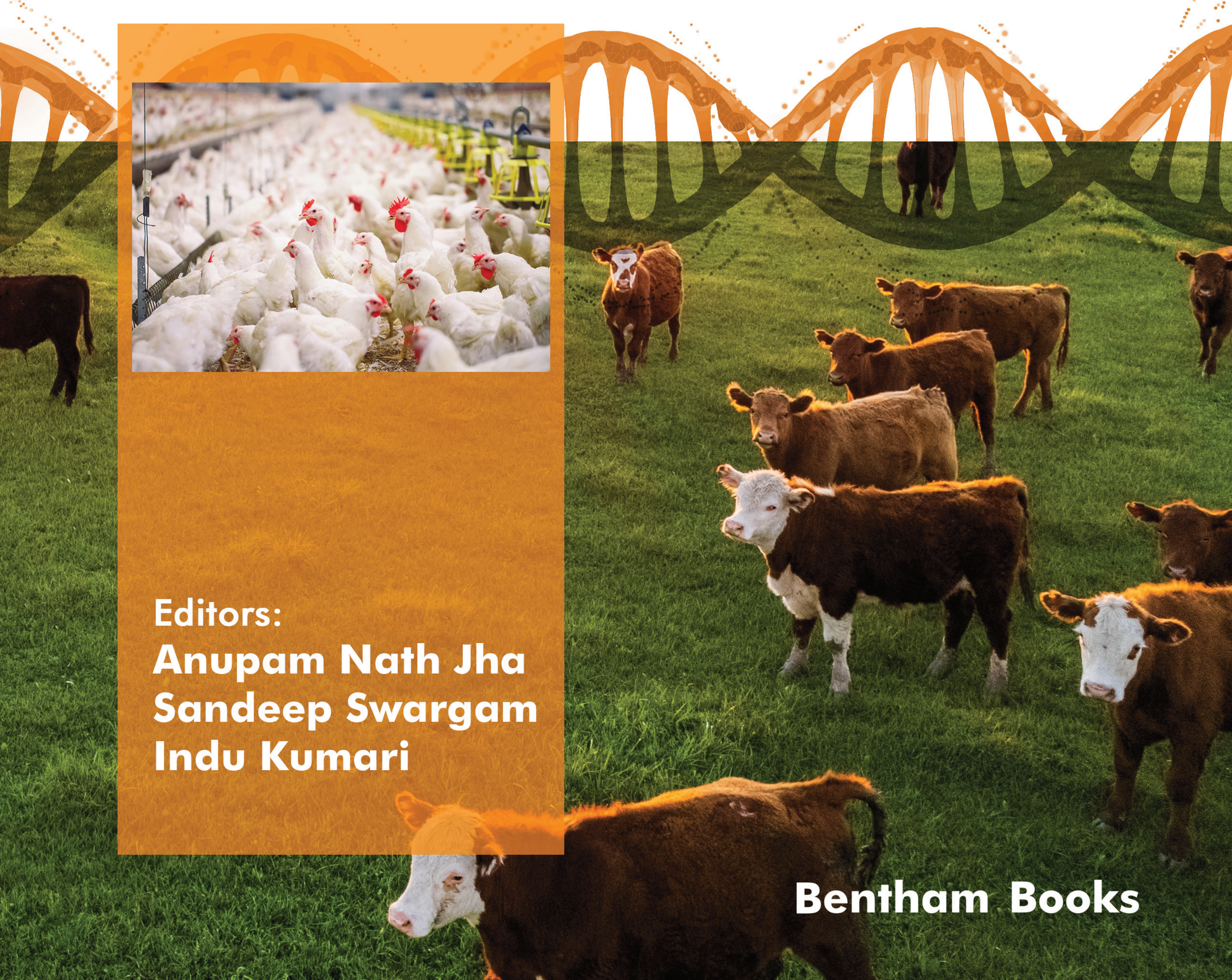
SYSTEMS BIOLOGY, BIOINFORMATICS AND LIVESTOCK SCIENCE



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FOREWORD 1

I was delighted when I received an invitation to write a foreword to the book "*Systems Biology and Bioinformatics and Livestock Sciences*". I enjoyed reading the draft of the book. The book renders comprehensive details of the most commonly used omics technologies used in livestock management and its integration with systems biology approaches. With the development of new-generation omics techniques and their use in livestock management and research, the application of systems biology in the field of livestock sciences is ever-increasing, which is aptly described in the book. The book will be a great source of knowledge for students (Graduate, Post-graduate, Doctoral), academicians of applied and veterinary sciences, early career scientists from bioinformatics, veterinary, basic sciences, applied animal sciences, data science, *etc*.

