ancient specimens. Sequencing data obtained are then aligned and analyzed with appropriate bioinformatics programs.

Single Nucleotide Polymorphisms

SNPs (Single Nucleotide Polymorphisms) are the most common form of polymorphism among individuals, arising approximately every 200 base pairs in livestock (Williams, 2005). A SNP marker is a single base change in a DNA sequence (Vignal, 2002). The main methods for the identification of new single nucleotide variations are direct sequencing of regions of interest and *in silico* research that allows the identification of SNPs through alignment and comparison of sequences using public sequence databases (Guryev et al., 2005). Expressed sequence tags (ESTs) including numerous copies of the same gene sequence can be used to identify SNPs *in silico* (Primmer, 2008). ESTs are becoming publicly available with increasing frequency; they represent a cheap and effective tool for identifying gene-linked markers and are available also for species not yet fully sequenced (Pariset et al., 2009c, 2010b). Today, millions of SNPs are discovered by resequencing different individuals by parallel sequencers. After sequencing, SNPs can be selected and a chip that allows the diagnosis of the alleles for a very low cost (well below 1/1000 of USD each, depending on market and species) can be devised. Y chromosome SNPs constitute another important source of uniparental markers (Nijman et al., 2008). Due to their abundance and to the recent availability of high throughput analysis technologies, SNP markers are being used more and more and have begun the most suitable markers for landscape genomics.

CNV

Copy Number Variation (CNV) refers to genomic structural variations that involve DNA segments ranging from 1 kb to 5 Mb (Feuk et al., 2006). The quantitative variants comprising insertions and deletions, as well as inversions and translocations, are relative to a reference genome sequence (Scherer et al., 2007)**.** CNVs represent an important source of genetic variation among individuals and cover more nucleotide sequences per genome compared to SNPs markers (Conrad et al., 2010). Some studies have demonstrated that CNVs can influence gene expression through position effects, and can be related to human diseases (Feuk et al., 2006; Zhang et al., 2009). The common methods for CNVs detection and analysis are SNP arrays and array comparative genome hybridization microarrays (CGH). The advantages of using the arrays are their low cost and high-density which make them ideal for large population screening (Perkel, 2011). About 29,000 CNVs have been identified in humans (Conrad et al., 2009), and it was estimated that two individual genomes have differences in CNVs on order of 500 to 1000 (Perkel, 2011). CNVs dataset have been identified in cattle using both high-density CGH and SNP array data. For example, CGH arrays have been used to identify 25 germline CNVs in three Holstein bulls (Liu et al., 2008); Liu et al. (2010) discovered over 200 candidate CNV regions some of which contribute to the breed formation and adaptation. Fadista et al. (2010) identified 304 CNV regions in 20 animals belonging to four cattle breeds. SNP data from Bovine HapMap Consortium samples were used to identify 682 candidate CNV regions in a diverse panel of 521 animals from 21 different breeds (Hou et al., 2011). Using the BovineSNP50 genotyping data 368 CNV regions from 265 Korean Hanwoo cattle and 682 candidate CNV regions in a diverse panel of 521 animals from 21 different breeds have been identified (Bae et al., 2010).

Landscape Genomics has proven ability to detect statistical signals that associate loci with environmental parameters in very different species, like *Hylobius abietis* and *Ovis aries* (Joost et al., 2007). The use of a high number of markers allows the identification of loci that may be under selection. In fact, loci under selection may be non-optimal for calculating population parameters while they can be useful in assessing local speciation, adaptation and, in the case of livestock, the effects of human selection (Storz, 2005; Joost et al., 2008; Pariset et al., 2009b; Manel et al., 2010). This approach presents differences when analyzing livestock or wild species (Bruford, 2004). Gene flow in natural populations depends on ecological characteristics and global or local environment, while for livestock it is influenced mainly by human activities (Manel et al., 2003; Storfer et al., 2007; Berthouly et al., 2009; Anderson et al., 2010). Present day livestock breeds are the result of years of human selection, adaptation to different environments and demographic effects as domestication, migration, selection of the more desired individuals, all contributing to the actual patterns of genetic diversity (Bruford et al., 2003).

Threats to biodiversity, in terms of extinction rate, destruction of ecosystems and habitat, or loss of genetic diversity, are increasing within the species utilized in agriculture. Livestock plays a fundamental role in human society, as source of both food and nitrogen and greenhouse gas contributing to environmental pollution and climate change (Joost et al., 2009). Livestock sector is losing genetic diversity as large-scale production expands (Taberlet et al., 2008; Joost et al., 2010; Anderson et al., 2010). After domestication process, livestock sector has changed remarkably because of the intense anthropogenic selection (Taberlet et al., 2008; Joost et al., 2011). As a consequence, farmers progressively substituted less productive local breeds with highly productive cosmopolitan breeds and progressively a significant number of native breeds disappeared (Simianer et al., 2003). It is more strategically important than ever to preserve as much of the livestock diversity as possible, to ensure a prompt and proper response to the needs of future generations. In this context, approaches based on the combination of genomics and spatial analysis is of great help.

2. Landscape analysis methods

Analysis techniques in landscape genetic employ various statistical approaches that can be applied using several statistical software, some of which are listed in Box 3. Statistical procedures for estimating genetic subdivision as AMOVA or F statistics (Wright, 1951; Excoffier et al., 1992) calculate divergence among populations. Statistical methods suitable for landscape analysis rely mostly on IBD, multivariate analysis and clustering models. They relate genetic variations to demographic data that can include aspects of the landscape.

2.1 IBD (isolation by distance)

The genetic structure of natural populations is influenced by the limited gene flow occurring when geographical distances increase between them. The non random mating is a result of the preferentially reproduction between geographically close individuals; this means that the genetic distance between individuals or populations is proportional to their spatial distance (isolation by distance). The IBD models are used to study demographic, migratory reproductive aspects of populations (Loiseau et al., 2009; Petit et al., 2001; Prugnolle et al.,

Box 2. GIS and GIScience
Geographical Information Systems (GIS) are specific systems designed to capture, store, manipulate, manage, analyze, and present digital geographically referenced data. In short, GIS constitute the merging of cartography, statistical analysis, and database technology. They belong to a rich set of methods, approaches and techniques, gathered together within a science (GIScience) to investigate the fundamental issues arising from the use of geographic information (Longley et al., 2001). GIScience consists of a two-sided discipline made up of its own technology driven research and development closely related to computer science (software, databases, formats, etc.), and of a collection of theories and statistical modelling approaches that explicitly use the spatial referencing of data (Goodchild & Haining, 2004).

2005). The presence of an IBD pattern is usually inferred using Mantel test (1967) which is a regression typically used to test for non-random associations between genetic differentiation (between pairs of individuals) and their geographical distance matrices (Manel et al., 2003; Guillot et al., 2009). A partial Mantel test is used to compare three or more variables allowing to identify, among a set of landscape variables, those that are associated with a significant levels of the genetic distance among individuals (Manel et al., 2003; Epps et al., 2005; Guillot et al., 2009).

Box 3. Software for Landscape genetics analysis	
BAPS (Corander et al., 2008)	BAPS is a program for Bayesian inference of the genetic structure in a population. BAPS assigns individuals to genetic clusters by either mixture or admixture models assuming HWE within cluster. The analyses can be done using a non-spatial, and spatial model for genetic discontinuities in populations. The spatial model requires that coordinate data is available for the clustered units (groups or individuals). (http://web.abo.fi/fak/mnf/mate/jc/software/baps.html)
Genclass (Piry et al., 2004)	Genclass uses Bayesian and likelihood approaches to detect migrants and to assign individuals to populations. Assumes HWE and calculates if a genotype can be excluded from a given population. (http://www.montpellier.inra.fr/URLB/index.html)
Structure (Pritchard et al., 2000)	Structure uses a Bayesan approach to investigate the population genetic structure using multi-locus genotype. Assuming HWE it infers the presence of distinct populations, detects new migrant and admixed individuals, assigns individuals to populations and studies hybrid zones. (http://pritch.bsd.uchicago.edu/software/structure2_1.html)
Geneland (Guillot et al., 2005)	Geneland is a R package that processes individual multilocus genetic data to detect population structure, assuming HWE and linkage equilibrium. Genland integrates spatial contiguity of individuals with a Bayesian genetic assignment. As a result, individuals are assigned to the genetic cluster not only on the basis of their genotype, but also of their geographic locations. The program provides a graphic with a spatial distribution of the subdivision. (http://www2.imm.dtu.dk/~gigu/Geneland/#)

Fdist (Beaumont & Nichols, 1996)	Fdist is a program for the identification of loci that might be under selection in structured populations. Fdist detect loci that show unusually low or high levels of genetic differentiation using the statistic of *Fst*. A plot of *Fst* and heterozigosity, using a coalescent model, identifies outlying *Fst* values. The program assumes an infinite or finite model of migration. (http://www.rubic.rdg.ac.uk/~mab/software.html)
Lamarc (Kuhner, 2006)	Lamarc is a program based on **l**ikelihood **a**nalysis to calculate effective population sizes assuming constant mutation rates among loci, a recombination rate, population exponential growth rates, and past migration rates assuming a stable migration structure. (http://evolution.gs.washington.edu/lamarc/lamarc_prog.html)
SAM (Joost et al., 2008)	SAM (Spatial Analysis Method) is an approach that gives the possibility to identify loci likely to be under natural selection. SAM analyzes the association between the allelic frequencies at molecular markers and data from various environmental variables. To this end SAM uses one or more environmental variable describing the sampling location and a molecular marker matrix. Using a logistic regression, this method associates the frequency of molecular markers with the environmental parameters at each site and highlights the potential markers linked to genomic regions involved in adaptation. (http://www.econogene.eu/software/sam/)
BayesAss (Wilson & Rannala, 2003)	BayesAss uses a Markov chain Monte Carlo (MCMC) method to estimates recent migration rates between populations. It also estimates each individual's immigrant ancestry, and inbreeding within populations. Loci are assumed to be in linkage equilibrium. (http://www.rannala.org/labpages/software.html)
BayeScan (Foll & Gagiotti, 2008)	BayeScan is a program that identifies candidate loci under natural selection from genetic data, using differences in allele frequencies between populations and it is based on the multinomial-Dirichlet model. BayeScan accepts different types of data: *(i)* codominant data (as SNPs or microsatellites), *(ii)* dominant binary data (as AFLPs) and *(iii)* AFLP amplification intensity, which are neither considered as dominant nor codominant. (http://cmpg.unibe.ch/software/bayescan/)
Allele in space (AIS). (Miller, 2005)	AIS is a program that combines information from genetic and spatial data. It performs some spatial analyses with genetic data: Mantel Tests, Spatial Autocorrelation Analyses, Allelic Aggregation Index Analyses (AAIA), Mommonier's Algorithm, and "Genetic Landscape Shape" interpolations. (http://www.marksgeneticsoftware.net/AISInfo.htm)
BATWING (Wilson et al., 2003)	BATWING uses a Markov chain Monte Carlo (MCMC) method to assess the past demography of populations based on multilocus genotypes. It estimates mutation rates, effective population sizes and growth rates, and times of population splitting events. (http://www.maths.abdn.ac.uk/~ijw)
NewHybrids (Anderson &	NewHybrids is a program for computing the posterior distribution that individuals fall into different hybrid categories. It uses a Bayesian

