

ESF GENOMIC-RESOURCES

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

Introduction

ESF GENOMIC RESOURCES Research Networking Programme (RNP) funded in 2012 two science meetings: the first one is a Summer School “Livestock Conservation Genomics”; the second one a scientific workshop on the Genotype-by-Environment Interactions and Adaptation of Farm Animals on Phenotypic and Molecular Level. We present here a report of these activities.

In 2013, GENOMIC RESOURCES decided to fund a special event: the organization of a SANDPIT meeting. We present here the content of the selected project in the following “What’s new?” section.

GENOMIC RESOURCES decided to fund 6 exchange visit grants in 2011. The results of the corresponding projects will be presented in the next issue of the GENOMIC RESOURCES Newsletter.

What’s new ?

Social science meets animal science: how to favor scientific integration and capacity building for sustainable conservation of farm animal genetic resources (FAnGR)? 9-11 September 2013

A three day meeting will be organized from 9 to 11th of September 2013 in Louvain-la-Neuve (Belgium).

Animation by a professional facilitator and original activities will facilitate to attain three main objectives: (1) a better mutual knowledge between social scientists and

animal geneticists, (2) exchange on successful case studies, (3) identify good rules of interaction.

Scientific summary

Animal breeders and social scientists are both working in a rapidly changing environment as new technologies -often linked to massive amounts of data- emerge, consumer demands change and global topics (climate change, global trade of animals and their products) arise.

Both researcher communities are confronted with complex adaptive systems, but each group has a different focus on these systems. While animal breeders tend to concentrate on technical solutions, social scientists put human beings and their attitudes, actions and behaviour in the centre of their research.

The key question of this proposal is “Can cooperation between animal scientists and social scientists help to deal better with the complexity of adaptive systems?”

In order to be in the position to give an answer to this question, both sides have to have a better understanding about concepts, approaches and methods of the different disciplines. One also has to notice that each group of scientists in itself very heterogeneous with different foci.

Therefore, for this workshop we decided to use as an overall conceptual framework “complex adaptive systems”, where different opinions and positions can be accommodated. Systems can be seen at various levels such as at genetic, individual, population level of farm animals, but also at farm, regional, national and international scale. Based on common understanding participants can develop in a very free setting new ideas. One facilitator

will guide participants through the workshop and will be responsible for ensuring an open space where everybody is free to express his/her opinion.

During these 3 days, the organizers would like to i) inform each other about methods and applications of systems analysis in each field ii) develop a mutual knowledge and understanding on research questions in different disciplines iii) share positive examples and iv) set up rules and guidelines for good practices. Based on these findings new research ideas can emerge and new research teams can be formed.

This workshop intends to provide researchers of different disciplines with different new methods that can support the conservation of FAnGR.

Key issues of the meeting are:

a. Systems analysis: this includes definitions of frameworks, borders and methodologies applied by both groups. The favourite types of methodologies applied by each group will be discussed, finding out whether these may be applied in the other.

b. From animal genetics to animal breeding: geneticists dealing with animal breeding very often do not consider the breeder (human), only think about the animal and its genetic composition. How to change this? Are joint research projects a way out?

c. Link to AnGR conservation: objective of conservation are sometimes in contradiction with objective of production. What is the point of view of both groups on this issue.

Expected outputs

- Share a common view on different aspects of complex adaptive systems
- A better mutual knowledge between social scientists and animal geneticists,

- Identification of good rules of interaction.
- Identification of possible new partnerships
- Identification of possible joint research topics

Details on the procedure chosen to select participants

An invitation e-mail will be directly sent out to possible interested persons to ask if they are interested in participating in the workshop.

Priority will be given to researchers who come from countries that financially support the programme (Austria, Belgium, Finland, Germany, Netherlands, Norway, Sweden, Switzerland and United Kingdom).

Applicants are requested to provide a motivation letter and propose possible case studies. The organizers will check that there is a balanced number of participants from both disciplines and that there is also a gender balance.

