



## Genomics to systems biology in animal and veterinary sciences: Progress, lessons and opportunities <sup>☆</sup>



Haja N. Kadarmideen <sup>\*</sup>

Section of Animal Genetics, Bioinformatics and Breeding, Department of Veterinary Clinical and Animal Sciences, Faculty of Health and Medical Sciences, University of Copenhagen, Grønnegårdsvej 7, 1870 Frederiksberg C, Denmark

### ARTICLE INFO

#### Keywords:

sgBLUP  
Genomic prediction  
Systems genetics  
Systems biology  
eQTL  
RNAseq

### ABSTRACT

Livestock genomics has gone through a paradigm shift since the advent of genome sequencing that includes Genome-Wide Association Studies (GWAS), Whole Genome Predictions (WGP) and Genomic Selection (GS). Beginning with a brief review of current progress and challenges in livestock GWAS, WGP and GS, opportunities for next generation methods are introduced that unravel the underlying systems genetics of complex traits and provide biologically meaningful and accurate predictions. Genome-Wide Epistasis Association (GWEA) and Weighted Interaction SNP Hub (WISH) network methods are introduced here to unravel complex trait genetics. These methods effectively address the problems of GWAS that have no ability to model and analyze genome-wide genetic interactions and thus do not capture any epistatic variance that could explain part of the missing heritability. Further, the *Systems genomic* BLUP (sgBLUP) prediction method is introduced in this paper as a next generation WGP or GS tool that can account for and differentiate SNPs with known biological roles in the phenotypic or disease outcomes and potentially increase the accuracy of prediction. It is emphasized that tools that link genetic variants to their functions, pathways and other biological roles will become even more important in the future. These tools include *FunctSNP*, *Postgwas* and *NCBI2R* which are briefly discussed. Genome-Wide Gene Expression (Transcriptomics) analyses using RNAseq technology are briefly discussed with some examples including results from our own pig experiments. In the last part of this review, systems genetics and systems biology approaches are introduced that involve joint modeling and analyses of multi-omics data types from genomics through transcriptomics (microarray and RNAseq), metabolomics to proteomics. It is shown using published studies that these systems approaches are valuable and powerful compared to stand-alone genomic methods in identifying key causal and highly predictive genetic variants for complex traits as well as in building up complex genetic regulatory networks. In all sections, some applications of next generation/-omics methods in livestock species (e.g. feed efficiency, growth, weight gain, fertility and disease resistance in cattle, pigs and sheep) are provided with references to relevant software and tools. In conclusion, this paper reviewed the current progress, lessons and challenges in livestock genomics and its ongoing transition to and opportunities for integrative systems genetics and systems biology in animal and veterinary sciences. Most of these integrative systems genetics and systems biology tools and methods presented here are equally applicable to plant and human genetics and systems biology.

© 2014 Elsevier B.V. Open access under [CC BY-NC-ND license](https://creativecommons.org/licenses/by-nc-nd/4.0/).

<sup>☆</sup> This paper is part of the special issue entitled: Genomics Applied to Livestock Production, Guest Edited by Jose Bento Sterman Ferraz.

<sup>\*</sup> Tel.: +45 35333577.

E-mail address: [hajak@sund.ku.dk](mailto:hajak@sund.ku.dk)