Thompson, 2002).	approach and assumes the HWE within parental populations. (http://ib.berkeley.edu/labs/slatkin/eriq/software/software.htm)
Migrate (Beerli, 2008)	The program estimates the effective population size and migration rates in different populations using maximum likelihood and Bayesian inference. It assumes constant migration rates. (http://popgen.sc.fsu.edu/)
IM (Hey & Nielsen, 2004)	IM program uses Bayesian inference to estimate the divergence time and migration occurred in the ancestry of two populations. The program assumes no linkage and recombination between loci**.** (http://genfaculty.rutgers.edu/hey/software)
Hickory (Holsinger et al., 2002)	Hickory is a program that estimates F population statistics from subdivided subpopulations. It uses a Bayesian approach and reports the posterior distribution of inbreeding coefficients and F_{ST}. (http://darwin.eeb.uconn.edu/hickory/hickory.html)

2.2 Spatial clustering

Spatial clustering models start by the assumptions that loci are in HWE and there is no admixture within clusters. They assign individuals assuming that some allele frequencies are cluster-specific. The early and still widely used program based on clustering is STRUCTURE (Pritchard et al., 2000). This program describes the genetic structure of populations using multilocus genotype data, assuming that there are K clusters, defined by allele frequencies at each locus. Modifications of the original model, recently reviewed by François & Durand (2010), include presence of genetic linkage (Falush et al., 2003; Hoggart et al., 2004; Corander & Tang, 2007), inbreeding (François et al., 2006), migration (Zhang, 2008), mutation (Shringarpure & Xing, 2009) and dominance (Falush et al,. 2007). Recently developed Bayesian clustering models such as those implemented in GENELAND (Guillot et al., 2005) and BAPS5 (Corander et al., 2008) take into account of individual geographic coordinates.

2.3 Multivariate analysis

Principal component analysis (PCA) is mainly used to represent individual or population-specific variations in allele distribution. Firstly used by Cavalli-Sforza and Edwards (1963), the method is again widely used to investigate population structure being computationally efficient and capable of handling wide datasets, where STRUCTURE requires high computational cost. PCA is still largely employed (Cavalli-Sforza et al., 1993, 1994; Novembre & Stephens, 2008) and recently applied to the study of population structure dealing with large datasets (Patterson et al., 2006; Lao et al., 2006; Jakobsson et al., 2008; Li et al., 2008; Novembre et al., 2008; Price et al., 2010), also in comparison with the Bayesian approach implemented in STRUCTURE (Price et al., 2006; Seldin et al., 2006). PCA represents population structure by means of genetic correlations among individuals. Another related method capable of detecting population structure is multidimensional-scaling (MDS) (Purcell et al., 2007; Li & Yu, 2008; Wang et al,. 2009), a method that explains observed genetic distance among individuals by the configuration of points and visually displays the structures hidden in the original data.

Box 4. Georeferenced data

Georeferenced data are geographic coordinates defining the location of investigated objects at the surface of the Earth. They constitute additional descriptors or variables in the data sets, generally X for longitude, Y for latitude and Z for altitude when recorded. Within a GIS, it is possible to simultaneously use different data sets. These datasets constitute separate information layers, whose overlay is possible only if their geographic components (X,Y) use the same projection system. A projection system is a method of representing the surface of a sphere on a plane, necessary for creating maps. Data sets from diverse national origins are produced in diverse projection systems, most often conforming to the geographical specificities of the country where the information is produced. Indeed, the location on the earth and the surface of a country influence the choice of the projection system. Given a frequent heterogeneity of data sets, the use of a common system facilitates the management and use of geodata. Such a universal projection system is longitude-latitude with a standard World Geodetic comprising a standard coordinate frame for the Earth, a standard spheroidal reference surface for raw altitude data, and a gravitational equipotential surface (the geoid) defining the nominal sea level. This system is made of latitude lines (parallels) that run horizontally, and of vertical longitude lines called meridians. Parallels are equidistant from each other, and each degree of latitude is approximately 111 km apart. Degrees of latitude are numbered from 0° to 90° north and south. Zero degrees is the equator, 90° north is the North Pole and 90° south is the South Pole. Meridians, on the other hand, converge at the poles and are widest at the equator (111 km apart). Zero degrees longitude is located at Greenwich, England. The degrees continue 180° east and 180° west, where they meet and form the International Date Line in the Pacific Ocean. To precisely locate points on the earth's surface, degrees longitude and latitude were divided into minutes (') and seconds ("). There are 60 minutes in each degree, and each minute is divided into 60 seconds. Seconds can be further divided into tenths, hundredths, or thousandths. Geographic coordinates can be displayed either in decimal degrees (e.g. 68.135°) or in sexagesimal system (degrees, minutes, and seconds: 68°8′6′′).

3. How landscape genetics/genomics can be used to infer history and migration of modern breeds

Domestication of many livestock species started about 10,000-5,000 years BP (Bruford et al., 2003). The localisation of the domestic centres can be traced back by simply observing the patterns of genetic diversity (GD) among individuals/populations of the species. GD is higher at the centre of domestication and decreases radiating from it. Landscape genetics is particularly powerful for the identification and illustration of these historical events. The domestication centres for the major livestock species have so far been assessed, e.g. goat (Naderi et al., 2008), sheep (Chessa et al., 2009), cattle (Ajmone- Marsan et al., 2010), pig (Larson et al., 2007), chicken (Kanginakudru et al., 2008), yak (Wiener et al., 2003). From domestication centres, livestock followed human migrations by demic expansion (Cavalli Sforza, 1966) or by active trade (Ajmone-Marsan et al., 2010). For the reconstruction of migration routes landscape genetics has been extensively used to infer also possible alternative routes through land or sea (Pariset et al., 2011). Since molecular markers include

sex specific ones, like Y chromosome and mtDNA markers, geographic maps of genetic diversity can be constructed for inferring male or female mediated gene flow (Hanotte et al., 2000). Landscape genetics can also provide the basis for ascertaining co-migration of livestock and humans. Pellecchia et al. (2007) found in Italian cattle haplotypes shared with Turkey breeds, nevertheless distance and discontinuity between the two countries. The data were interpreted as co-migration of Etruscan people along with their cattle around 3000 years BP, therefore corroborating the hypothesis of the middle-East origin of this people. Wild yak are believed to have been domesticated about 5000 years ago in the Qinghai-Tibet Plateau and then dispersed to occupy their current distribution (Zhang, 1989; Wiener et al., 2003). Xuebin et al. (2005) report lack of evidence for recent bottleneck in any of yak populations studied suggesting that the low level of genetic differentiation and the high level of diversity within populations observed today is more likely explained by the recent origin of these populations from a common ancestral population with large effective population size.

4. The importance of landscape genomics in livestock: Main differences with respect to wild animals

Landscape genetics has been mainly applied to the study of the genetic structure in wild populations, where components such as habitat preference can be assessed. In landscape genetics the matrix of habitat, morphological, climatic (etc.) features is considered as a major cause of biological and ecological processes influencing the population structure of wild population (Holderegger & Wagner, 2008). Recently, the field of livestock landscape genomics, where data such as environmental, socio-economic and demographic characteristics are geo-referenced, has boosted during the last decade (Joost et al., 2009).

In livestock the study of adaptation of different breeds to the environment is of crucial importance in order to support production systems based on adapted breeds reducing impact on the environment, and making better goods available to consumers: landscape genomics, studying the animal genome coupled with the description of landscape (including biotic, abiotic, human and market influences), offers a tool to identify the genotypes suitable to a given environment (Joost & Negrini, 2010). Within the landscape genomics studies in livestock, the Econogene project (http://www.econogene.eu) developed a programme with the aim of promoting the sustainable conservation of genetic resources in sheep and goats. Combining a molecular analysis of biodiversity, socio-economics and geostatistical systems the project defined strategies of genetic management and rural development.

Landscape genomics in livestock depends on the topography and on farmer market preferences and social structure. When analysing domesticated populations, characteristics of farms and farmers, as their isolation or farmers' practices, could affect the genetic structure of the animals. For example, the geographical location of farmers may facilitate or reduce animal exchanges influencing the gene flow. When dealing with livestock populations it would then be useful collecting as environmental factors human activities such as human density, roads or hunting activities (Bertouly et al., 2009).

One of the differences between landscape analysis in wild and domesticated species is that, in the latter, anthropic selection plays a relevant role. Therefore many loci reflect the

domestication history of the species and are influenced by the human needs for certain characteristics. As a consequence, a high percentage of loci purposely chosen for influencing potentially selected traits could result under selection (Pariset et al., 2009a). This will be discussed in the next paragraph.

Box 5. GPS

The Global Positioning System (GPS) is a worldwide radio-navigation system developed and maintained by the U.S. government, formed from a constellation of 27 satellites (24 in operation and three extras in case one fails) and their ground stations. Initially designed for military applications, a decision directive was signed by President Clinton in 1996 describing GPS as an international information utility.
Each of these satellites circles the globe at about 19'300 km, making two complete rotations of the Earth every day. The orbits are arranged so that at any time and anywhere, there are at least four satellites visible in the sky.
Radio signals are sent from orbiting satellites to Earth. GPS receivers on the ground can collect and convert these radio signals into position, velocity, and time information and calculate positions accurate to a matter of meters.
To this end, a GPS receiver has to locate four or more of these satellites, figure out the distance to each, and use this information to deduce its own location by means of triangulation (or trilateration). To triangulate, a GPS receiver measures distance using the travel time of radio signals. GPS accuracy is affected by a number of factors, including satellite positions, noise in the radio signal, atmospheric conditions, and natural barriers to the signal. These factors can create an error between 1 to 10 meters and may result from interferences caused by a physical obstacle near the receiver or a radio emission on the same frequency. For instance, objects such as mountains or buildings can also error sometimes up to 30 meters. The most accurate determination of position occurs when the satellite and receiver have a clear view of each other and no other objects interfere.

5. Detection and consequences of artificial selection in livestock

Landscape genomics needs the simultaneous study of a high number of markers, mainly neutral but including also genes under selection. This combination of loci with different characteristics can aid in understanding the action of evolutionary forces (selection, drift, migration) influencing the genetics of livestock populations. In this matter we are helped by the fact that many innovative tools, such as medium or high density SNP chips, are now available for many domesticated species (cattle, pig, sheep, chicken already available; goat in progress - see Box 7) and custom chip (see Box 7) are sold at relatively low cost.