In case of interest please contact philippe.baret@uclouvain.be

Scientific workshop Report

“Genotype-by-Environment Interactions and Adaptation of Farm Animals on Phenotypic and Molecular Level” Tuusula, Finland, 7- 8 November 2012

NordGen, the Nordic Genetic Resource Center, organized in collaboration with the University of Helsinki a two-day scientific workshop “Genotype-by-Environment Interactions and Farm Animal Adaptation on Phenotypic and Molecular Levels”. The

workshop was held in Tuusula, Gustavelund Hotel and Conference Center on the 7th-8th of November 2012. The overall goal of the workshop was to deepen the understanding of genotype-by-environment interactions and adaptation potential of farm animal genetic resources (AnGR) in the face of climate change, and to stimulate networking between stakeholders for future research strategy building. This workshop also served as a mid-term seminar for the Nordic project “Nordic Research Network on Animal Genetic Resources in the Adaptation to Climate Change” (AnGR-NordicNET). This is a project funded by NordForsk with participation from the Nordic countries.

The workshop was organized in three sessions: 1) Genotype-by-Environment Interactions, 2) Farm Animal Adaptation on Phenotypic and Genetic Levels and 3) Genotype-by-Environment Interactions in Practical Breeding and Conservation Programs. Each of the sessions had three or four invited speakers. Additionally, a poster session was arranged where 11 posters were presented.

The workshop provided a multidisciplinary view merging state of the art knowledge on quantitative, population and molecular genetics within both domestic and natural populations to increase understanding of the climate change impacts, adaptation and mitigation with respect to the sustainable use of farm AnGR. More specifically, the first session presented genotype-by-environment interactions in the model organism *Drosophila melanogaster* as well as summarized examples of GxE from farm animal populations with the focus on heat stress. Status report from AnGR-NordicNET presented the data available for the assessment of GxE effects on alternative fertility traits based on activity recordings of individual cows together with production data and traditional fertility data using reaction norm methods. Session II focused on adaptation potential and signs

of adaptation of both natural and domestic animal populations, introducing the development of theory for studies of adaptation, by using experiences from natural populations. Participants were introduced to landscape genomics and shown how this method provides new and structured knowledge on the environmental forces acting on the genome. Results from AnGR-NordicNET summarized results from a study utilizing SNP data to examine population stratification and possible genome-wide signals of selection. Session III offered a broad overview on challenges and solutions of tackling genotype-by-environment interactions in practical breeding programs for plants, fish and pigs. The last lecture of the workshop put the goals and efforts of the AnGR-NordicNET into the context of the workshop. Furthermore, the future challenges of animal breeding in the face of climate change and population growth were discussed.

Poster session successfully supplemented the topics discussed during the three sessions, with a high and very active participation. Abstracts of the invited talks as well as papers presented as posters have been published in the Proceedings, edited by Anne Præbel and Torsten Nygård Kristensen. Electronic versions of the proceedings, presentations and posters are available on NordGen’s homepages <http://nordgen.org/index.php/skand/content/view/full/2249>

1.1. Scientific content of the workshop

Session I: Genotype-by-environment interactions

“Three invited talks were presented in Session I. In this session definition of GxE and investigations done using the model organism *Drosophila melanogaster* as well as examples of GxE from farm animal populations with the focus on heat stress and genetic stress (inbreeding) were presented.

GxE interactions are defined as different performance of genotypes (breeds or individuals within a breed) in different environments. The way that trait expression varies over an environmental gradient for a given genotype is called its norm of reaction. The main question of GxE and AnGR in the face of climate change is whether the genotypes and breeds we have selected in the past are still superior in the future where the environment will be different from the past and present. To be able to answer this question, it is imperative to 1) investigate whether significant GxE effect exists in the traits of interest, 2) quantify GxE, 3) estimate its effect in the current production systems and 4) find solutions how to overcome(utilize)the impediment of (the benefit of) a particular GxE in livestock production to guarantee sustainable use of AnGR.The talks in this session concentrated on the questions 1) and 2).Questions 3) and 4) were discussed in Session III.

