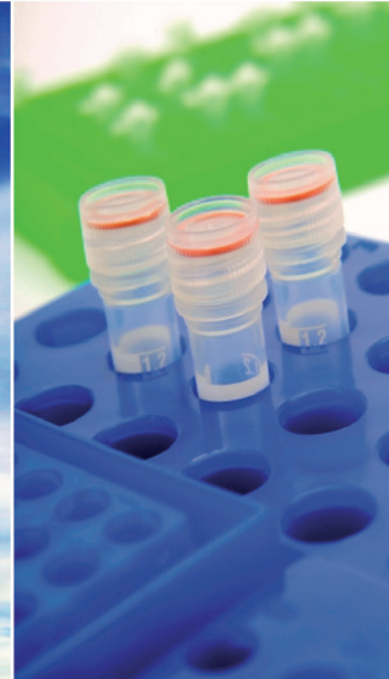


**ADVANCES IN FARM ANIMAL GENOMIC RESOURCES
(GENOMIC-RESOURCES)**

Standing Committee for Life, Earth and Environmental
Sciences (LESC)



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Introduction

GENOMIC-RESOURCES is a four-year ESF Research Networking Programme (RNP). Its main objective is to contribute to the education of a new generation of scientists in cutting edge approaches to the characterisation, evaluation, management and conservation of Farm Animal Genetic Resources (FAnGR).

Training is organised at the European level through summer schools and workshops addressing specific interdisciplinary topics and by offering visiting researcher mobility grants and training programmes in one of the partner institutions.

It is planned that visiting researchers will work and learn novel tools and methods offered by recent advances in molecular technologies, statistical and econometric approaches, Geographic Information Systems and integrated data analysis. Participants from different EU countries offer a structured interdisciplinary research and training network covering all these different branches.

Main research themes comprise:

- i) characterisation;
- ii) economic evaluation;
- iii) exploitation and conservation of FAnGR.

Emphasis will be placed on training future research leaders to design and manage research programmes in an interdisciplinary perspective by providing complementary skills such as basics of socio-economy to geneticists and vice versa. Project management skills will also be addressed.

The running period of the ESF GENOMIC-RESOURCES Research Networking Programme is four years, from June 2010 to June 2014.