The book is appropriately divided into four sections with different chapters. Each chapter in the first section is an introduction to various OMICs techniques and their integration into Systems Biology for Livestock Research. The editors have followed a pedagogic approach to highlight the core practices of OMICs and systems biology, which have been employed in the livestock sciences or can be applied in the future to enhance livestock yield and production. The systematically divided book sections initially introduce the readers to the basics of systems biology. The last section of the book is a section on the future of systems biology in livestock science. It elaborates on recent developments in systems biology, high throughput technologies, its integrated analysis using artificial intelligence algorithms and other modern techniques. The well-written, unique and informative book is bound to attract global readership.

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FOREWORD 2

I am immensely delighted to write this foreword for the book titled “Systems Biology and Bioinformatics and Livestock Sciences” edited by Drs. Anupam Nath Jha, Sandeep Swargam, and Indu Kumari. This book is an amalgamation of integrated omics with systems biology, within which readers from interdisciplinary sciences will find valuable information on the application of system biology for livestock sciences, including but not limited to signaling transduction cascades, metabolic pathways, mathematical modeling, disease management, and increased cattle production. As next-generation sequencing has taken the scientific community to a new era, integrated sciences have emerged with a better course of action for research scientists of animal sciences to better understand the health of cattle and increase the yield (milk and meat). This field is currently explored by scientists and scholars in veterinary, bioinformatics, and basic sciences. The chapters in review provide a critical analysis of the ongoing studies, tools and techniques that are being developed. The databases developed for livestock animals and disease-causing pathogens (bacteria and viruses) have been discussed in detail in the chapters. Genomics, transcriptomics, proteomics, metabolomics, translational omics, single-cell transcriptomics, and integration of artificial intelligence-machine learning with system biology and livestock are the terms that are used and elaborated in the chapters. The authors of Systems Biology and Bioinformatics and Livestock Sciences clearly demonstrate the impact system biology can have in the reproduction, early biological development, and immunological studies of livestock.

This book is intended to be helpful to students and early/mid-career scientists from veterinary, bioinformatics, animal, basic and applied sciences. This book will be a noteworthy component of the interdisciplinary sciences in India and worldwide. I believe the book will reach a broad audience, and there will be readers who will gain significant knowledge and insights into this important field of science (both basic and applied) because of their collective efforts.

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PREFACE

In the next decade, the demand for animal products will be nearly double. Livestock sciences must evolve to produce more livestock products as the world's population rises. Thus, it is crucial to utilize the latest techniques of omics, systems biology, and bioinformatics interventions to improve livestock production and meet demand. To address key challenges with respect to livestock health and diseases, one must utilize experimental data along with advanced computational approaches. The complementary methods shall aid in deciphering the intricacies of biological under-wiring in livestock animals and help in their probable mitigation and prevention of diseases.

The book is divided into four sections with 13 chapters. Section A: Introduction to systems biology and its perspectives comprises 3 chapters wherein the authors throw light on the introduction of systems biology and bioinformatics approaches for scientists involved in animal science research. It was followed by two other chapters that emphasize computational modeling methods and physiome modeling relevant to biological investigations. Section B: Systems Biology to study livestock and related diseases includes 4 chapters focused on the investigation of the gut microbiome, viral diseases, livestock animals, and fisheries with the tools of omics and systems biology. Section C: Integration of recent and developing techniques with Systems Biology for better outcomes highlights different techniques of proteomics, single-cell sequencing and nanobiotechnology in livestock health and sciences. Section D: Future Aspects of Systems Biology in Livestock Sciences sheds light on the application of advanced methods of systems biology, including genomics and AI/ML, in animal sciences and their future prospects.