First invited talk was given by Torsten Nygård Kristensen on investigations of GxE interactions using the model organism *Drosophila melanogaster*. *Drosophila* has its genome mapped and sequenced, extra copy and knock-out lines are also available. *Drosophila* has a short life cycle and is handled easily and in high numbers. Additionally, despite of different genome size, chromosome number and physiology etc., there is high degree of similarity between *Drosophila* and mammals at the genetic level. Investigations with this model organism have shown significant GxE in locomotor activity and metabolic rate over a range of temperatures, and egg to adult viability in benign and hot environments. Genome wide association studies have revealed that many SNPs explain significant amount of variation only under specific environmental conditions. Additionally, environmental temperature has been shown to affect heritability estimates for egg to adult

viability of both temperate and tropical populations. Lowest estimates were obtained in the most stressful environment. A special case of GxE, namely IxE (inbreeding-by-environment interaction), where inbreeding depression is more severe under stressful conditions, has been detected in *Drosophila*.

Ignacy Misztal summarized numerous investigations of GxE in dairy cattle with a special focus on heat stress. It has been shown that temperate and heat tolerance genetics are moderately antagonistic ($r \sim 0.40$). This means genetic re-ranking of animals in regular and warm environments. It has also been shown that selection of fluid milk on hot areas will result in use of less heat-tolerant sires and detrimental selection in long-term. Genetic variance of milk, protein and fat production increases up to three-fold from first to third parity under heat stress (increase of 5 °C from regular). Selection has resulted in a strong genetic improvement in milk yield and simultaneous genetic deterioration in heat tolerance relative to milk yield (weak effect) and number of days open and conception rate (large effect). In dairy cattle (trait: days open) the opposite relationship between heat stress and magnitude of heritability estimates has been shown than in *Drosophila*: higher h^2 estimates were obtained under heat stress conditions.

Analysis of GxE is not straightforward and careful modeling is important to conclude whether detected GxE is reality or relict from the statistical analysis. Heat stress related GxE is detected, both in model organism *Drosophila* and various livestock species, in production traits and especially in fitness traits. Incomplete knowledge of GxE may undermine successful breeding programs through use of biased estimates of genetic parameters, genetic deterioration of economically important traits under unfavorable estimates of genetic parameters, genetic deterioration of economically important traits under unfavorable conditions or existence of

unidentified components of GxE such as IxE. Response to climate changes should be tackled by both management and genetics. Selection for future challenges is possible with careful modeling and genomic selection.

Session II: Farm Animal Adaptation on Phenotypic and Genetic Levels

First talk of Session II was given by Scott McCairns. He used examples from natural populations to illustrate how adaptive population divergence through natural selection occurs over environmental gradients and may be verified in laboratory conditions as maximized fitness in native conditions (or reduced fitness in the reciprocal treatment/environment). F_{ST} can define a baseline of neutral population divergence, whereas divergence in quantitative traits can be expressed by Q_{ST} . Q_{ST} values larger than F_{ST} infer directional selection. New predator community, novel host or food resource or a new biophysical environment may promote adaptive evolution. It has been predicted with natural populations that phenotypic plasticity alone is unlikely to be sufficient to compensate for predicted environmental changes. Cairn's presentation underlines the importance of genetic diversity for maintaining the adaptive potential of farm AnGR.

Stéphane Joost gave a talk on landscape genomics: an approach where a set of environmental variables describing specific locations are regressed on the genetic profile of each sampled individual. The association between alleles and climatic variables gives information on the environmental forces acting on the genome and permits to seek genomic regions influencing the ability of animals to cope with and adapt to specific environmental conditions. Joost's results from a large collaborative project on goats using landscape genomics approach (ECOGENE) showed four AFLP loci possibly under selection; these loci were

coupled with climatic variables such as solar radiation, frequency of precipitation and diurnal temperature range. If the genotype of an animal shows signatures of selection for traits significantly associated with an animal's habitat, more attention could be paid to choosing animals/breeds that are adapted to specific climatic conditions.

In the third presentation Terhi Iso-Touru showed results from a study where whole-genome SNP data was used to investigate 1) population structure among 10 Eurasian cattle breeds and 2) to detect signs of selection. Population structure analysis demonstrated the genetic difference of Yakutian cattle from other breeds. Additionally, several previously found QTL-regions showed high SNP-wise F_{ST} values inferring to directional selection. One interesting gene, *ELOVL0*, is situated within such a region, but further molecular level studies are needed to verify whether this or other genes in the region are involved in cold adaptation in cattle.