Recently many authors emphasized the need of accompanying the analysis of neutral markers with those of loci under selection, which may directly reflect environmental change (Kohn et al., 2006; Hoffmann & Willi, 2008; Primmer, 2009). The analysis of population genetic measures like Wright's *F* statistics (Wright, 1978; Weir & Cockerham, 1984) as continuous distributions across a genome (Storz, 2005; Foll & Gaggiotti, 2008; Excoffier et al., 2009) can help in identifying genomic regions showing significant differentiation among populations, thus regions that have likely been under natural selection (Nielsen et al., 2007;

Box 6. Next Generation Sequencing

Next generation sequencing (NGS) generates hundreds of millions of sequence reads in parallel. New NGS technologies are based on production of 'libraries' obtained by breaking the entire genome into small pieces which are then ligated to designated adapters. The DNA templates are read randomly during DNA synthesis (sequencing-by-synthesis) (Zang et al., 2011). Several NGS platform recently developed allow larger-scale DNA sequencing:

454 sequencing

The 454 system developed by Roche was the first commercial platform. During library construction the DNA is fragmented and ligated to adapters. The fragments are linked to microbeads that have millions of oligomers complementary to the adaptor sequences and then amplified by emulsion PCR (Dressman et al., 2003; Margulies et al., 2005). The 454 Genome Sequencer uses the pyrosequencing technology in which the nucleotide addition leads to a pyrophosphate release that triggers an enzymatic cascade and consequently a light signal (Ronaghi et al., 1998). The 454 platform gives a length reads of 500bp and 400-600 Mb per run.
(http://www.454.com).

Illumina

Illumina – Solexa sequencing technology is a platform based on massively parallel sequencing of millions of fragments using reversible terminator-based sequencing chemistry (modified Sanger). This technology uses a bridge amplification in which the fragmented genomic DNA is arranged on an optically surface and amplified to create a high density sequencing flow cell. The sequencing system uses reversible terminator dideossinucleotides with removable fluorescent dyes. The Illumina HiSeq 2000 Genome Analyzer produces single reads of 2 x 100 bp (pair-end reads), and generates about 200 giga basepair (Gb) of short sequences per run with accuracy of 99%.
(http://www.solexa.com).

ABI solid

The SOLiD platform uses the emulsion PCR in which the amplicons are captured on small magnetic beads (1μm). The sequencing reaction is catalyzed by a DNA ligase and relies on serial ligation of labelled oligonucleotides. SOLiD4 platform produces 80-100 Gbp per run and read length of up to 50 bp with system accuracy greater than 99.94%.
(http://www.solid.appliedbiosystems.com).

Ion Torrent

Ion Torrent technology uses a new approach to sequencing based on the detection of hydrogen ions released by DNA polymerization process. A semiconductor chip captures voltage measurements due to hydrogen ions and directly convert the chemical information to digital sequence information. Ion Torrent offers different sequencing chip densities producing from 10 Mb to more than 1 Gb of sequences. The technology produces a read length of 200bp, and it is expected to get read length of 400bp in 2012.
(http://www.iontorrent.com/).

Bonin, 2008; Akey, 2009) that can be used to identify candidate genes for functional analysis (Akey et al., 2002; Vigouroux et al., 2002; Roberge et al., 2007; Bonin et al., 2009; Bigham et al., 2010).

The methods of Fdist and SAM were used to detect signatures of selection in goats, confirming the usefulness of both methods in outlier loci identification (Pariset et al., 2009b). By adding or removing neutral markers from datasets it could be possible to individuate the effects of the forces acting on a population (Pariset et al., 2009a, 2011). This will work in an efficient way if the number of markers is high, as in the case of landscape genomics.

On a short timescale, migration-drift equilibrium should result in the conservation of genetic differentiation. Differentiation between populations would increase with drift occurrence and decrease in the case of migration.

In the evolution of functional traits, diversification occurs as a result of chance and selective processes. In wild populations, founder effects can result in stochastic evolution acting against adaptive evolution; then founder effects can be assessed by testing for the signature of natural selection. This is not the case in livestock, where human selection acts sometimes against stochastic and natural selection. Particularly during the last century, the livestock sector has undergone striking changes as large-scale production expanded, leading to the formation of well-defined breeds, exposed to intense anthropogenic selection. Selective breeding in fact results in the increase of the phenotypes with desired characteristics (and sometimes with undesired characteristics, as in the case of CVM in Holstein cattle, see Agerholm et al., 2004). This will be better analysed in the next paragraph.

Therefore human selection can have effects similar to those of bottleneck and genetic drift, particularly amplified by the fact that sex ratio is strongly biased and by the progress of management practices, the introduction of artificial insemination and embryo transfer, resulting in reduced allelic diversity and heterozygosity, a non-random sample of the genes in the population and the loss of rare alleles (Nei et al., 1975; Allendorf, 1986; England et al., 2003).

Bottleneck detection is mainly used for the interpretation of historical demography of wild populations and for endangered wild species management (Hundertmark & Daele, 2010). Anyway its detection results of crucial importance also in livestock, where local and typical flocks are represented by small number of animals. In fact, a significant number of cattle, sheep, and goat breeds already disappeared and many are presently endangered (FAO, 2007) because farmers progressively substitute the less productive, locally adapted, native breeds with highly productive cosmopolitan breeds and progressively abandon marginal areas (Taberlet et al., 2008).

6. Landscape analysis and regions associated with adaptation and disease resistance

Landscape genetics can be useful at identifying environmental and landscape components in the spreading of diseases, for example tracking hosts to assess aetiological agents spread (Archie et al., 2009), providing data relevant for health, studying epidemiology of zoonoses, understanding the spread of disease, designing optimal surveillance and control programs and identifying interactions affecting spatial patterns of disease incidence (Guillot et al.,

2009). SAM could assist the discovery of genomic regions linked to quantitative trait loci implicated in selection and adaptation (e.g. for disease resistance). One striking example in Scottish Blackface sheep is the identification of an allele at locus DYMS1 (from the major histocompatibility complex), associated with the number of wet days using SAM (Joost et al., 2007). In a previous study Buitkamp and collaborators found this locus linked to parasite resistance in the same sheep breed (Buitkamp et al., 1996). After *Ostertagia circumcincta* infection the faecal egg counts were associated with the major histocompatibility complex alleles (Buitkamp et al. 1996). By using both SAM and Fdist methods, Joost et al. (2007) detected an outlier allele at locus OARJMP29 that has been showed to be implicated in a disease resistance. The SAM method can also contribute to monitor and control the infectious disease processes (Biek & Real, 2010). The spatially explicit Bayesian clustering methods were used to analyse the genetic structure of European wild boar affected by classical swine fever in order to identify geographical barriers for disease management units. The results showed an overestimation of genetic structure when using Bayesian clustering methods in data sets characterized by isolation by distance. This bias could lead to the erroneous delimitation of management or conservation units (Frantz et al., 2009).

Cringoli et al. (2007) used the landscape genomics approach to understand the role of sheep in the cystic echinococcosis disease transmission to cattle and buffalo. The authors found a higher incidence of the disease in cattle and buffaloes farms that showed a close proximity with the sheep farms in the studied area. Moreover the higher prevalence found in cattle compared to water buffalo farms is explained by the lower distance between the sheep and cattle farms than those between the sheep and water buffalo.

An example of how landscape genomics can provide analytical tools in the mapping of diseases is reported by Tum et al. (2007). The authors compared the maps produced using geographic information systems and field measurements to predict the levels of risk of fasciolosis due to *Fasciola gigantica* in Cambodia cattle and buffalo. They found a good correlation between the two methods indicating the power of using GIS (Box 2).

7. An overview of geographical patterns of livestock genetic diversity

The loss of diversity of livestock breeds is affected by genetic drift, inbreeding, introgression, natural and artificial selection (Bruford, 2004). The application of landscape genomics is suitable to develop our understanding of the mechanisms leading to livestock genetic change (Luikart et al., 2003).

Unlike cattle or water buffaloes, sheep and goats are raised by almost all ethnic groups, representing suitable systems to study the effect of farmer connectivity on livestock genetic structure. Berthouly et al. (2009) reported the effects of gene flow due to the spatial distribution of ethnic groups, farmer ethnicity and husbandry practices on goat spatial pattern. Good examples of application of spatial genomics to sheep and goats was performed by the Econogene project (http://www.econogene.eu) (Pariset et al. 2006; Bertaglia et al., 2007; Peter et al., 2007; Cañon et al., 2007; Pariset et al., 2011). Within the same project Joost et al. (2007) analysed European sheep breeds and found 40 alleles significantly associated with at least one environmental parameter; Pariset et al. (2009b) using different landscape genomics approaches identified adaptive variation in goat, which is characterized by a large range of climatic conditions in the rearing areas and by a history of intense trade.

Box 7. High-throughput SNP genotyping in livestock

New DNA sequencing technologies have recently made feasible the discovery of SNPs virtually in all species. Millions of SNPs have been discovered in recent years and deposited in the NCBI (National Center for Biotechnology Information) database dbSNPs (http://www.ncbi.nlm.nih.gov/projects/SNP/).

Technological progresses now make available tools for typing hundreds of thousands of SNPs in the same individual. Some of the techniques described in Box 1 are suitable for high-throughput SNP genotyping; however one of the most efficient systems to analyse many SNPs simultaneously is microarray/chip analysis (Perkel, 2008). Hundreds of probes synthesized on a single chip allow the analysis of many SNPs simultaneously.

Affymetrix and Illumina systems offer the densest platforms for SNP genotyping in livestock. Using data from the bovine HapMap project, Affymetrix has produced a 25K SNP panel. This chip can analyze approximately 25000 SNPs discovered by sequencing the bovine genome. The Illumina technology allows the analysis of thousands of SNPs and recently became the most popular platform. The Illumina iSelect BeadChip are thus more functional for large amounts of SNP genotyping assays and achieve high densities that include tens of thousands of point mutations distributed throughout the genome. Illumina has developed several panels for the SNP genotyping including the GoldenGate Bovine3K BeadChip that provides 2,900 SNPs, the BovineSNP50 BeadChip consisting of 54,609 informative SNP probes that uniformly span the entire bovine genome, the BovineHD BeadChip which is the most comprehensive genome-wide genotyping array with more than 777,000 informative SNP across bovine genome; the PorcineSNP60 BeadChip with 62,000 SNP validated in seven economically important pig breeds; the 60k SNP BeadChip in chicken; the OvineSNP50 BeadChip with 52,000 SNP partially discovered by sequencing 60 animals from 15 breeds and partially derived from the ovine draft genome and the GoatSNP50 chip that will be released by December 2011. Low density SNP chips are also available from a selection of markers from the largest devices. Imputation methods allow to reconstruct the more dense genotype with accuracy higher than 95% (Nothnagel et al., 2009).

Currently commercial microarray platforms allow the development of custom genotyping array. Illumina provides the platform Golden Gate to identify 384 to 3,072 SNPs per sample and Affymetrix provides MyGeneChip Custom Arrays.