To summarize, in order to advance the field, the current edition offers a comprehensive compilation of the existing, ongoing approaches and future prospects of omics along with systems biology. In addition, to provide avenues for systems biology in the field of livestock sciences, these chapters and critical analyses will likely motivate further research in the area apart from benefiting a wide range of other scientific disciplines.

We want to express our gratitude to our esteemed contributors for giving their valuable and scientific aptitude to contribute to the chapters related to omics and systems biology studies in this post-Covid era where we are still struggling to attain our old state of mind. It would not have been developed into a ready reference for researchers in the animal science field without contributors.

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ABOUT-THE-EDITORS

Dr. Anupam Nath Jha is a computational biologist specialising in molecular dynamics (MD) simulations of nanomaterials and proteins, including protein modelling and their structural elucidations. His area of specialization also includes metabolic pathway analysis using systems biology approaches. He has significantly contributed to the computational biology scenario and has completed many major research projects concerning infectious diseases, protein-nanoparticle interactions and protein design. Dr. Jha is currently serving as assistant professor (Grade III) in the Department of Molecular Biology and Biotechnology, Tezpur University. His basic education is in physics and has done Ph.D. in computational biophysics from Indian Institute of Science (IISc), Bangalore.

Dr. Sandeep Swargam is currently working as an assistant professor at the Centre for Computational Biology and Bioinformatics, School of Life Sciences, Central University of Himachal Pradesh, Shahpur and Dharamshala, Himachal Pradesh. India. His area of specialization includes next generation sequencing with pipeline development and structural biology including molecular modelling, molecular docking, simulations and big data analytics. Previously, he worked as a bioinformatics specialist at INSACOG Unit, National Centre for Disease Control, New Delhi, Ministry of Health and Family Welfare. Govt. of India, where he worked on COVID genomic surveillance and WGS analysis. Before that he worked as scientist-B at Jamia Hamdard University and his research work focused on the WGS analysis of clinical Mtb samples from the North-Eastern region of India. In collaboration with the Indian Council of Medical Research (ICMR), Head Quarters, he developed a MycovarP pipeline for the analysis of M.tb WGS data.

Dr. Indu Kumari is working as data curator at Indian Biological Data Centre, RCB, Faridabad. Before this, she was working as scientist C at Central Molecular Lab, Govind Ballabh Pant Institute of Postgraduate Medical Education & Research, New Delhi. She was working there on whole-exome sequencing of colorectal cancer. Prior to this, she was working at National Institute of Pathology, Delhi. During this she has worked on clinical patient's *Mycobacterium tuberculosis* (M.tb) whole genome sequenced (WGS) data collected from the North-Eastern region of India. In addition to this, she also analyzed the global WGS data of M.tb available in public domain like ENA. MycoVarP: a pipeline for the analysis of M.tb WGS data has also been developed. She is an editorial reviewer for international journals. Her interdisciplinary research interests include fish biology, plant-microbe interactions, molecular docking and simulations, structural, bioinformatics, next generation sequence analysis and big data analysis.

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CHAPTER 1

An Introduction to the Integration of Systems Biology and OMICS data for Animal Scientists

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Abstract: Systems biology integrates the data of all the omics studies and provides the avenues to understand the biology of an organism at higher levels like at tissue, organ or organism level. In the last decade, studies of genomics, transcriptomics, proteomics and metabolomics have been carried out. Only a limited amount of this big data has been analyzed, which is mainly focused on the genotype (single nucleotide polymorphism) level like minor allele frequency, copy number variation and structural variants. The analysis in transcriptomics is limited to differentially expressed genes and their ontology. Proteomics is focused on virulent factors, proteins involved in the disease progression and immunomodulation. However, in the case of livestock animals, there is a need to develop pipelines for the analysis of the omics data. With the integration of omics data into systems biology studies, there is a need to develop algorithms to carry out gene interaction and protein interaction studies and to build interaction networks. The pathway analysis of a system requires the well-defined interacting hub and edges of the protein system of an organism. Developing AI-ML models for drug discovery is required to target the pathogens of livestock animals. In the present era, the research is moving towards single-cell sequencing of the cells and tissues to explore the genetic heterogeneity in the micro-environment of the tissue and spatial biology of the tissue. This chapter will introduce the reader to different aspects of omics technology and its role in systems biology for better livestock management.