Session III: Farm Animal Adaptation on Phenotypic and Genetic Levels

The aim of the third session was to present challenges and solutions of tackling genotype-by-environment interactions in practical breeding and conservation programs.

In plant breeding GxE can be coped with using three alternative strategies. The first strategy is to develop a variety which performs consistently well in a range of environments ("Jack of all trades, master of none" genotype). This is equivalent to a selection of multiple traits and the rate of progress is determined by the divergence of the environments. The second strategy is to subdivide environments into groups so that there is little GxE within each group. This means setting up multiple breeding programs. The third strategy is to evaluate a common set of breeding material across environments but make specific recommendations for each environment.

Rognli also gave an overview of the statistical methods used to estimate GxE in plant breeding and how these methods are utilized in strategy selection.

Bjarne Gjerde summarized the GxE investigations done within fish selective breeding programs. Fish are often reared in different environments than their parents, and individuals from the same year-class are exposed to a set of environmental conditions during different life stages. Therefore, GxE may be more important in fish farming than in species reared under more controlled and stable conditions. Many studies show substantial GxE in various fish species in economically important traits (growth, sexual maturity, disease resistance), but more studies are required for most species and traits. In his talk Gjerde emphasized the importance of analytical evaluation whether it is enough that breeding evaluation is based on testing at several commercial environments, or is it necessary to establish a separate breeding nucleus for a particular type of environment.

Pieter Knap presented the overview of scenarios of relating variation originating from genotype, environment and GxE and their implications on AnGR. In the cases where the effect of environment is greater than that of interaction, there is an incentive to improve the environment. If the effect of interaction exceeds that of the environment there is an incentive to match the genotype to the environment either by selecting in or selecting on data from the response environment. To take into account the environmental sensitivity of productivity, in addition to the conventional EBV, a new type of a breeding goal is actually set up. Average performance in commercial conditions combines the genetic potential of the nucleus with the environmental sensitivity of productivity in commercial conditions deviating from those experienced in

nucleus. Although optimal, inclusion of sensitivity EBVs in the total merit index is not feasible in modern pig breeding and alternative methods have to be used to match the selection to the response environment. Individual reaction norm slopes show that better individuals perform “increasingly better” in better environments. Thus genetic variation can be detected, exploited and valued more easily in a good environment.

In the last presentation, by Theo Meuwissen, the climate change and population growth challenges to livestock production were summarized. Production increase and improvement of cost effectiveness of livestock production are imperative to meet the challenges in the future. Additionally, there is an increased need to utilize waste products as input as well as marginal land. In the future, more focus will be on animal welfare and health and reduction of greenhouse gas emissions originating from livestock production. A great challenge for animal breeding lies ahead as the animals need to be adapted to these challenges. Rapid changes are required. This necessitates envisagement of new breeding directions as soon as possible. Animal breeding must work towards both mitigation and adaptation issues (including investigations of GxE) through sustainable and effective use of AnGR, genomic selection (GS) and GS-introgression.

Poster session

Eleven posters were presented in the poster session that was arranged in addition to the invited talks. Posters successfully supplemented the contents of the sessions on different aspects of GxE on different terrestrial livestock species as well as in fish. The full titles of the posters together with main results/conclusions of each poster were as follows (see next page).

Effects of genotype-by-environment interactions on lameness and pneumonia incidences in Dorper, Turcana and F1 cross-breeds lambs during heat stress exposure

- Genotype plays a major role in the incidence of both lameness and pneumonia in fattening lambs reared extensively during heat stress exposure.

Are responses to selection in lines divergently selected for residual feed intake in growing pigs affected by GxE interactions when bred in a tropical environment?

- Tropical stress had major impacts on the metabolism. Depressive effect of tropical environment was especially pronounced in early stages of growth for pigs selected for reduced residual feed intake.

Genetic variation in heat stress tolerance of Holsteins producing under a continental temperate environment

- It is possible to select for reduced thermal sensitivity using any of the six indicators of heat stress evaluated in this study.