Sequenom MassARRAY platform combines a primer extension chemistry with the MALDI-TOF mass spectrometry to characterize genotypes with the highest levels of reproducibility. It is possible to multiplex up to 40 SNPs in a single well and process up to 384 samples in parallel.

Fluidigm performs TaqMan SNP genotyping and offer some benefits including the low cost per genotype and high-sample throughput for low- to mid-multiplex SNP genotyping.

Kijas et al. (2009) used a SNP panel to analyse sheep nuclear genome, providing the indication that breeds cluster into large groups based on geographic origin, and that SNPs can successfully identify population substructures within individual breeds. Sheep generally show a moderate geographic structure and a high genetic variability within breeds (Kijas et al., 2009) compared to cattle (Achilli et al., 2009). This can be explained by the easiness of transportation of sheep compared to cattle. Anyway, using a different

dataset, Pariset et al. (2011) show a good correspondence of breeds to geographical locations.

The geographical patterns in sheep breeds has been also analysed by Tapio et al. (2010) who performed a Bayesian clustering analysis on 52 sheep breeds from the Eurasian subcontinent using 20 microsatellite markers. They found three genetic clusters: Nordic, Composite and Fat-tailed. The differentiation of the Fat-tailed cluster from the others indicates restricted gene flow between steppe or mountain environments in central Eurasia and cooler and moister northern areas of the continent.

Most of the information about history of the species have been gathered using mtDNA. In a recent study Meadows et al. (2011) analyzed complete mtDNA sequences from each haplogroup previously identified in domestic sheep, and from a sample of their wild relatives. Bayesian, maximum likelihood revealed that among various mtDNA components the control region is the more suitable to detect the true relationship between sheep.

A recent study on retrovirus integrations (Chessa et al., 2009) has provided information on the introduction of sheep into Europe, indicating an early arrival of the primitive sheep populations (European mouflons, North-Atlantic Island breeds) and a subsequent advent of wool producing sheep.

Other examples of geographical patterns in livestock concern goat populations studies. The phylogenetic history and population structure of domestic goats was assessed using both mtDNA and nuclear markers. Cañón et al. (2006) analysed thirty microsatellites in 1426 goats from 45 traditional or rare breeds in 15 European and Middle Eastern countries. They found at least four discrete clusters using Bayesian-based clustering analysis and multivariate analysis. About 41% of the genetic variability among the breeds could be explained by their geographical origin. The analysis of mtDNA polymorphism in the domestic goat revealed six different haplogroups that have been found also in its wild ancestor (Naderi et al., 2008), suggesting that the domestication process occurred over a very large area encompassing eastern Anatolia and North-West Iran (Taberlet et al., 2011).

Among livestock, buffalo plays a fundamental role in the agricultural economy. The study of geographical pattern in buffalo population can contribute to breeding management. Gargani et al. (2009) analyzed six Turkish water buffalo populations using a set of 26 heterologous (bovine) microsatellite markers. Principal component and Bayesian cluster approach revealed three genetically distinct groups with a good correspondence of population to geographical locations. The analysis of mtDNA from different Indian breeds revealed that the river buffalo was domesticated in the Western region of the Indian subcontinent and that different maternal lineages contributed to the domestication process (Kumar et al., 2007).

The genetic diversity and the geographical patterns in cattle has been compared using different molecular markers. Mitochondrial DNA and microsatellite loci, for example, showed that taurine and zebu cattle were domesticated independently (Bradley et al., 1996). The selective breeding and genetic isolation of taurine cattle leads to the formation of many specialized dairy and beef breeds, with a complex spatial pattern of genetic differentiation.

Pariset et al. (2010a) assessed the relationship among some Podolic breeds and verified whether their genetic state reflects their history using SNP polymorphisms. The Bayesian

inference assignment confirmed that the set of chosen SNPs is able to distinguish among the breeds and that the breeds are genetically distinct. Gautier et al. (2010) investigated the genetic diversity of cattle breeds analysing 47 populations from different parts of the world with 44,706 autosomal SNPs markers. The differentiation of the African taurine, the European taurine and zebus, indicated a support for three distinct domestication centres. Spatial principal component (sPCA) analysis and spatial metric multidimensional scaling (sMDS) was applied to 101 cattle breeds using microsatellite markers (Laloë et al., 2010). The results showed a strong geographic structure along a southeast to northwest cline, corresponding to a gradient from Indian zebu to European taurine cattle. The diversity and differentiation of the African Ankole Longhorn cattle breed have been analysed on the basis of genotypic and spatial distance data by Ndumu et al. (2008). Using analyses on distance-based and model-based methods they found an isolated sub-population that it is well differentiated from the others.

In yak, cattle microsatellites are commonly used for the study of genetic diversity (Ritz et al., 2000; Dorji et al., 2002; Xuebin et al., 2005; Qi, 2004, Nguyen et al., 2005). Population structure of nine Chinese yak breeds were analyzed by means of 16 microsatellite markers and the Neighbor-Joining phylogenetic tree constructed based on Nei's standard genetic distances revealed a separation in 3 clusters (Zhang et al., 2008). Recently, a study of mitochondrial DNA haplotypes identified taurine cattle mtDNA in two samples of Tibetan yak and yak maiwë populations (Lai et al., 2007). Qi et al. (2008), using three different methods, show the results of admixture in populations of yak-cattle across the range of the species geographical distribution using mtDNA haplotypes and 17 autosomal microsatellites. Cattle bulls are commonly used to hybridize with yak cows at relatively high altitudes, while reciprocal crossing is adopted at a lower altitude of their distribution range (Davaa, 1996; Tshering et al., 1996). Some factors influence the variation of frequency of cattle introgression in yak between and among regions. For example, a generally low frequency of cattle introgression was observed at relatively high altitudes (about 3500 meters) (Wiener et al., 2003; Qi et al., 2008). Today, the yak geographical distribution extends from the southern slopes of the Himalayas to the Altai mountains Hangai of Mongolia and Russia, and the Pamir and Tianshan mountains and the Qilian Mountains Minshan (Wiener et al., 2003). The Mongolian and Russian yak populations may have originated from a large effective population size and frequent gene flow between two populations that live close to each other. Xuebin et al. (2005) report lack of evidence for recent bottleneck in any of yak populations studied suggesting that the low level of genetic differentiation and the high level of diversity within populations observed today is more likely explained by the recent origin of these populations from a common ancestral population with large effective population size.

8. Livestock conservation

Landscape genetic investigations are particularly useful in the management and conservation of species (Bruggeman et al., 2009; Segelbacher et al., 2010), even if the examples of landscape approaches to practical conservation management of species are still a few and mainly focused on wild species (Epps et al., 2005; Segelbacher et al., 2008).

Threats to biodiversity in terms of extinction rate, destruction of ecosystems and habitat, or loss of genetic diversity are increasing within the species utilized in agriculture. Since mid-

1800s, the modern breed concept and its application to breeding and husbandry practices led to the formation of well-defined breeds, exposed to intense anthropogenic selection and during the last century the livestock sector has undergone striking changes as large-scale production expanded. This has led farmers to progressively substitute the less productive, locally adapted, native breeds with highly productive cosmopolitan breeds and to progressively abandon marginal areas. Therefore a significant number of cattle, sheep, and goat breeds already disappeared and many are presently endangered (Taberlet et al., 2008). According to the Food and Agriculture Organization of the United Nations (FAO), a total of 1491 livestock breeds world-wide are classified as being either critically endangered, critical-maintained, endangered, or endangered-maintained; it is likely that a high number of breeds are being, and will be lost in the near future, suffering of the effects of rapid climate change, increasing market demand and human demographic expansion. It is then strategically important to preserve as much the farm animal diversity as possible, and this will be better accomplished with the aid of landscape genomic studies. Landscape genomics, by combining geo-referencing of breed distributions, spatial genetic diversity, climatic, ecological, epidemiological and production system information (Hanotte & Jianlin, 2005) will help in formulate priority decisions for in situ breed conservation. It could help to understand the genetic basis of animal adaptation to the environment, and the co-evolution of livestock and their production systems (Joost & Negrini, 2010).

Breeding systems on genetic management of threatened species needs to be fully evaluated (Frankham, 2010). SNP markers (see Box 1 and 7) open up new perspectives to livestock genomics, in particular for the investigation of genome diversity within and among individuals and populations, population structure, search of causative genes, and for the identification of signatures left by selection. They can also fulfil what has been envisaged in the recent past by Bertaglia et al. (2007) when only a reduced set of markers were known, i.e. the possibility to geographically map the socio-economy of rural areas and the genetic variation patterns of livestock, in order to match policies of intervention with the capability of the system to be driven to a more sustainable status.

9. References

Achilli, A., Bonfiglio, S., Olivieri, A., Malusà, A., Pala, M., Kashani, B.H., Perego, U.A., Ajmone-Marsan, P., Lotta, L., Semino, O., Bandelt, H.J., Ferretti, L., & Torroni, A. (2009). The Multifaceted Origin of Taurine Cattle Reflected by the Mitochondrial Genome. *PLoS ONE*, vol. 4, No. 6, e5753.

Adachi, A., & Kawamoto, Y. (1992). Hybridization of yak and cattle among the Sherpas in Solu and Khumbu, Nepal. *Report of the Society for Researches on Native Livestock*, vol. 14, pp. 79–87.

Agerholm, J.S., Andersen, O., Almskou, M.B., Bendixen, C., Arnbjerg, J., & Aamand, G.P. (2004). Evaluation of the inheritance of the complex vertebral malformation syndrome by breeding studies. *Acta Veterinaria Scandinava*, vol. 45, pp. 33-137.

Ajmone-Marsan, P., Gorni, C., Milanesi, E., Mazza, R., van Eijk, M.J., Peleman, J.D., & Williams, J.L. (2008). Assessment of AFLP marker behaviour in enriching STS radiation hybrid maps. *Animal Genetics*, vol. 39, pp. 383-394.

Ajmone-Marsan, P., Garcia, J.F., & Lenstra, J.A. (2010). On the origin of cattle: How aurochs became cattle and colonized the world. *Evolutionary Anthropology: Issues, News, and Reviews*, vol. 19, No. 4, pp. 148-157.

Ajmone-Marsan, P., Negrini, R., Crepaldi, P., Milanesi, E., Gorni, C., Valentini, A., & Cicogna, M. (2001). Assessing genetic diversity in Italian goat populations using AFLP markers. *Animal Genetics*, vol. 32, pp. 281-288.

Akey, J.M. (2009). Constructing genomic maps of positive selection in humans: where do we go from here? *Genome Research*, vol. 19, pp. 711–722.

Akey, J.M., Zhang, G., Zhang, K., Jin, L., & Shriver, M.D. (2002). Interrogating a high-density SNP map for signatures of natural selection. *Genome Research*, vol. 12, pp. 1805-1814.