Keywords: Database, Genomics, Omics, Proteomics, System biology, Transcriptomics.

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INTRODUCTION

The ongoing era is the advancing next generation sequencing (NGS) which started from Sanger sequencing that was taken over by targeted and whole genome sequencing (WGS). At present, the scientific community has shifted to single-cell sequencing and spatial transcriptomics. This ever-increasing big data is obtained from the reductionist approach. Therefore, there is a need to integrate the latest information on biological systems which is present in several databases and metadatabases like NCBI, ENA, DDBJ and China National GeneBank DataBase (CNGBdb). There are several genome databases available for animals. And these available open data sources provide details of genomics, transcriptomics, proteomics, metabolomics, translatomics, function of enzyme and protein, interactome (protein-ligand, protein-protein, DNA-protein and RNA-protein interactions), drug-associated single nucleotide variants (SNVs) and gene ontologies. The integration of the available data of livestock is required, which is possible through the application of mathematical modelling and system biology approaches. It is the necessity of the present era as the human population is estimated to rise to 11.2 billion by 2100, as given by the Food and Agriculture Organisation of the United Nations (FAO) (https://population.un.org/wpp /Publications/Files/Key_Findings_WPP_2015.pdf). Population growth along with global climate change causes pressure on the global food system. This can be achieved by integrating different fields of omics to bring improved and better food from the lab to common people. To achieve this objective, we need to improve animal health and welfare through sustainable practices. The enhanced food quality can be achieved by improving breeding strategies by selecting the accurate genotype to access the phenotype in farmed terrestrial and aquatic animal species. There is a Functional Annotation of ANimal Genomes (FAANG) project ongoing to fulfil these objectives [1]. There is a need to start such projects in different parts of the world so that the quality of food and the reproductive ability of the livestock can be improved. There are studies that were carried out by single technique like WGS, targeted or whole exome sequencing (WES), targeted/whole transcriptomic sequencing, targeted/whole methylome sequencing (epigenetic changes), proteome profiling, and metabolomics. In addition to this, there are integrated studies which have tried to improve the meat, milk quality and health of the livestock. However, the integration of the genome into the phenome will help to develop some working models that can be applied by system biology for better livestock production.

The book has been divided into four sections which introduce the readers to system biology, its application in livestock and diseases, the amalgamation of various techniques with system biology and its future perspectives as well. In the present era, the experimental work is moving from genome-level sequencing to single-cell sequencing. In experimental biology, we are trying to move towards a holistic approach by shifting towards single-cell sequencing and spatial tissue analysis. We will discuss all the chapters in brief in this chapter.

We will discuss briefly the contents of the book chapters, which include:

Modeling Approaches in Computational Biology, Including Silicon Cell Models, Physiome Project: A Global System Biology Network Initiative, Genome to Systems Biology in Livestock Management, Host-food-Gut Microbiome Interactions by Systematic approaches, Multi trait genetic evaluation of economic traits in ruminants, Role and Importance of Nano-biotechnology and System Biology for Livestock Science, Animal–Pathogen Interactions, Proteomics in animal health and diseases: An update, Machine learning-based AI approaches to veterinary drug discovery for system-wide prediction of the drugable proteome, System biology-based understanding of gut microbiome role in cattle production and health, Application and Development of CRISPR-cas9 based genome engineering in farm animals.

SECTION A: INTRODUCTION TO SYSTEMS BIOLOGY AND ITS PERSPECTIVES

Chapter 1. Systems Biology and Bioinformatics for Animal Scientists

System biology is a holistic approach to correlating the individual livestock's omics levels of different units involved in the central dogma process of the cell. This integration of genome to phenome and functional annotation of the genetic units may help the scientific community to bring better quality features of the livestock to the farm end. This integration process starts from genome-epigenome (methylome)- transcriptome- metabolome- proteome- phenotype or disease variaome [2]. Different omics approaches employed in the current research are listed in Table **1**.

Table 1. Different 'omic' levels used in systems biology analyses.