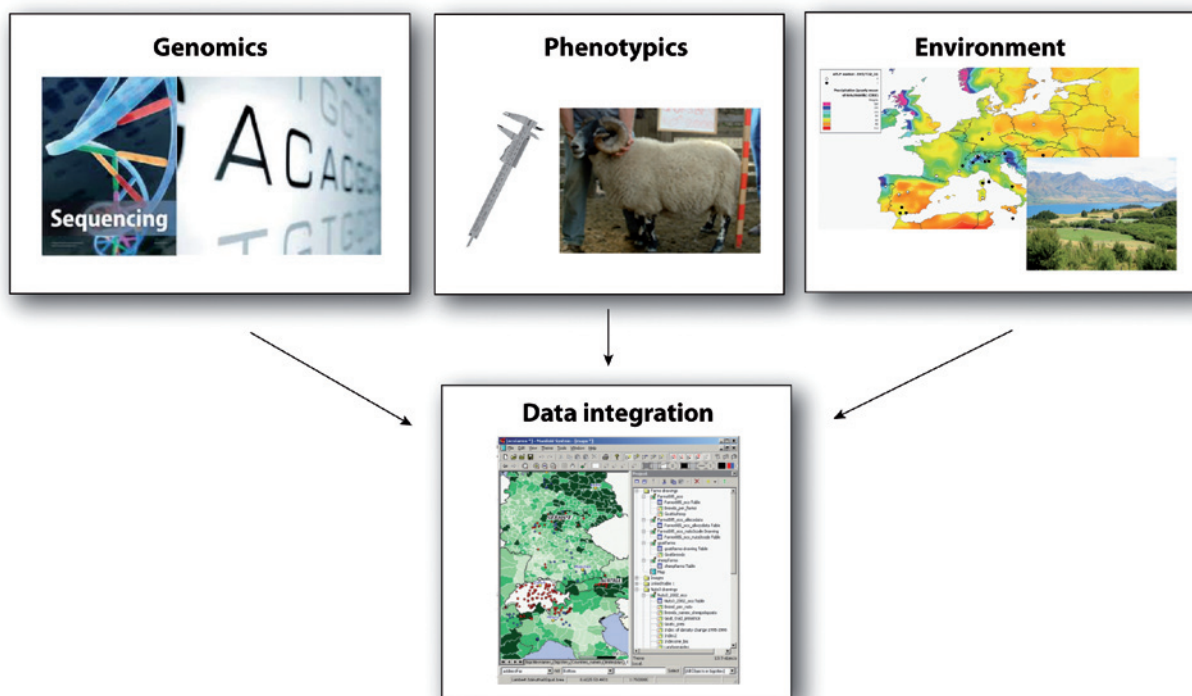


Figure 1. The study and management of Farm Animal Genetic Resources (FAnGR) is a multidisciplinary issue involving genomics, phenotypic evaluation, and elements from natural and socio-economic environments.

Background

The history of livestock started with the domestication of their wild ancestors: a restricted number of species allowed themselves to be tamed and entered a symbiotic relationship with the human species. In exchange for food, shelter and protection, they provided us with meat, milk, eggs, hides, wool, feathers and draught power, thus contributing considerably to our economic and cultural development.

Depending on the species, domestication took place in different areas and periods, with the largest contribution from Southwest Asia 8,000 to 10,000 years ago (Fig. 2). After domestication, livestock spread over all inhabited regions of the Earth, accompanying human migrations or conquests and becoming also trade objects. This required an adaptation to different climates and varying styles of husbandry and resulted in an enormous phenotypic diversity.

Approximately 200 years ago, the situation started to change with the rise of the concept of breeds. Animals from the same breed were selected for the same visible characteristics, and crossing of animals with different phenotypes was seriously reduced. This resulted in the formation of many different breeds, mostly genetically isolated from other populations. A few decades ago, selection pressure was increased again with intensive production focusing on a limited range of types and a subsequent loss of genetic diversity. For short-term economic reasons, farmers have abandoned traditional breeds. As a consequence, during the 20th century at least 28% of farm animal breeds became extinct, rare or endangered. A substantial number of autochthonous breeds are still classified as 'critical' in developed countries.

The situation is even more alarming in developing countries, where autochthonous breeds adapted to local environments and diseases are being replaced by industrial breeds. In the most marginal areas, FAnGR are considered to be essential for viable and sustainable land use and, in the developing world, a major pathway out of poverty.

Historic documentation from the period before the breed formation is scarce. As a consequence, reconstruction of the history of livestock populations depends critically on archaeological, archaeozoological and DNA analysis of extant populations. Scientific research into genetic diversity takes advantage of the rapid advances in molecular genetics. Studies of mitochondrial DNA, microsatellite DNA profiling and Y chromosomes have revealed many details on the process of domestication, on the diversity retained by breeds and on relationships between breeds. However, we only see a small part of the genetic information and the advent of new technologies is most timely in order to answer many essential questions. High-throughput SNP (single-nucleotide

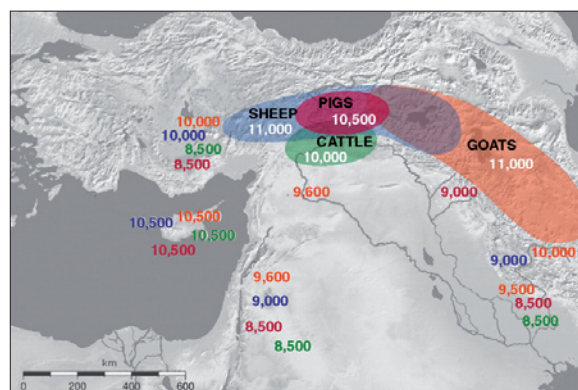


Figure 2. Map of Mesopotamia showing times of domestication (Zeder, 2008, PNAS, 105: 11597-11604).

polymorphism) genotyping is about to be available for all major farm animal species. The recent development of sequencing techniques and the availability of a huge amount of genomic data calls for new methods of data management and analysis and for new ideas for the extraction of information relevant for proper choices in conservation and valuation of FAnGR. To make sense of this genetic information in practical conditions, integration of geo-environmental and socio-economical data are key elements. The study and management of FAnGR is indeed a major multidisciplinary issue.