Allendorf, F.W., Hohenlohe, P.A., & Luikart, G. (2010). Genomics and the future of conservation genetics. *Genetics*, vol. 11, pp. 697-709.

Allendorf, F.W. (1986). Genetic drift and the loss of alleles versus heterozygosity. *Zoo Biology*, vol. 5, pp. 181–190.

Anderson, E.C., & Thompson, E.A. (2002). A model-based method for identifying species hybrids using multilocus genetic data. *Genetics*, vol. 160, pp. 1217–1229.

Archie, E.A., Luikart, G., & Ezenwa, V.O. (2009). Infecting epidemiology with genetics: a new frontier in disease ecology. *Trends in Ecology & Evolution*, vol. 24, pp. 21–30.

Bae, J.S., Cheong, H.S., Kim, L.H., NamGung, S., Park, T.J., Chun, J.Y., Kim, J.Y., Pasaje, C.F.A., Lee, J.S., & Shin, H.D. (2010). Identification of copy number variations and common deletion polymorphisms in cattle. *BMC Genomics*, vol. 11, p.232.

Beaumont, M.A., & Nichols, R.A. *(1996)*. Evaluating loci for use in the genetic analysis of population structure. *Proceedings of the Royal Society B: Biological Sciences,* vol. 263, pp. 1619–1626.

Beerli, P. (2008). Migrate-N, Version 2.4. Available from: (http://popgen.sc.fsu.edu/).

Bertaglia, M., Joost, S., Roosen, J., & the Econogene Consortium. (2007). Identifying European Marginal Areas in the Context of Local Sheep and Goat Breeds Conservation: A Geographic Information System Approach. *Agricultural Systems*, vol. 94, pp. 657-670.

Berthouly, C., Do Ngoc, D., Thévenon, S., Bouchel, D., Van, T.N., Danes, C., Grosbois, V., Thanh, H.H., Chi, C.V., & Maillard, J.C. (2009). How does farmer connectivity influence livestock genetic structure? A case-study in a Vietnamese goat population. *Molecular Ecology,* vol. 18, pp. 3980-3991.

Bigham, A., Bauchet, M., Pinto, D., Mao, X., Akey, J.M., Mei, R., Scherer, S.W., Julian, C.G., Wilson, M.J., López-Herráez, D., Brutsaert, T., Parra, E.J., Moore, L.G., & Shriver, M.D. (2010). Identifying signatures of natural selection in Tibetan and Andean populations using dense genome scan data. *PLoS Genetics*, vol. 6, e1001116.

Bonin, A. (2008). Population genomics: a new generation of genome scans to bridge the gap with functional genomics. *Molecular Ecology*, vol. 17, pp. 3583–3584.

Bonin, A., Paris, M., Tetreau, G., David, J.P., & Després, L. (2009). Candidate genes revealed by a genome scan for mosquito resistance to a bacterial insecticide: sequence and gene expression variations. *BMC Genomic*s, vol. 10, p. 551.

Botstein, D., White, R.L., Skolnick, M., & Davis R.W. (1980). Construction of a genetic linkage map in man using restriction fragment length polymorphisms. *The American Journal of Human Genetics*, vol. 32, pp. 314–331.

Bruford, M.W. (2004). Conservation genetics of UK livestock: from molecules to management, In: *Farm Animal Genetic Resources,* Eds G. Simm, B. Villanueva and S. Townsend, pp. 151-169, Nottingham University Press, Nottingham, UK.

Bruford, M.W., Bradley, D.G., & Luikart, G. (2003). Dna markers reveal the complexity of livestock domestication. *Nature*, vol. 4, pp. 900-910.

Buitkamp, J., Filmether, P., Stear, M.J., & Epplen, J.T. (1996). Class I and class II Major histocompatibility complex alleles are associated with faecal egg counts following natural, predominantly *Ostertargia circumcincta* infection. *Parasitology Research*, vol. 82, pp. 693–696.

Cañón, J., García, D., García-Atance, M.A., Obexer-Ruff, G., Lenstra, J.A., Ajmone-Marsan, P., Dunner, S., & the Econogene Consortium (2006). Geographical partitioning of goat diversity in Europe and the Middle East. *Animal Genetics,* vol. 37, pp. 327–334.

Cavalli-Sforza, L.L., & Edwards, A.W.F. (1963). Analysis of human evolution. *Proceedings of the XI International Congress of Genetics, The Hague, Genetics Today,* vol. 3, pp. 923–933.

Cavalli-Sforza, L.L. (1966). Population Structure and Human Evolution. *Proceedings of the Royal Society of London Series B-Biological Sciences,* vol. 164, pp. 362–379.

Cavalli-Sforza, L.L., Menozzi, P., & Piazza, A. (1993). Demic expansions and human evolution. *Science*, vol. 259, pp. 639–646.

Cavalli-Sforza, L.L., Menozzi, P., & Piazza, A. (1994). The History and Geography of Human Genes. Princeton University Press.

Chessa, B., Pereira, F., Arnaud, F., Amorim, A., Goyache, F., Mainland, I., Kao, R.R., Pemberton, J.M., Beraldi, D., Stear, M., Alberti, A., Pittau, M., Banabazi, M.H., Kazwala, R., Zhang, Y-P., Arranz, J.J., Ali, B.A., Wang, Z., Uzun, M., Dione, M., Olsaker, I., Holm, L-E., Saarma, U., Ahmad, S., Marzanov, N., Eythorsdottir, E., Holland, M., Ajmone-Marsan, P., Bruford, M.W., Kantanen, J., Spencer, T.E., & Palmarini, M. (2009). Revealing the history of sheep domestication using retrovirus integrations. *Science*, vol. 324, pp. 532-536.

Cingoli, G., Rinaldi, L., Musella, V., Veneziano, V., Maurelli, M.P., Di Pietro, F., Frisiello, M., & Di Pietro, S. (2007). Geo-referencing livestock farms as tool for studying cystic echinococcosis epidemiology in cattle and water buffaloes from southern Italy. *Geospatial Health,* vol. 2, No. 1, pp. 105-111.

Conrad, D.F., Pinto, D., Redon, R., Feuk, L., Gokcumen, O., Zhang, Y., Aerts, J., Andrews, T.D., Barnes, C., Campbell, P., Fitzgerald, T., Hu, M., Ihm, C.H., Kristiansson, K., Macarthur, D.G., Macdonald, J.R., Onyiah, I., Pang, A.W., Robson, S., Stirrups, K., Valsesia, A., Walter, K., Wei, J., Wellcome Trust Case Control Consortium, Tyler-Smith, C., Carter, N.P., Lee, C., Scherer, S.W., & Hurles, M.E. (2010). Origins and functional impact of copy number variation in the human genome. *Nature*, vol. 464, pp. 704-712.

Corander, J., & Tang, J. (2007). Bayesian analysis of population structure based on linked molecular information. *Mathematical Biosciences*, vol. 205, pp. 19-31.

Corander, J., Siren J., & Arjas, E. (2008). Bayesian spatial modeling of genetic population structure. *Computational Statistics*, vol. 23, No. 1, pp. 111–129.

Davaa, M. (1996). Conservation and Management of Domestic yak Genetic Diversity in Mongolia. *Proceedings of a Workshop on Conservation and Management of Yak Genetic Diversity*, pp. 41–46, Kathmandu, Nepal, 29-31 October 1996.

Dorji, T., Goddard, M., Perkins, J., Robinson, N., & Roder, W. (2002). Genetic diversity in bhutanese yak (*Bos Grunniens*) populations using microsatellite markers. *Proceedings of the third International Congress on Yak,* pp. 197–201, Lhasa, P.R. China, 4-9 September, 2000.

Dressman, D., Yan, H., Traverso, G., Kinzler, K.W., & Vogelstein, B. (2003). Transforming single DNA molecules into fluorescent magnetic particles for detection and enumeration of genetic variations. *Proceedings of the National Academy of Science of the Unite States of America*, vol. 100, pp. 8817–8822.

England, P.R., Osler, G.H.R., Woodsworth, L.M., Montgomery, M.E., Briscole, D.A., & Frankham, R. (2003). Effects of intense versus diffuse population bottlenecks on microsatellite genetic diversity and evolutionary potential. *Conservation Genetics*, vol. 4, pp. 595–604.

Epps, C.W., Palsboll, P.J., Wehausen, J.D., Roderick, G.K., Ramey, I.R., & McCullough, D.R. (2005). Highways block gene flow and cause a rapid decline in genetic diversity of desert bighorn sheep. *Ecology Letters,* vol. 8, pp. 1029–1038.

Excoffier, L., Smouse, P.E., & Quattro, J.M. (1992). Analysis of molecular variance inferred from metric distances among DNA haplotypes: application to human mitochondrial DNA restriction data. *Genetics,* vol. 131, pp. 479-491.

Excoffier, L., Hofer, T., & Foll, M. (2009). Detecting loci under selection in a hierarchically structured population. *Heredity*, vol. 103, pp. 285–298.

Fadista, J., Thomsen, B., Holm, L.E., & Bendixen, C. (2010). Copy number variation in the bovine genome. *BMC Genomics*, vol. 11, p. 284.

Falush, D., Stephens, M., & Pritchard, J.K. (2003). Inference of population structure using multilocus genotype data: linked loci and correlated allele frequencies. *Genetics*, vol. 164, pp. 1567–1587.

Falush, D., Stephens, M., & Pritchard, J.K. (2007). Inference of population structure using multilocus genotype data: dominant markers and null alleles. *Molecular Ecology Notes*, vol. 7, pp. 574-578.

Feuk, L., Carson, A.R., & Scherer, S.W. (2006). Structural variation in the human genome. *Nature Reviews Genetetics*, vol. 7, pp. 85-97.

Foll, M., & Gaggiotti, O. (2008). A genome-scan method to identify selected loci appropriate for both dominant and codominant markers: a Bayesian perspective. *Genetics*, vol. 180, pp. 977–993.

Fordyce, S.L., Ávila-Arcos, M.C., Rockenbauer, E., Børsting, C., Frank-Hansen, R., Petersen, F.T., Willerslev, E., Hansen, A.J., Morling, N., & Gilbert, M.T.P. (2011). High-throughput sequencing of core STR loci for forensic genetic investigations using the Roche Genome Sequencer FLX platform. *Biotechniques*, vol. 51, pp. 127-133.

François, O., & Durand, E. (2010). The state of the art - Spatially explicit Bayesian clustering models in population genetics. *Molecular Ecology Resources*, vol. 10, pp. 773-784.

François, O., Ancelet, S., & Guillot, G. (2006). Bayesian clustering using hidden Markov random fields in spatial population genetics. *Genetics*, vol. 174, pp. 805-816.

Frankham, R. (2010). Where are we in conservation genetics and where do we need to go? *Conservetion Genetics*, vol. 11, pp. 661–663.