Genetics of micro-environmental sensitivity in body weight of farmed rainbow trout

- Genetic improvement for body weight does not cause a concomitant increase in micro-environmental sensitivity. There may be high potential to simultaneously improve weight gain and increase its uniformity if both criteria are included in a selection index.

Genotype by environment interactions of claw health in Swedish dairy cattle in tie stalls and loose-housing

- There are only weak indications of genotype-by-environment interactions for claw health in these two housing systems (loose housing and in tie stalls).

Diseases induce genotype-by-environment interactions in production traits of farm animals

- Genotype-by-environment interactions induced by tolerance should be accounted for in breeding programs with multiple testing and nucleus environments having different levels of pathogen pressure.

A method to define environmental groupings for UK sheep farms to allow the assessment of genotype x environment (GxE) effects

- Multivariate analysis of the results identified 5 homogenous clusters of farm environments.

A Europe-wide experiment for assessing the impact of genotype-environment interactions on the vitality of honey bee colonies

- The local bee strains showed overall higher fitness in local environments underlining the value of the conservation work of local honey bee breeds as a resource for successful and profitable bee keeping in the future.

Breed by environment and gender by environment interaction effects affect pre-weaning mortality in two Norwegian sheep breeds

- There was substantial re-ranking of risks for males and females in the different environments.

Challenges of estimation of international breeding values due to genotype-by-environment interactions in dairy cattle

- Random regression model facilitating exploitation of principal component and factor analytic approaches provides a highly parsimonious structure for the (co)variance matrix compared to the standard multi-trait model and a decrease in the estimation time and standard errors of the estimates.

Environmental stability of responses created by line selection: Finnish rainbow trout Growth vs. Delayed Maturity -lines in Vietnam

- Estimates of genetic correlations for growth and survival revealed substantial GxE, but showed clearly that there exist genotypes that are superior in all environments.

1.2 Assessment of the results and impact of the event on the future directions of the field

During the meeting it was clearly shown that a substantial GxE exists in many of the economically important traits in plants, terrestrial farm animals as well as in aquaculture species. As long as the production environment can be controlled, relative to the practical and economical aspects, effects of GxE can be overcome simply by adjusting the environment to the animals' optimum. Nevertheless, disregarding existing GxE may have a great negative effect on the profitability of agricultural businesses. Genetic parameters are dependent on the environment they are estimated in. Use of biased estimates of genetic parameters for the genetic evaluation of a particular group of selection candidates may negatively affect the genetic progress. Furthermore, if selection and production are performed in different environments, existence of GxE strongly deteriorates the production predictions and impairs the profitability. Degree of control and stability of production environment vary between species (e.g., broilers vs. sea water aquaculture) and production systems (intensive vs. extensive). Furthermore, future challenges brought by population growth and climate change are likely to demand substantial strategy changes in livestock production. In an animal breeding framework this will call for adjustments or total overhaul of breeding programs, re-definition of breeding goals, utilization of

fastest breeding techniques available. A profound understanding of GxE is indispensable. In conclusion, more GxE investigations in most of the species are necessary to understand, quantify and utilize or solve the GxE challenges in livestock production.

To increase the sustainability and robustness of animal production systems to the harmful effects of climate change, an increased accessibility to a wide diversity AnGR is needed. Without a delay, envisioning a future strategy for conservation, utilization and investigation of AnGR within adaptation and mitigation issues which focus on the potential of farm animal species and breeds to adapt to a changing environment is imperative. This includes interdisciplinary collaboration with climate researchers, economists etc. to understand the predicted climate change scenarios and their effects on the whole agriculture business, and specifically on farm animal production. Similar value should be put on education, relevant dissemination of research knowledge and maintenance of already established research networks.