Whole genome analysis

During the last decade, animal genetics has moved from analysis of a handful of genetic polymorphisms or candidate gene loci, towards genome scans and whole genome sequencing. The 1,000 human genomes project has put in place the infrastructure for whole genome scale population studies in farm animals (Nature 467: 28 October 2010). This landmark study opens the way for similar analysis of common and rare genetic variants in domestic species. During this important period in agricultural development, analysis of genetic diversity in commercial and marginal breeds will allow identification of millions of potentially informative single nucleotide polymorphisms and thousands of structural variants. As genome sequencing is becoming more technically feasible, the cost is also becoming much more affordable. This will lead to a 'democratisation' of genome data, enabling any country or interested party to analyse and exploit the genome of their own genetic resources.

Markers

The use of molecular genetic markers has evolved rapidly since the 1960s when allozymes (soluble enzyme electrophoresis) were first discovered and, as we have progressed through restriction enzyme polymorphisms in the 1970s to DNA fingerprinting in the 1980s and DNA profiling using STR markers in the 1990s, statistical analysis of genetic variation has become very sophisticated and model-driven. In the last decade, the advent of high-density SNP genome maps in livestock has moved the science along even further and now analysis of more than 50,000 SNPs in a single reaction for cattle and sheep is routine. However, the population genetic analysis of these markers is challenging due to the sheer amount of data and the computational intensity of many current statistical methods. The biggest challenge in the near future will be the development of approaches that optimally utilise the enormous datasets and generate novel information on the evolutionary history of breeds and domestic species.

Ancient DNA

Archaeological collections of osteological materials of domesticated animals and their wild ancestors, fibre and leather may store genetic information that can provide otherwise unobtainable insights into the past history of domesticated animals. The historic DNA provides information about the heterogeneity and genetic ancestries of past animal populations. For example, ancient DNA analysis has led to insights into the origins of domesticated wild ancestral populations and possible prehistoric backcrossing between domesticated and wild ancestral

populations. In addition, ancient DNA analysis is a tool to explore temporal changes in genetic diversity within domesticated animal populations and can provide useful information on the current animal genetic biodiversity.

The archaeogenetics data for domesticated animal studies come typically from analyses of short DNA segments in the hypervariable mitochondrial control region, but the more challenging analysis of nuclear DNA has already been achieved. In general, ancient DNA experiments are demanding. The accepted criteria for ancient DNA work include, for example, reproducibility and the use of negative controls in order to demonstrate that the amplified DNA did not come from contaminants introduced during the experiment.

Epigenetics

Phenotypic variation is traditionally divided into components that are under control of genetic and environmental variation, in addition to variation not readily attributable to either. Epigenetic phenomena are likely to contribute to this 'intangible variation'. Epigenetic effects are caused by chemical modifications to DNA that do not change the DNA sequence but alter the probability of gene transcription. These include methylation of cytosines and modification of the DNA binding proteins, which modulate the accessibility of DNA to transcription complexes. Technologies in epigenomic research include genomic analysis of DNA methylation, chromatin-associated proteins and chromatin higher-order structures. Besides the well-known epigenetic aspects like gene silencing and genomic imprinting, a role of epigenetics has recently been identified in foetal adaptation and transgenerational inheritance of acquired phenotypes. The progressive elucidation of epigenetic molecular mechanisms in different organisms will be a major research goal.

Phenotypes

To characterise breeds and learn about their potential utilities in the respective environments, measures of body size and conformation, yields and qualities of products and their social behaviour need to be recorded. A comprehensive and detailed description of phenotypes, linked with new molecular technologies, allows unprecedented insights into the genetics of traits and the reaction of particular breeds to changing environments.

Classical traits

Traits that have been recorded traditionally to characterise breeds and ecotypes are body size and conformation. Weights, distances (e.g., height at withers) and circumferences (e.g., of the chest) are measured routinely. Information on age at measurement is often available, allowing inference about growth curves. Quantities and qualities of products are often recorded as part of the genetic management of livestock breeds. Typical products in such systems are milk, meat and fibre. Information is available for commercial, transboundary breeds but not always for local and endangered breeds. In industrial breeds data are also recorded on fertility and somatic cell count as measure of mastitis.