## 1. Introduction

Food production from livestock will be the primary driver in alleviating the concerns raised by a rapidly increasing human population's demand for food of animal origin. For efficient animal production and reproduction, there are challenges to be overcome for a better understanding of how animal production can contribute more effectively to the bio-economy. Animal breeding and genomics play a critical role in producing animal raw materials (meat, milk, eggs and their products) to meet current and future demands of food security for all human beings, while ensuring sustainable use of natural resources and less environmental impact. The genomic revolution in livestock was an aftermath of the human genomic revolution vis-à-vis genome sequencing projects. In the last 20 years, we have seen an astonishing development in livestock genomic technologies. Quantitative Trait Loci (QTL) mapping in the early 1990s spurred a lot of enthusiasm that saw several hundred research projects identifying QTLs in livestock species. The Animal QTL database (<http://www.animalgenome.org/QTLdb/>) reported several thousands of QTLs for major livestock species; however, most of these QTLs were detected using sparse microsatellite markers with large confidence intervals covering several megabases of the genome containing dozens to hundreds of genes and variants. Therefore, it was difficult to detect genes causing substantial quantitative trait variation which, in turn, initiated re-mapping and fine mapping of the initially mapped QTLs (see review by Georges, 2007). Subsequently, the release of whole genome sequences of major livestock species like cattle (*The Bovine Genome Sequencing and Analysis Consortium et al., 2009*), sheep (*The International Sheep Genomics et al., 2010*) and pig (*Groenen et al., 2012*) have led to a paradigm shift in availability of high-throughput genetic markers ranging from 10,000 to 50,000, 100,000 and up to one million Single Nucleotide Polymorphisms (SNP) markers today. These markers are genotyped using high-throughput Affymetrix or Illumina genotyping platforms (DNA arrays or SNPchips). In the first phase, the high-density SNP genotype data were mainly used in conducting Genome-Wide Association Studies (GWAS) that match genetic variants, with or without pedigree records, with the observed phenotype and provide estimates for hundreds of thousands of markers on each phenotype considered. In humans, GWAS has identified hundreds of associations of common genetic variants with over 100 diseases and traits (<http://www.genome.gov/gwasstudies>). A consistent quest for variants that explain more of the disease or trait heritability has resulted in assaying increasingly higher-density SNP arrays with more than one million SNPs and dramatic increases in population sample sizes. In human genetics, the focus had been on precise delineation of causal variants that alter human phenotypes, particularly diseases, and on those variants that provide crucial insights into the biology connecting genotype and phenotype. In livestock species, the use of GWAS has been limited in the context of how it can be applied to breeding for improved performance and disease resistance. In both humans and animals, there are hundreds of success stories and the hype in GWAS is still unprecedented.

Functional genomics or transcriptomics studies that are based on microarray gene expression profiling (MGEP) has been and still is popular in livestock species. MGEP uses high-throughput transcriptomic arrays containing up to 30,000 transcripts to reveal underlying genetic (co) regulation in a set of biological conditions that clearly relate to phenotypic differences or disease states. These hybridization-based approaches typically involve incubating fluorescently labeled cDNA with custom-made microarrays or commercial high-density oligo microarrays. The focus of MGEP studies have been on those transcripts that provide holistic insights into the functional biology connecting genes throughout the genome and phenotypic or disease outcomes and eventually provide drug targets or biomarkers.

The SNP chip or microarray-based genomics and transcriptomics studies in livestock are being rapidly replaced by next-generation sequencing (NGS) technologies as robust genome/transcriptome sequencing technology platforms are widely and cheaply available and rapidly parallel development in statistical- and computational-biology and bioinformatics methods and tools to analyze NGS data. The NGS technology provides enormous opportunities for livestock sciences to move forward and make a transition to systems biology but also pose formidable challenges.

In summary, the sheer volume of genomic and transcriptomic data from hundreds of thousands of breeding animals in cattle, sheep, pigs and poultry and the availability of large-scale phenotyping for a range of complex and economically important traits has resulted in major challenges and opportunities for livestock production. This review paper is organized as follows: In the first part, I will briefly outline Genome-Wide Association Studies (GWAS) and Genomic Selection (GS) methods with some existing challenges and examples from our groups' own studies. In the second part, which is one of the two main focus areas of this paper, I will outline next generation genomics wherein GWAS and genomic selection are based on complex statistical-computational genetic methods and on the next generation sequencing technologies for both genomic and transcriptomic profiling. In the third part, the other main focus of this paper, I will introduce livestock systems genetics and systems biology where networks construction (on genomic and transcriptomic datasets) and an integration of multiple data types from genomics through transcriptomics, metabolomics, and proteomics are shown to be valuable approaches to identifying key causal and highly predictive genetic variants for complex traits. In all sections, I have highlighted some of the software and tools that can be used.

## 2. Genome-wide association studies and genomic selection

### 2.1. GWAS—Single SNP and haplotype approaches

GWAS rely on a natural phenomenon of population-wide linkage disequilibrium (LD) between genetic (SNP) markers and causal variants, quantitative trait loci (QTL) or nucleotide (QTN). GWAS require larger samples of individuals than those required for linkage-QTL studies, because (1) population-wide

Download English Version:

<https://daneshyari.com/en/article/5790148>

Download Persian Version:

<https://daneshyari.com/article/5790148>

[Daneshyari.com](https://daneshyari.com)