Abstracts of the invited talks as well as papers presented as posters have been published in the Proceedings, edited by Anne Præbel and Torsten Nygård Kristensen. Electronic version of the proceedings, presentations and posters are available on NordGen's homepages <http://nordgen.org/index.php/skand/content/view/full/2249>

Summer School Report

“Livestock Conservation Genomics”: Hotel Luna, Pag Island, Croatia, 1-10 October 2012

The summer school entitled “Livestock Conservation Genomics: Data, Tools and Trends“, jointly organised by the Faculty of Agriculture, University of Zagreb (Svetosimunska 25, 10 000 Zagreb, Croatia, Prof. Ino Curik) and University of Natural Resources and Life Sciences Vienna (Gregor Mendel Str. 33, A-1180 Vienna, Austria, Prof. Johann Sölkner) was held from 1st to 7th October in 2012, in Hotel "Luna" on the Pag Island, Croatia. The surrounding nature and quality of the hotel provided a pleasant working atmosphere and ambient. With a total number of 31 participants and 13 lecturers representing 12 countries (including Argentina and USA) the school was quite international event.

While mainly represented by animal scientists there were scientists from other disciplines of applied biology (ecology, veterinary, molecular genetics, etc...). Although participants were mainly PhD students, there were several professors (7) and senior scientists (3), as well as several students (3), attending the school. In addition, majority of lecturers have fully attended the school during all 7 days while three lecturers have attended the school for a considerable time. This positive mixture of young and experience researchers in the audience assured a number of stimulating discussions at the high scientific level. A total number of 8 grants were provided to the PhD students coming from institutions from Austria, Croatia (2), France (2), Germany, Netherlands and Sweden. The content of the school was structured into

theoretical lectures, software demonstrations and paper discussions and was targeting to update basic topics of conservation genetics with respect to newly available information (SNP chips and sequence data). The school started with required introduction to the school program schedule and timetable (Prof. Ino Čurik), followed by the updating overview of molecular techniques and methods providing DNA information (Prof. Paolo Ajmone Marsan). In the afternoon, we continued with explanation and tips required when starting to analyse and manipulate data coming from SNP chips (Dr. Gabor Meszaros and Ana María Pérez O'Brien). This part has been supplemented with software demonstrations and practical exercises. The second day, theoretical backgrounds, concepts and new possibilities on linkage disequilibrium and population effective size (Prof. Henner Simianer) and inbreeding and relatedness (Prof. Ino Čurik) have been presented. Theoretical aspects were followed by the software demonstration related to the calculation of all those parameters (Christian Reimer, Maja Ferencakovic). In the evening we had quite stimulating journal club discussion on the effective population size. On the third day, Prof. Johannes Lenstra and Prof. Johann Sölkner provided comprehensive empirical overview on the population structure and admixture followed by software demonstrations (Anamarija Frkonja). Assist. Prof Gregor Gorjanc presented the concept of imputation and phasing together with demonstration of its calculations. The Wednesday has finished with the journal club on population structure of sheep populations. On Friday, whole day was devoted to the sequence data analyses and detection of selection signatures (Dr. Carl-John Rubin).

The Friday finished with the journal club presenting possibilities of sequence analyses in poultry. On Saturday, Assoc. Prof. Patrik Waldmann made introduction

to the theory and calculation used in GWAS, while Prof. Johann Sölkner (theory and examples) and Maja Ferenčakovic (calculation demonstration) presented possibilities of autozygosity mapping in “detecting” deleterious genes. On the last day, Prof. Michelle Tixier-Boichard nicely presented future trends and perspectives. At the end Prof. Johann Sölkner made closing speech and together with Prof. Ino Curik provided certificates of the school attendance. On Thursday, we had working excursion visit to the sheep breeding (Pag Islan Sheep), cheese factory and old olive trees.

2.1 Description of the scientific content of and discussions at the event

The quality of the school was assured by the large number of lecturers (13) engaged. In choosing lecturers, particular care was taken on the fact that lecturers have been previously shown their expertise in the lectured subject (scientific publications and experience in working with SNP chips or/and sequencing data was required). The school started with introduction to the schedule and timetable of the school programme (Prof. Ino Curik). During the introduction each participant and lecturer provided individual presentation of the working subject of interest and institution he/she is coming from. Acknowledgments were made to all countries financing the program GENOMICRESOURCES as well as to all lecturers accepting to participate as there was no single rejection. Prof Paolo Ajmone-Marsan continued with introduction to genetic data explaining: basic DNA and genetic concepts reminder, related terminology, types of data, sequencing and SNP genotyping techniques together with types of variation (copy number variations, insertions, deletions and polymorphic sites). It was pointed that we are witnessing severe price reduction per genotyped SNP, so in the near future we can expect radical changes in the methodology of obtaining molecular