The efficiency of production, e.g., the total energy consumed in feed relative to the energy stored in the product, is economically important, but information is frequently missing. Information on the length of productive life is mostly available but often ignored.

New traits

Rapid development of technologies allows recording of traits related to the metabolic condition of animals, at least for limited numbers of samples. Relevant traits may include methane production, nitrogen and phosphorus excretions as components of the environmental footprints. Blood parameters provide information on, inter alia, energy balance and health status of animals. Near or mid infrared spectra of animal products are about to become available and may give information about traits related to product quality (e.g., fatty acid composition of milk). Remote sensing techniques allow us to learn about the social behaviour of animals, particularly interesting for species foraging on pasture.

Information on disease diagnoses of animals is of particular economic interest. EU regulations request veterinarians to leave information on each diagnosis, including the animal ID, on farm. This information is already being collected routinely in Nordic countries but has been deemed impossible everywhere else. This attitude is changing. Disease diagnosis information has been collected in Austria since 2006 and may be available soon in other countries.



Figure 3. Scottish Blackface sheep in Rochester, UK (© Econogene).

Phenotyping

Classical tools of phenotyping are weighing scales, measuring sticks (see Fig. 3), measuring tapes and sliding callipers. The qualities of products are measured with specialised equipment like milk and fibre analysers. Instruments originally developed for human medicine, like ultrasound machines, X-ray and CT scanners, are used to compile information about body composition and skeletal properties. Blood testing is applied to learn about metabolic characters. Near or mid infrared spectrography of milk, blood, urine or meat is yet to be implemented as a comparatively accurate and inexpensive tool for learning about properties of products as well as disease related traits.

Measurement or recording is mostly not a one-time exercise, but occurs repeatedly over time (e.g., across duration of growth, lactation or lifetime). Strategies need to be devised depending on the nature of the characterisation exercise. For example, for analysis of growth curves, cross-sectional approaches, i.e., measuring a large number of animals with known ages, may be as informative as longitudinal approaches of repeatedly measuring the same batch of animals.

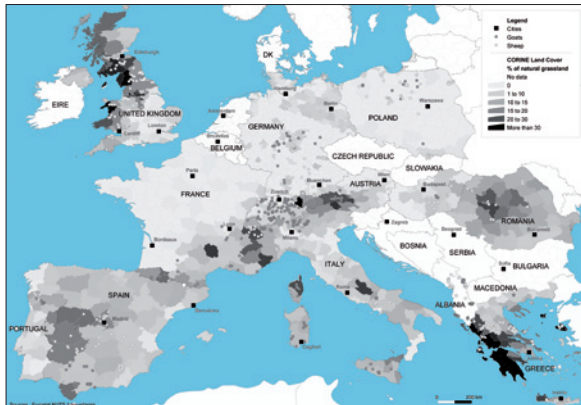


Figure 4. Geographic map showing the percent of natural grassland (CORINE land cover) within NUTS level 3 administrative boundaries of 8 EU countries (Bertaglia *et al.*, 2007, Agricultural Systems).

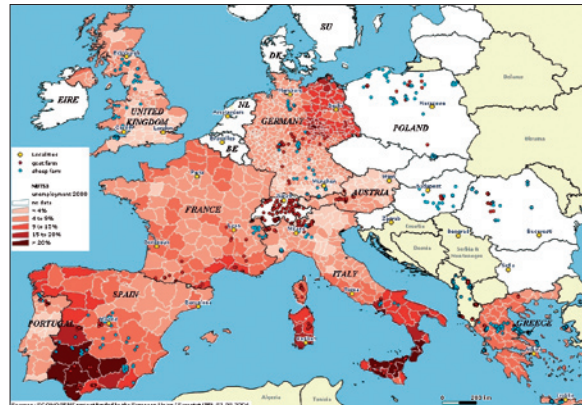


Figure 5. Geographic map showing the unemployment rate of European NUTS3 regions in 2000 compared to the spatial distribution of farms where sheep and goats were sampled in the context of the EU FP5 ECONOGENE project (Bertaglia *et al.*, 2007, Agricultural Systems).

The environment in which livestock populations are reared plays an important role in animal health and productivity.