Sr. No.	Description of the Omic Technique
1.	Whole genome sequence- total gene of an organism
2.	Epigenome- change in the total methylome
3.	Targeted or whole transcriptome (mRNa, lncRNA, hnRNA and miRNA) and epitranscriptomics
4.	Proteome
5.	Translatome (*all translating mRNAs)*
6.	Metabolome
7.	Microbiome (bucaal cavity and gut microbiome)

CHAPTER 2

Application of Multi-scale Modeling Techniques in System Biology

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Abstract: Systems biology intends to portray as well as comprehend biology around the globe, where biological processes are acknowledged as the outcome of complex mechanisms which occur on multiple dimensions beginning with the molecular level and reaching to ecosystem level. Biological information in systems biology comes from overlying but distinct scientific areas, each with its own style of expressing the events under research. Simulation and modeling are computer-aided methods that are precious for the quantitative and integrative description, prediction, and exploration of these mechanisms. In addition, Multi-level and hybrid models have been developed to meet both improved accuracy and capability of making good knowledge bases, which turned out to be a valuable tool in computational systems biology. Various methods, including the silicon model, have been developed in many scientific disciplines for solving multi-scale problems, which is appropriate to continuum-based modeling strategies. The association between system properties is depicted using continuous mathematical equations in which heterogeneous microscopic elements, such as persons, are modelled using individual units. We summarized multi-scale methodologies and their application in biotechnology and drug development applications in view of emphasizing the importance of studying systems as a whole with the role of artificial intelligence and biostatistical aspects in this review.

Keywords: Artificial intelligence, Biostatistical aspects, Multi-scale modeling, System biology, Silicon model.

INTRODUCTION

Bioinformatics, computer biology and system biology are the integrative fields that establish and apply computational approaches to evaluate huge volumes of biological data, *i.e.,* genetic sequences, cell populations, and so on, in order to make innovative discoveries. Analytical techniques, mathematical modeling and

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simulation are some of the computational methods used in these disciplines [1, 2] (Fig. **1**).