information as well as in analysing such data. Additionally, structural variations such as are copy number variations can be important source of phenotypic variation which was, up to recently, not considered at all. Ana María Pérez O’Brien explained in details what information we do receive from the SNP Chip analyses while Dr. Gabor Meszaros explained the manipulation of data and provided R scripts useful when working with large SNP chip related data files. The concept of linkage disequilibrium and population effective size was explained by Prof. Henner Simianer who also have shown some new opportunities in calculating effective population size and demographic history from the SNP chip data. Later his PhD student Christian Reimer demonstrated calculation of linkage disequilibrium and population effective size using Beagle program. Prof. Ino Curik explained in details the concept of inbreeding and relatedness on the individual and population level together with presentation of the calculation of inbreeding from Runs of Homozygosity, so called ROHs, (theoretical explanation and empirical results). The new concept of shifting individual inbreeding level was shown graphically (“SpagettIno graph”). His PhD student Maja Ferenčakovic explained how to calculate inbreeding from molecular information (ROHs) as well as how to calculate genomic relationship matrix by the method of VanRaden. In the journal club, Belen Jimenez Mena presented the paper: “Flury et al. (2010). Effective population size of an indigenous Swiss cattle breed estimated from linkage disequilibrium. *J. Anim. Breed. Genet.*, 127: 339–347.”. Huge discussion has arisen on the fragility of effective population size concept used by FAO as criteria for endangered populations as well as on the confidence interval in the estimating effective population size from the linkage disequilibrium. Prof. Johannes Lenstra has made detail description,

including the newest molecular information (SNP chip), on the current population structure and history status for cattle, sheep, goat and horse populations. Prof. Johann Sölkner introduced the concept of admixture on the research examples related to cattle. The concept was further supplemented by Anamarija Frkonja demonstrating calculations required. Availability of the large number of markers is a powerful tool in detecting admixed individuals but there is still not reliable method to provide precise estimation of time (remote generations) since admixture. On the other side admixture provides potentials in detecting adaptive selection signals. Assist. Prof. Gregor Gorjanc has presented methods used in determining haplotype phases as well as methods used to impute missing genotypes. He further demonstrated AlphaPhase as a program involved in haplotype phasing. At the end of the day, PhD student Tesfaye Getachew presented paper “Kijas et al. (2012). Genome-Wide Analysis of the World’s Sheep Breeds Reveals High Levels of Historic Mixture and Strong Recent Selection. PLoS Biol., 10: e1001258.”.

Discussion was related to the paper but was later extended to the domestication origin and population structure of other domestic species. After three intensive days, on Thursday, we were visiting cheese factory “Sirana Gligora” famous for the production of the worldwide multi-awarded cheeses. After passing through all processing units of cheese production we tasted 7 types of cheese produced there. Following, we have visited a classical sheep breeder in the Pag Island. Our excursion ended by visiting one of the oldest olive tree orchard (50 000 – 80 000 trees with estimated number of 300 subspecies based on DNA analyses) with trees being up to 1600 years old. In his first talk, Dr. Carl-Johan Rubin provided a nice overview over several methods used for detection of selection; a) based on the referent genome (differentiation on FST

values; levels of heterozygosity; long haplotype tests, EHH; site frequency spectrum, Tajima’s D test; and comparison with divergence, HKA and McDonalds-Kreitman test) and b) based on the absence of referent genome. The later approach was presented in details on the analyses performed on the sequences data derived from the pooled poultry populations samples. The second theoretical talk of Dr Carl-John Rubin was related to the structural variants, particularly to copy number variations influencing phenotypes. Both talks were extremely stimulating and introducing quite new approaches and methodologies, not regularly used by animal scientists. In the afternoon, there was demonstration of software’s used in the analyses of sequences. All demonstrations were based on the poultry sequence data provided from the research published in the paper “Rubin et al. (2010). Whole-genome re-sequencing reveals loci under selection during chicken domestication. Nature, 464: 587-593.”. The same paper was later presented in a journal club discussion by a PhD student Mirte Bosse. Very interesting discussion has been arisen, questioning what should be the main goal of an conservation program as well as discussion questioning usefulness of adaptive based approach versus neutral variation (mainly used in the last decade). Later discussion become more imaginative, for example, what if we would base long-term conservation strategy on the storing of sequence information of endangered breeds or what if we would target the individuals with the highest DNA content in the conservation, etc... On Saturday, Assoc. Prof. Patrik Waldmann continued with critical presentation of widely applied strategies known as GWAS in estimating SNPs affecting phenotypic variation. His theoretical presentation was supported by exercises using written R scripts and simulated data. Large number of extremely useful R scripts has been provided. The