Agro-environmental

Geo-environmental data (temperature, precipitation, land cover, solar radiation, relative humidity, etc.) can be used to map disease-risk areas, to predict parasite outbreaks and to characterise production environments to enable the unbiased comparative analysis of the performance of breeds. Moreover, this type of information is essential for understanding the adaptation of livestock to their local environmental conditions and is therefore important for many decisions in FAnGR management and conservation.

Socio-economic

The conservation of farm animal genetic resources cannot succeed without the consideration of economic drivers in the farm livestock system. Survival of specific breeds depends on their economic value in livestock markets. The latter have changed considerably due to the industrialisation and globalisation of livestock production systems, which have undergone change from more land-based types of agriculture to industrial farming systems, a substitution of local breeds by higher yielding ones, a more homogenous supply of quality for livestock product processing meeting modern consumer needs and an increase in global livestock product trade. Genetic resources need, however, to be seen as a common pool resource and it is hence important to understand the public good dilemma involved in the

conservation of farm animal genetic resources. Appropriate economic and political measures can help to solve this dilemma. A rational approach should consider measures of the option value related to the future uses of genetic diversity. Possible solutions in the political arena rely on the enforcement of intellectual property rights, the development of demand for specific quality differentiated products as local meats, the support of mixed farming systems and the efficient management of animal diseases.

Data Integration

In livestock genetic resource conservation, decisions about conservation priorities are based on the simultaneous analysis of several different criteria that may contribute to long-term sustainable breeding conditions. This requires complementary data on population and evolutionary genetics, animal husbandry practices, socio-economic and environmental information, usually over a broad geographic range. These different sources and categories of data are often considered separately, although their integration facilitates and optimises the processes used to establish priorities in the conservation of livestock genetic resources. These different types of information can be explored and compared according to their geographic coordinates.

Database

Data integration consists of combining data sets obtained from different sources and providing the user with a unified view. Therefore, data must be stored in specific databases software named Geographical Information Systems (GIS) able to manage geographic information and to perform tasks specific to geographic coordinates (computing distances or spatial buffers around objects of interest, determining inclusions or exclusions, etc.). Geographic databases are also able to calculate elementary statistical operations.

Tools

GIS are specialised computer systems for the storage, retrieval, analysis and display of large volumes of spa-

tial data. GIS are designed to overlay complementary information and to study the relationships between the different information layers. A number of GIS software exist, including statistical packages or easily connectable to standard statistical software (*Animal Genetics* 41, Suppl. 1, 2010).

Exploratory spatial data analysis (ESDA) is a specific category of GIS tool to facilitate the understanding of the geographic distribution of genetic diversity among livestock breeds as well as its variation according to different environmental parameters or to diverse socio-economic situations. This approach employs a variety of mostly graphical techniques to maximise insight into a data set to uncover underlying structures, extract important variables or detect outliers and anomalies. Instead of assuming a known model and checking if data conform, EDA proposes a more direct approach of allowing the data itself to reveal its underlying structure, stimulated by spontaneous successive rough hypothesis outlines produced by researchers.

Statistics

With the integration of separate categories of data and the implementation of statistical comparison of their behaviour, a major challenge is to understand the relationships between the chosen variables. For that purpose, a) the right variables must be chosen to describe the system being considered, b) the dependent and the independent variables must show sufficient variation, and c) spatial covariations of different variables must be detected either by using univariate analysis such as correlation, one factor ANOVA, or multivariate approaches.

The goal of the latter is to arrange objects or variables in relation to each other (ordination, scaling), to classify objects into groups (classification, clustering, prediction), or to test hypotheses about relationship between response and predictor variables.

Multi-criteria analysis

Multi-criteria decision analysis combines the information from several criteria in order to form a single evaluation integrated index. This is useful to support decision makers, who usually face several and often conflicting evaluations like prioritisation in conservation processes. The approach includes qualitative as well as quantitative aspects of the problem to be solved in the decision-making process. It can be used to rank options, to identify a single preferred one, to list a limited number of alternatives for a subsequent evaluation, or simply to distinguish acceptable from unacceptable effects of the different options.