Frantz, A.C., Cellina, S., Krier, A., Schley, L., & Burke, T. (2009). Using spatial Bayesian methods to determine the genetic structure of a continuously distributed

population: clusters or isolation by distance? *Journal of Applied Ecology*, vol. 46, pp. 493–505.

Galtier, N., Nabholz, B., Glémin, S., & Hurst, G. (2009). Mitochondrial DNA as a marker of molecular diversity: a reappraisal. *Molecular Ecology*, vol. 18, 4541-4550.

Gargani, M., Pariset, L., Soysal, M.I., Ozkan, E., & Valentini, A. (2009). Genetic variation and relationships among Turkish water buffalo populations. *Animal Genetics*, vol. 41, pp. 93–96.

Gonçalves, G.L., Moreira, G.R.P., Freitas, T.R.O., Hepp, D., Passos, D.T., & Weimer, T.A. (2010). Mitochondrial and nuclear DNA analyses reveal population differentiation in Brazilian Creole sheep. *Animal Genetics*, vol. 41, pp. 308-310.

Goodchild, M.F., & Haining, R.P. (2004). GIS and Spatial Data Analysis: Converging Perspectives. *Papers in Regional Science*, vol. 83, pp. 363– 385.

Greger, L., Albarella, U., Dobney, K., Rowley-Conwy, P., Schibler, J., Tresset, A., Vigne, J-D., Edwards, C.J., Schlumbaum, A., Dinu, A., Balaçsescu, A., Dolman, G., Tagliacozzo, A., Manaseryan, N., Miracle, P., Van Wijngaarden-Bakker, L., Masseti, M., Bradley, D.G., & Cooper, A. (2007). Ancient DNA, pig domestication, and the spread of the Neolithic into Europe. *Proceedings of the National Academy of Sciences*, vol. 104, No. 39, pp. 15276 -15281.

Guillot, G., Mortier, F., & Estoup, A. (2005). Geneland: a computer package for landscape genetics. *Molecular Ecology Notes*, vol. 5, No. 3, pp. 712-715.

Guillot, G., Leblois, R., Coulon, A., & Frantz A.C. (2009). Statistical methods in spatial genetics. *Molecular Ecology*, vol. 18, pp. 4734–4756.

Guryev, V., Berezikov, E. & Cuppen, E. (2005). CASCAD: A database of annotated single nucleotide polymorphisms associated with expressed sequences. *BMC Genomics*, vol. 6, p. 10.

Hanotte, O., & Jianlin, H. (2005). Genetic characterization of livestock populations and its use in conservation decision-making. *The role of biotechnology,* pp. 131-136, Villa Gualino, Turin, Italy, 5-7 March 2000.

Hanotte, O., Tawah, C.L., Bradley, D.G., Okomo, M., Verjee, Y., Ochieng, J., & Rege, J.E.O. (2000). Geographic distribution and frequency of a taurine *Bos taurus* and an indicine *Bos indicus* Y specific allele amongst sub-Saharan African cattle breeds. *Molecular Ecology*, vol. 9, pp. 387–396.

Helyar, S.J., Hemmer-Hansen, J., Bekkevold, D., Taylor, M.I., Ogden, R., Limborg, M.T., Cariani, A., Maes, G.E., Diopere, E., Carvalho, G.R. & Nielsen, E.E. (2011). Application of SNPs for population genetics of non-model organisms: new opportunities and challenges. *Molecular Ecology Resources*, vol. 11, pp. 123–136.

Hewitt, G.M. (2004). Genetic consequences of climatic oscillations in the Quaternary. *Philosophical Transactions of the Royal Society B*: *Biological Sciences*, vol. 359, pp. 183–195.

Hey, J., & Nielsen, R. (2004). Multilocus methods for estimating population sizes, migration rates and divergence time, with applications to the divergence of *Drosophila pseudoobscura* and *D. persimilis*. *Genetics*, vol. 167, pp. 747-760.

Hoffmann, A.A., & Willi, Y. (2008). Detecting genetic responses to environmental change. *Nature Reviews Genetics*, vol. 9, pp. 421–432.

Hoggart, C.J., Shriver, M.D., Kittles, R.A., Clayton, D.G., & McKeigue, P.M. (2004). Design and analysis of admixture mapping studies. *American Journal of Human Genetics*, vol. 74, pp. 965–978.

Holderegger, R., & Wagner, H.H. (2006). A brief guide to landscape genetics. *Landscape Ecology*, vol. 21, pp. 793–796.

Holderegger, R., & Wagner, H.H. (2008). Landcspe genetics. *Bioscience,* vol. 58, pp. 199-207.

Holsinger, K.E., & Lewis, P.O. (2003). Hickory: a package for analysis of population genetic data v1.0. University of Connecticut, Storrs: Distributed by the authors.

Hou, Y., Liu, G.E., Bickhart, D.M., Cardone, M.F., Wang, K., Kim, E., Matukumalli, L.K., Ventura, M., Song, J., VanRaden, P.M., Sonstegard, T.S., & Van Tassell, C.P. (2011). Genomic characteristics of cattle copy number variations. *BMC Genomics*, vol. 12, p. 127.

Hundertmark, K.J., & Van Daele, L.J. (2010). Founder effect and bottleneck signatures in an introduced, insular population of elk. *Conservation Genetics,* vol. 11, pp. 139–147.

Jenkins, S., & Gibson, N. (2002). High-throughput SNP genotyping. *Comparative and Functional Genomics*, vol. 3, pp. 57–66.

Joost, S., & Negrini, R. (2010). Early Stirrings of Landscape Genomics: Awaiting Next-next Generation Sequencing Platforms before Take-off. *Sustainable Improvement of Animal Production and Health.* Eds. N.E. Odongo, M. Garcia & G.J. Viljoen, pp. 185–189, Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture, Rome, Italy.

Joost, S., Bonin, A., Bruford, M.W., Després, L., Conord, C., Erhardt, G., & Taberlet, P. (2007). A spatial analysis method (SAM) to detect candidate loci for selection: towards a landscape genomics approach to adaptation. *Molecular Ecology,* vol. 16, pp. 3955–3969.

Joost, S., Kalbermatten, M., & Bonin, A. (2008). Spatial Analysis Method (SAM): a software tool combining molecular and environmental data to identify candidate loci for selection. *Molecular Ecology Resources*, vol. 8, pp. 957–960.

Joost, S., Colli, L., Baret, P.V., Garcia, J.F., Boettcher P.J., Tixier-Boichard, M., Ajmone-Marsan, P., & the Globaldiv Consortium. (2010). Integrating geo-referenced multiscale and multidisciplinary data for the management of biodiversity in livestock genetic resources. *Animal Genetics*, vol. 41, pp. 47–63.

Joost, S., Colli, L., Bonin, A., Biebach, I., Allendorf, F., Hoffmann, I., Hanotte, O., Taberlet, P., Bruford, M., & the Globaldiv Consortium. (2011). Promoting collaboration between livestock and wildlife conservation genetics communities. *Conservation Genetics Resources*, vol. 3, pp. 785–788.

Kanginakudru, S., Metta, M., Jakati, R.D., & Nagaraju, J. (2008). Genetic evidence from Indian red jungle fowl corroborates multiple domestication of modern day chicken. *BMC Evolutionary Biology*, vol. 8, p. 174.

Kijas, J.W., Townley, D., Dalrymple, B.P., Heaton, M.P., Maddox, J.F., McGrath, A., Wilson, P., Ingersoll, R.G., McCulloch, R., McWilliam, S., Tang, D., McEwan, J., Cockett, N., Oddy, V.H., Nicholas, F.W., Raadsma, H., & International Sheep Genomics Consortium. (2009). A genome wide survey of SNP variation reveals the genetic structure of sheep breeds. *PLoS On*e, vol. 4, e4668.

Kohn, M.H., Murphy, W.J., Ostrander, E.A., & Wayne, R.K. (2006). Genomics and conservation genetics. *Trends in Ecology and Evolution*, vol. 21, pp. 629–637.

Kokoris, M., Dix, K., Moynihan, K., Mathis, J., Erwin, B., Grass, P., Hines, B., & Duesterhoeft, A. (2000). Highthroughput SNP genotyping with the Masscode system. *Molecular Diagnosis*, vol. 5, pp. 329–340.

Kuhner, M.K. (2006). LAMARC 2.0: maximum likelihood and Bayesian estimation of population parameters. *Bioinformatics applications note*, vol. 22, pp. 768–770.

Kumar, S., Nagarajan, M., Sandhu, J.S., Kumar, N., Behl, V., & Nishanth, G. (2007). Mitochondrial DNA analyses of Indian water buffalo support a distinct genetic origin of river and swamp buffalo. *Animal Genetics*, vol. 38, pp. 227–232.

Larson, G., Albarella, U., Dobney, K., Rowley-Conwy, P., Schibler, J., Tresset, A., Vigne, J.D., Edwards, C.J., Schlumbaum, A., Dinu, A., Bălăçsescu, A., Dolman, G., Tagliacozzo, A., Manaseryan, N., Miracle, P., Wijngaarden-Bakker, L.V., Masseti, M., Bradley, D.G., & Cooper, A. (2007). Ancient DNA, pig domestication, and the spread of the Neolithic into Europe. *Proceedings of the National Academy of Science of the United States of America*, vol. 104, pp. 15276–15281.

Lai, S.J., Chen, S.Y., Liu, Y.P., & Yao, Y.G. (2007). Mitochondrial DNA sequence diversity and origin of Chinese domestic yak. *Animal Genetics*, vol. 38, pp. 77–80.

Li, J.Z., Absher D.M., Tang, H., Southwick, A.M., Casto, A.M., Ramachandran, S., Cann, H.M., Barsh, G.S., Feldman, M. Cavalli-Sforza, L.L., & Myers, R.M. (2008). Worldwide Human Relationships Inferred from Genome-Wide Patterns of Variation. *Science*, vol. 319, No. 5866, pp. 1100-1104.

Li, Q., & Yu, K. (2008). Improved correction for population stratification in genome-wide association studies by identifying hidden population structures. *Genetic Epidemiology*, vol. 32, pp. 215-226.

Liu, G.E., Van Tassell, C.P., Sonstegard, T.S., Li, R.W., Alexander, L.J., Keele, J.W., Matukumalli, L.K., Smith, T.P., & Gasbarre, L.C. (2008). Detection of germline and somatic copy number variations in cattle. *Developments in Biologicals*, vol. 132, pp. 231-237.

Liu, G.E., Hou, Y., Zhu, B., Cardone, M.F., Jiang, L., Cellamare, A., Mitra, A., Alexander, L.J., Coutinho, L.L, Dell'Aquila, M.L., Lacalandra, G., Li, R.W., Matukumalli, L.K., Nonneman, D., Regitano, L.C.A., Smith, T.P.L., Song, J., Sonstegard, T.S., Van Tassell, C.P., Ventura, M., Eichler, E.E., McDaneld, T.G., & Keele, J.W. (2010). Analysis of copy number variations among diverse cattle breeds. *Genome Research*, vol. 20, pp. 693-703.