power of SNP chip information to detect detrimental single gene defects has been demonstrated by Prof. Johann Sölkner on the example where degenerative axonopathy in Tyrolain Grey cattle has been associated to the gene mutation. Furthermore, some strategies to perform mapping of inbreeding depression due to single gene were also shown, although methodology was still not fully developed. The practical issues and software demonstration in autozygosity mapping were demonstrated by Maja Ferencakovic. On the last day, Prof. Michelle Tixier-Boichard nicely presented future trends and perspectives related to the conservation genetics.

Firstly, conceptual framework for conservation genomics in livestock has been explained. Secondly, the important research questions and major issues to be addressed using genomic approaches have been pointed. Thirdly, current technological trends and challenges has been addressed. Furthermore, societal challenges have been considered and at the end future conservation strategies were discussed from the point of gene-banking, biotechnology and up to definitions of phenotypes. The lecture was supported by the number of literature citations. At the end Prof. Johann Sölkner made closing speech and together with Prof. Ino Curik provided certificates of attendance. Through the usage of Dropbox, as well as the usage of USB stick (given in "the school materials bag"), all participants were provided with all presentations (pdf or/and pptx), together with all software's applied and training datasets.

2.2 Assessment of the results and impact of the event on the future directions of the field

The thematic of the school was very much on the cutting age technology, so, we expect benefits from the educational, research and industrial sides. The intensive program lasted seven days and

systematically covered a number of basic topics in conservation genetics (molecular genotyping and sequencing, linkage disequilibrium, effective population size, inbreeding, relatedness, population structure, admixture, detection of adaptive variation, detection of detrimental defects, estimation of complex trait variability) from the aspects of genomics and newly developed possibilities (SNP chips and sequences). In this way, the curriculum of one subject at the master and/or PhD level, covering the field of "Livestock Conservation Genomics", has been built. Thus, we expect that a number of lectured subjects will be incorporated in the future academic programs taught at EU Universities, particularly as considerable number of relevant academic stuff has attended whole school program.

Topics describing achievements in sequencing technology and development of molecular technologies were highly stimulating and surprising (in a positive way) for the majority of participants. At least in my institution we are re-evaluating our current development strategies. For example how much efforts and to what extent should we invest into building computing and calculation facilities and skills (developments/platforms/languages) versus how much should we invest into building of molecular genetics capacities? For a number of participants, practical's and software demonstrations were helpful, further, encouraging and facilitating future researches. The location and low price of the school enabled participation of a large number of East European participants (Croatia, Hungary, Slovenia, and Slovakia) to catch up with new scientific developments. We hope this is bringing to the creation of a more homogenized scientific research space within the Europe. The internationality of the participants and lecturers provided certain level of networking among researchers that have not been collaborated previously. Thus, we have already been informed about

initialisations of several projects and research exchanges established during the school, particularly with respect to the incoming grant applications within the GENOMIC-RESOURCES program (it would be interesting to monitor next grant applications related to the participants attending the school). Discussions were simulative and quite opened, enabling young scientists as well as experienced scientists to critically confront ideas and arguments. Probably, the best example is discussion on the effective population size where there was general agreement that current numbers used ($N_e=50$) are not sufficient criteria in determining the conservation status of the breed.

The conclusion was that it is necessary to develop better approaches, measures and methods to evaluate endangeredness of a breed. Finally, we believe that the summer school was successful in providing Ph.D. students and researchers in animal genetics, conservation and breeding not yet conversant the analysis of SNP and sequence data with a toolbox of methods and softwares to address questions relevant in the conservation of livestock.

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