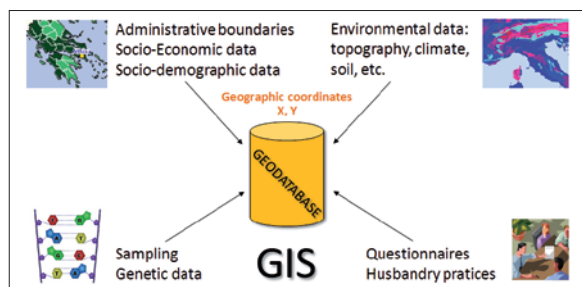


Figure 6. Different thematic components can be integrated within a geographic database.

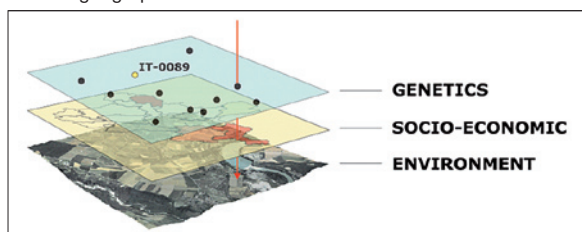


Figure 7. The integrative function of Geographic Information Systems (GIS).

Copy Number Variation

The current focus on SNPs as the new currency of genetic diversity should not divert our attention from a new source of molecular variation, the copy number variation (CNV). These have so far been studied mainly in humans and mice, but recently also in cattle and pigs. A detailed comparison of the genome of different cattle showed that hundreds of CNVs per genome involve segments of 1 kb to millions of base pairs. A sizable fraction of the CNV regions even contain functional genes, many of which are in cattle involved in environmental response. Interestingly, several reports indicate an association of human SNPs with neuropsychiatric disorders, obesity and several other pathogenic traits. So unlike most microsatellites and SNPs, CNV are not just innocent bystanders that deny causal relationship to variable traits, but are likely to be involved actively in phenotypic diversity. Other interesting observations are (1) a mutation rate of up to 10⁻³ per generation for a few percent of the human CNVs, (2) indications for somatic CNV variation, and (3) differences between monozygotic twins. This may suggest that CNV is a continuous source of new diversity and, challenging current concepts, that genetic variation is more than a heritage of the past. As formulated 2,500 years ago by the Greek philosopher Heraclitus and his followers: Παντα ρει και ουδεν μενει [all things change and nothing remains].



Yakutian Cattle in the land of permafrost

Siberia's last remaining indigenous breed of domestic cattle, Yakutian Cattle, inhabit the lands surrounding the Lena River in Sakha Republic (Yakutia) in the Russian Federation. A Finnish multidisciplinary team of researchers investigated genetic divergence of the Yakutian Cattle from other Eurasian breeds and evaluated their socio-cultural values.

The Yakutian Cattle are endangered and the current census size of the breed is 1,200 animals. Up to 74% of the Yakutian Cattle are distributed in the Eveno-Bytantay district locating about 150 km north of the Arctic Circle. In this region, the permafrost depth is several hundred meters. The breed is adapted to the harsh Siberian environment, long and cold winters and short summers. Yakutian is a purebred aboriginal breed and produces milk and meat. It is also used as draught animal.

The neutral genetic diversity of the Yakutian Cattle was examined by analysing autosomal, Y-chromosomal microsatellites and mtDNA D-loop sequences. Data were compared with Eurasian cattle breeds. Materials for identifying socio-cultural values of the breed were obtained from several different sources. Interviews were conducted with animal owners, villagers, researchers, animal breeding experts, local residents and public officers in the Eveno-Bytantay District and in Yakutsk, the capital of the Sakha Republic. Two anthropological field trips were conducted. In addition, demographic data were investigated as well as media analysis, history and literature research conducted.

Six different values in the Yakutian Cattle were identified: ecological, economic, social, political, cultural and ethical. At the local level the values of the cattle were more related to everyday livelihood strategies of single households and families, whereas the representatives of the republic, in line with the newspapers, highlighted the importance of the cattle for food production and for national identity. Thus, individuals at different levels were in favour of conserving the cattle for different reasons. Local residents and experts were more concerned about developing economically sustainable cattle production, whereas the experts in Yakutsk were concerned about the conservation of genetic resources. Genetic studies have indicated that Yakutian Cattle show genetic distinctiveness and have high genetic value for the maintenance of cattle diversity. The shared desire to preserve this breed has led to the elaboration of the world's very first domestic breed conservation law.

Figure 8. Yakutian Cattle (Picture: Anu Osva).

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