Loiseau, L., Richard, M., Garnier, S., Chastel, O., Julliard, R., Zoorob, R., & Sorci, G. (2009). Diversifying selection on mhc class I in the house sparrow (*Passer domesticus*). *Molecular Ecology*, vol. 18, pp. 1331-1340.

Longley, P.A., Goodchild, M.F., Maguire, D.J., & Rhind, D.W. (2001). Geographic Information Systems and Science, Chichester, Wiley.

Luikart, G., Allendorf, F.W., Cornuet, J.M., & Sherwin, W.B. (1998). Distortion of allele frequency distributions provides a test for recent population bottlenecks. *Journal of Heredity*, vol. 89, pp. 238–247.

Luikart, G., England, P.R., Tallmon, D., Jordan, S., & Taberlet, P. (2003). The power and promise of population genomics: From genotyping to genome typing. *Nature Reviews Genetics*, vol.4, pp. 981-994.

Manel, S., Joost, S., Epperson, B.K., Holderegger, R., Storfer, A., Rosenberg, M.S., Scribner, K., Bonin, A., & Fortin, M.J. (2010). Perspective on the use of landscape genetics to

detect genetic adaptive variation in the field. *Molecular Ecology*, vol. 19, pp. 3760-3772.

Manel, S., Schwartz, K., Luikart, G., & Taberlet, P. (2003). Landscape genetics: Combining landscape ecology and population genetics. *Trends in Ecology and Evolution*, vol. 18, pp. 189–197.

Margulies, M., Egholm, M., Altman, W.E., Attiya, S., Bader, J.S., Bemben, L.A., Berka, J., Braverman, M.S., Chen, Y.J., Chen, Z., Dewell, S.B., Du, L., Fierro, J.M., Gomes X.V., Godwin, B.C., He, W., Helgesen, S., Ho, C.H., Irzyk, G.P., Jando, S.C., Alenquer, M.L., Jarvie, T.P., Jirage, K.B., Kim, J.B., Knight, J.R., Lanza, J.R., Leamon, J.H., Lefkowitz, S.M., Lei, M., Li, J., Lohman, K.L., Lu, H., Makhijani, V.B., McDade, K.E., McKenna, M.P., Myers, E.W., Nickerson, E., Nobile, J.R., Plant, R., Puc, B.P., Ronan, M.T., Roth, G.T., Sarkis, G.J., Simpson, J.W., Srinivasan, M., Tartaro, K.R., Tomasz, A., Vogt, K.A., Volkmer, G.A., Wang, S.H., Wang, Y., Weiner, M.P., Yu, P., Begley, R.F., & Rothberg, J.M. (2005). Genome sequencing in microfabricated high-density picolitre reactors. *Nature*, vol. 437, pp. 376–380.

Meadows, J.R.S., Hiendleder, S., & Kijas, J.W. (2011). Haplogroup relationships between domestic and wild sheep resolved using a mitogenome panel. *Heredity*, vol. 106, pp. 700-706.

Miller, M.P. (2005). Alleles In Space (AIS): Computer Software for the Joint Analysis of Interindividual Spatial and Genetic Information. *Journal of Heredity*, vol. 96, No. 6, pp. 722-724.

Naderi, S., Rezaei, H.R., Pompanon, F., Blum, M.G., Negrini, R., Naghash, H.R., Balkiz, O., Mashkour, M., Gaggiotti, O.E., Ajmone-Marsan, P., Kence, A., Vigne, J.D., & Taberlet, P. (2008). The goat domestication process inferred from large-scale mitochondrial DNA analysis of wild and domestic individuals. *Proceedings of the National Academy of Science of the United States of America*, vol. 105, No. 46, pp. 17659-17664.

Negrini, R., Milanesi, E., Colli, L., Pellecchia, M., Nicoloso, L., Crepaldi, P., Lenstra, J.A., & Ajmone-Marsan, P. (2007). Breed assignment of Italian cattle using biallelic AFLP markers. *Animal Genetics*, vol. 38, pp. 147-153.

Nei, M., Maruyama, T., & Chakraborty, R. (1975). The bottleneck effect and genetic variability in populations. *Evolution*, vol. 29, pp. 1-10.

Nguyen, T.T., Genini, S., Menetrey, F., Malek, M., Vogeli, P., Goe, M.R., & Stranzinger, G. (2005). Application of bovine microsatellite markers for genetic diversity analysis of Swiss yak (*Poephagus grunniens*). *Animal Genetics,* vol. 36, pp. 484–489.

Nielsen, R., Hellmann, I., Hubisz, M., Bustamante, C., & Clark, A.G. (2007). Recent and ongoing selection in the human genome. *Nature Reviews Genetics*, vol. 8, pp. 857–868.

Nijman, I.J., Van Boxtel, D.C.J., Lisette, M., Van Cann, L.M., Marnoch, Y., Cuppen, E., & Lenstra, J.A. (2008). Phylogeny of Y chromosomes from bovine species. *Cladistics*, vol. 24, No. 5, pp. 723-726.

Novembre, J., & Stephens, M. (2008). Interpreting principal component analyses of spatial population genetic variation. *Nature Genetics*, vol. 40, pp. 646–649.

Oleksyk, T.K., Smith, M.W., & O'Brien, S.J. (2010). Genome-wide scans for footprints of natural selection. *Philosophical Transactions of the Royal Society B*, vol. 365, pp. 185-205.

Olivier, M. (2005). The Invader assay for SNP genotyping. *Mutation Research*, vol. 573, pp. 103-110.

Pariset, L., Cappuccio, I., Ajmone Marsan, P., Dunner, S., Luikart, G., Obexer-Ruff, G., Peter, C., Marletta, D., Pilla, F., Valentini A., & the Econogene Consortium (2006). Assessment of population structure by single nucleotide polymorphisms (SNPs) in goat breeds. *Journal of Chromatography B*, vol. 833, pp. 117-120.

Pariset, L., Cuteri, A., Ligda, C., Ajmone Marsan, P., Valentini, A., & the Econogene Consortium (2009a). Geographical patterning of sixteen goat breeds from Italy, Albania and Greece assessed by Single Nucleotide Polymorphisms. *BMC Ecology*, vol. 9, p. 20.

Pariset, L., Joost, S., Ajmone Marsan, P., & Valentini, A. (2009b). Landscape genomics and biased FST approaches reveal Single Nucleotide Polymorphisms under selection in goat breeds of North-East Mediterranean. *BMC Genetics*, vol. 10, p. 7.

Pariset, L., Chillemi, G., Bongiorni, S., Spica, V.R., & Valentini, A. (2009c). Microarrays and high throughput transcriptomic analysis for species with limited knowledge of genomic sequences. *New Biotechnology*, vol. 25, No. 5, pp. 272-279.

Pariset, L., Mariotti, M., Nardone, A., Soysal, M.I., Ozkan, E., Williams, J.L., Dunner, S., Leveziel, H., Maroti-Agots, A., Bodò, I., & Valentini A. (2010a). Relationships of podolic cattle breeds assessed by Single Nucleotide Polymorphisms (SNPs) genotyping. *Journal Animal breeding and Genetics*, vol. 127, pp. 481-488.

Pariset, L., Bueno, S., Bongiorni, S., & Valentini, A. (2010b). Not working on mice or humans? A pipeline to rapidly generate species- specific microarrays from sequence databases. *G.I.T. Laboratory Journal Europe* 1-2/2010, pp. 020-021. http://www.laboratory-journal.com/science/informationstechnologie-it/not-working-mice-or-humans.

Pariset, L., Mariotti, M., Gargani, M., Joost, S., Negrini, R., Perez, T., Bruford, M., Ajmone Marsan, P., Valentini, A., & the Econogene Consortium (2011). Genetic diversity of sheep breeds from Italy, Albania and Greece assessed by mitochondrial DNA and nuclear polymorphisms (SNPs). *TheScientificWorldJOURNAL*, vol. 11, pp. 1641-1659.

Pellecchia, M., Negrini, R., Colli, L., Patrini, M., Milanesi, E., Achilli, A., Bertorelle, G., Cavalli-Sforza, L.L., Piazza, A., & Torroni, A. (2007). The mystery of Etruscan origins: novel clues from *Bos taurus* mitochondrial DNA. *Proceedings of the Royal Society B*, vol. 274, No. 1614, pp. 1175–1179.

Perkel, J.M. (2008). SNP genotyping: six technologies that keyed a revolution. *Nature Methods*, vol. 5, pp. 447-453.

Perkel, J.M. (2011). Copy Number Variants: Mapping the Genome's 'Land Mines'. *BioTechniques*, vol. 51, pp. 21–24.

Peter, C., Bruford, M., Perez, T., Dalamitra, S., Hewitt, G., Erhardt, G., & the Econogene Consortium (2007). Genetic diversity and subdivision of 57 European and Middle-Eastern sheep breeds. *Animal Genetics*, vol. 38, pp. 37–44.

Petit, C., Freville, H., Mignot, A., Colas, B., Riba, M., Imbert, E., Hurterez-Bousses, S., Virevaire, M., & Olivieri, I. (2001). Gene flow and local adaptation in two endemic plant species. *Biological Conservation*, vol. 100, pp. 21-34.

Piry, S., Alapetite, A., Cornuet, J.M., Paetkau, D., Baudouin, L., & Estoup, A. (2004). GeneClass2: A Software for Genetic Assignment and First-Generation Migrant Detection. *Journal of Heredity*, vol. 95, pp. 536-539.

Price, A.L., Patterson, N.J., Plenge, R.M., Weinblatt, M.E., Shadick, N.A., & Reich, D. (2006). Principal components analysis corrects for stratification in genome-wide association studies. *Nature Genetics*, vol. 38, No. 8, pp. 904-909.

Price, A.L., Kryukov, G.V., de Bakker, P.I.W., Purcell, S.M., Staples, J., Wei, J.L., & Sunyaev, S.R. (2010). Pooled Association Tests for Rare Variants in Exon-Resequencing Studies. *The American Journal of Human Genetics*, vol. 86, No. 6, pp. 832-838.

Primmer, C.R. (2009). From conservation genetics to conservation genomics. *Annals of the New York Academy of Science*, vol. 1162, pp. 357-368.

Pritchard, J.K., Stephens, M., & Donnelly, P. (2000). Inference of population structure using multilocus genotype data. *Genetics*, vol. 155, pp. 945–959.

Prugnolle, F., Theron, A., Pointier, J., Jabbour-Zahab, R., Jarne, P., Durand, P., & de Meeûs, T. (2005). Dispersal in a parasitic worm and its two hosts: Consequence for local adaptation. *Evolution*, vol. 59, pp. 296-303.

Purcell, S., Neale, B., Todd-Brown, K., Thomas, L., Ferreira, M.A.R., Bender, D., Maller, J., Sklar, P., de Bakker, P.I.W., Daly, M.J., & Sham, P.C. (2007). PLINK: a toolset for whole-genome association and population-based linkage analyses. *The American Journal of Human Genetics*, vol. 81, pp. 559–575.

Qi, X-B. (2004). Genetic Diversity, Differentiation and Relationship of Domestic yak Populations - a Microsatellite and Mitochondrial DNA Study. Lanzhou, P.R. China: Lanzhou University.

Qi, X-B., Jianlin, H., Wang, G., Rege, J.E.O., & Hanotte, O. (2008). Assessment of cattle genetic introgression into domestic yak populations using mitochondrial and microsatellite DNA markers. *Animal Genetics*, vol. 41, pp. 242–252.

Rasool, G., Khan, B.A., & Jasra, A.W. (2002). Yak Pastoralism in Pakistan. Nairobi, Kenya: International Livestock Research Institute (ILRI). *Proceedings of the third International Congress on Yak*, pp. 95–99, Lhasa, P.R. China, 4-9 September, 2000.

Ritz, L.R., Glowatzki-Mullis, M.L., MacHugh, D.E., & Gaillard, C. (2000). Phylogenetic analysis of the tribe Bovini using microsatellites. *Animal Genetics,* vol. 31, pp.178–185.

Roberge, C., Guderley, H., & Bernatchez, L. (2007) Genomewide identification of genes under directional selection: gene transcription Qst scan in diverging Atlantic salmon subpopulations. *Genetics*, vol. 177, pp. 1011–1022.

Biek, R., & Real, L.A. (2010). The landscape genetics of infectious disease emergence and spread. *Molecular Ecology*, vol. 19, pp. 3515–3531.

Ronaghi, M., Uhlen, M., & Nyren, P. (1998). A sequencing method based on real-time pyrophosphate. *Science*, vol. 281, pp. 363–365.

Schwartz, M.K., Copeland, J.P., Anderson, N.J., Squires, J.R., Inman, R.M., Mckelvey, K.S., Pilgrim, K.L., Waits, L.P., & Cushman, S.A. (2009). Wolverine gene flow across a narrow climatic niche. *Ecology*, vol. 90, No. 11, pp. 3222-3232.

Segelbacher, G., Tomiuk, J., & Manel, S. (2008). Temporal and spatial analyses disclose consequences of habitat fragmentation on the genetic diversity in capercaillie (*Tetrao urogallus*). *Molecular Ecology*, vol. 17, pp. 2356–2367.

Segelbacher, G., Cushman, S., Epperson, B., Fortin, M.J., Francois, O., Hard, O., Holderegger, R., Taberlet, P., Waits, L.P., & Manel, S. (2010.) Landscape Genetics: concepts and Challenges in a Conservation Context. *Conservation Genetics*, vol. 11, pp. 375–385.

Seldin, M.F., Shigeta, R., Villoslada, P., Selmi, C., Tuomilehto, J., Silva, G., Belmont, J.W., Klareskog, L., & Gregersen, P.K. (2006). European population substructure: clustering of Northern and Southern populations. *PLoS Genetics*, vol. 2, pp. 1339–1351.

Simianer, H., Marti, S.B., Gibson, J., Hanotte, O., & Rege J.E.O. (2003). An approach to the optimal allocation of conservation funds to minimize loss of genetic diversity between livestock breeds. *Ecological Economics,* vol. 45, pp. 377-392.

Storfer, A., Murphy, M.A., Evans, J.S., Goldberg, C.S., Robinson, S., Spear, S.F., Dezzani, R., Delmelle, E., Vierling, L., & Waits, L.P. (2007). Putting the "landscape" in landscape genetics. *Heredity*, vol. 98, pp. 128-142.

Storz, J.F. (2005). Using genome scans of DNA polymorphism to infer adaptive population divergence. *Molecular Ecology*, vol. 14, pp. 671–688.

Syvanen, A.C. (1998). Solid-phase minisequencing as a tool to detect DNA polymorphism. *Methods in Molecular Biology,* vol. 98, pp. 291–298.

Taberlet, P., Valentini, A., Rezaei, H.R., Naderi, S., Pompanon, F., Negrini, R., & Ajmone-Marsan, P. (2008). Are cattle, sheep, and goats endangered species? *Molecular Ecology*, vol. 17, pp. 275-284.

Taberlet, P., Coissac, E., Pansu, J., & Pompanon, F. (2011). Conservation genetics of cattle, sheep, and goats. *Comptes Rendus Biologies*, vol. 334, No. 3, pp. 247-254.

Tapio, M., Ozerov, M., Tapio, I., Toro, M.A., Marzanov, N., Cinkulov, M., Goncharenko, G., Kiselyova, T., Murawski, M., & Kantanen, J. (2010). Microsatellite-based genetic diversity and population structure of domestic sheep in Northern Eurasia. *BMC Genetics,* vol. 11, pp. 76-86.

Tautz, D., & Renz, M. (1984). Simple sequences are ubiquitous repetitive components of eukaryotic genomes. *Nucleic Acid Research*, vol. 12, pp. 4127–4138.

Tshering, L., Gyamtsho, P., & Gyeltshen, T. (1996). Yaks in Bhutan. *Proceedings of a Workshop on Conservation and Management of Yak Genetic Diversity*, pp. 13–24, Kathmandu, Nepal: 29-31 October, 1996.

Tum, S., Puotinen, M.L., Skerratt, L.F., Chan, B., & Sothoeun, S. (2007). Validation of a geographic information system model for mapping the risk of fasciolosis in cattle and buffaloes in Cambodia. *Veterinary Parasitology*, vol. 143, pp. 364–367.

Vignal, A., Milan, D., SanCristobal, M., & Eggen, A. (2002). A review on SNP and other types of molecular markers and their use in animal genetics. *Genetic Selection and Evolution*, vol. 34, pp. 275-305.

Vigouroux, Y., McMullen, M., Hittinger, C.T., Houchins, K., Schulz, L., Kresovich, S., Matsuoka, Y., & Doebley, J. (2002). Identifying genes of agronomic importance in maize by screening microsatellites for evidence of selection during domestication. *Proceedings of the National Academy of Sciences*, vol. 99, pp. 9650-9655.

Vos, P., Hogers, R., Bleeker, M., Reijans, M., van de Lee, T., Hornes, M., Frijters, A., Pot, J., Peleman, J., & Zabeau, M. (1995). AFLP: a new technique for DNA fingerprinting. *Nucleic Acid Research*, vol. 23, pp. 4407-4444.

Wang, I.J. (2011). Choosing appropriate genetic markers and analytical methods for testing landscape genetic hypotheses. *Molecular Ecology*, vol. 20, No. 12, pp. 2480–2482.

Wang, Y.H., Yang, K.C., Bridgman, C.L., & Lin, L.K. (2008). Habitat suitability modelling to correlate gene flow with landscape connectivity. *Landscape Ecology*, vol. 23, pp. 989–1000.

Weir, B.S., & Cockerham, C.C. (1984). Estimating F-statistics for the analysis of population structure. *Evolution*, vol. 38, pp. 1358–1370.

Wiener, G., Jianlin, H., & Ruijun, L. (2003). The Yak. The Regional Office for Asia and the Pacific. Bangkok, Thailand: Food and Agriculture Organization of the United Nations.

Williams, J.L. (2005). The use of marker-assisted selection in animal breeding and biotechnology. *Revue Scientifique et Technique*, vol. 24, pp. 379-391.

Wilson, G.A., & Rannala, B. (2003). Bayesian inference of recent migration rates using multilocus genotypes. *Genetics*, vol. 163, pp. 1177–1191.

Wilson, I.J., Weale, M.E., & Balding, D.J. (2003). Inferences from DNA data: population histories, evolutionary processes and forensic match probabilities. *Journal of the Royal Statistical Society: Series A (Statistics in Society)*, vol. 166, pp. 155–188.

Wright, S. (1951). The genetical structure of populations. *Annals of Eugenics*, vol. 15, pp. 323–354.

Wright, S. (1978). Evolution and the genetics of populations. Chicago: University of Chicago Press.

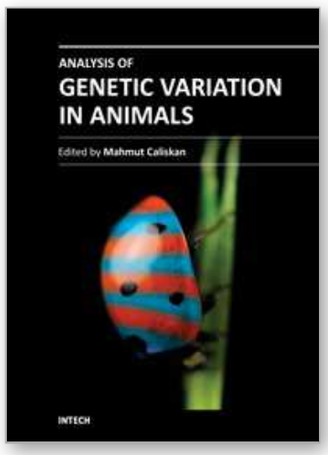
Xuebin, Q., Jianlin, H., Rege, J.E.O., & Hanotte, O. (2002). Y-Chromosome Specific Microsatellite Polymorphisms in Chinese yak. *Proceedings of 7th World Congress on Genetics Applied to Livestock Production*, pp. 509–512.

Xuebin, Q., Jianlin, H., Lkhagva, B., Chekarova, I., Badamdorj, D., Rege, J.E., & Hanotte, O. (2005). Genetic diversity and differentiation of Mongolian and Russian yak populations. *Journal of Animal Breeding and Genetics*, vol. 122, pp. 117–216.

Zhang, F., Gu, W., Hurles, M.E., & Lupski, J.R. (2009). Copy number variation in human health, disease, and evolution. *Annual Review of Genomics and Human Genetics*, vol. 10, pp. 451-481.

Zhang, G., Chen, W., Xue, M., Wang, Z., Chang, H., Han, X., Liao, X., & Wang, D. (2008). Analysis of genetic diversity and population structure of Chinese yak breeds (*Bos grunniens*) using microsatellite markers. *Journal of Genetics and Genomics*, vol. 35, pp. 233-238.

Zhang, J., Chiodini, R., Badr, A. & Zhang, G. (2011). The impact of next-generation sequencing on genomics. *Journal of Genetics and Genomics,* vol. 38, No. 3, pp. 95-109.



Analysis of Genetic Variation in Animals
Edited by Prof. Mahmut Caliskan

ISBN 978-953-51-0093-5
Hard cover, 360 pages
Publisher InTech
Published online 29, February, 2012
Published in print edition February, 2012

Analysis of Genetic Variation in Animals includes chapters revealing the magnitude of genetic variation existing in animal populations. The genetic diversity between and within populations displayed by molecular markers receive extensive interest due to the usefulness of this information in breeding and conservation programs. In this concept molecular markers give valuable information. The increasing availability of PCR-based molecular markers allows the detailed analyses and evaluation of genetic diversity in animals and also, the detection of genes influencing economically important traits. The purpose of the book is to provide a glimpse into the dynamic process of genetic variation in animals by presenting the thoughts of scientists who are engaged in the generation of new idea and techniques employed for the assessment of genetic diversity, often from very different perspectives. The book should prove useful to students, researchers, and experts in the area of conservation biology, genetic diversity, and molecular biology.

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

IntechOpen