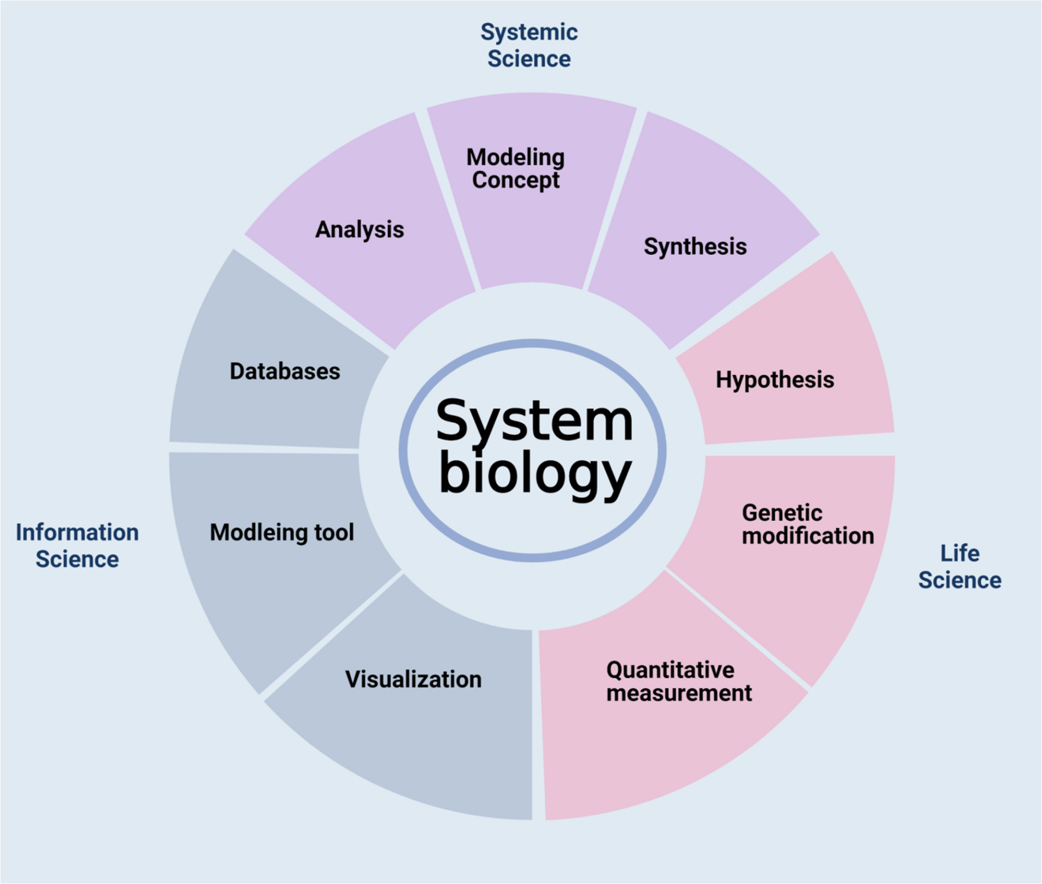

Fig. (1). System biology includes information science, life science and Systemic science.

In system biology, biological entities are interpreted as multiplex holistic systems in which activity may not be simplified to the linear sum total of their parts' functions [3]. It aims to determine how biological system features might be viewed as functions of macromolecular component characteristics and interactions. In this integration, computer models play a crucial role [4]. The study of enzyme-catalyzed reaction pathways and a new signal transduction pathway has dominated Systems biology. It is widely used in the integrative elucidation of increasingly large post genomic datasets, which are widely accepted as useful in computer aided modeling of molecular systems, if not necessary, components of biological research [5, 6] and are used in a broad range of fields [7 - 13].

Local interactions between sub-parts in an intricated biological structure give rise to general characteristics [14]. The spatial similarity of the sub-parts favors these interactions in general. As a result, one of the biological features that ought to be considered when modeling biological systems is spatiality [15]. The likelihood of these two elements interacting is an outcome of their dimensional closeness, and the probability governing such events committed to be principally considered in the modeling task [16].

In biologically complex systems, distinct techniques have developed to regulate the probable interactions of biological components interacting. Compartmentalization is one of them [17, 18]. Biological processes are divided into compartments, and the boundaries linking compartments specifically control the channel of molecules, changing the probability density of molecular encounters over space. This must be expressed in a model as the ability to articulate encapsulation and limited communication of each and every sub-part [19]. This must be expressed in a model as the ability to articulate encapsulation and exclusive communication of each and every sub-part [19].

Functional activation does not always translate spatial proximity between molecules. In general, the activation of certain functions can necessitate biochemical interactions between molecules that result in structural changes that amend their functional state. Bimolecular structural characteristics are ciphered into the genome. As a result, the quality and quantity of actors along with their relationships, are defined by the information gathered. The use of genomic data is controlled at various layers and by various mechanisms, all of which are in a flexible graded relationship. The graded relative relations that make up such a dynamic interplay of laws fluctuate in accordance with the process situation. It matches the epigenetic regulation concept in its broadest sense; anything that occurs among a genotype and the phenotypes [20]. As a result, biological models must be able to portray context-dependent and flexible hierarchies in an efficient manner.

ELEMENTS OF SYSTEM BIOLOGY

As a holistic approach, systems biology entails modeling and investigation of metabolic pathways and also involves various regulatory as well as signal transduction pathways in order to strengthen understanding of cellular behavior. Additionally, there are a range of layers of abstraction at whichever these systems can be modeled within a range of techniques available depending on both the quality and quantity of offered information.

Reconstruction of these pathways, which involves combining data from various sources to produce a depiction of various chemical events that underpin biological

CHAPTER 3

The Perspective of Physiome Modelling in Systems Biology: New Horizon

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Abstract: Scientific understanding has rapidly expanded in the new biological age, with the rapid advancement of genomic science and molecular biology, It is a challenge to reintegrate the enormous quantity of information and data that was generated from works related to genomics, transcriptomics, proteomics, and metabolomics in order to effectively explain the organism and connect molecular processes with higher-level biological phenomena. Scientific understanding has expanded quickly in the new biological age due to the rapid advancement of genomic science and molecular biology. This inspired contemporary interest in systems biology, which investigates organisms as integrated systems made up of dynamic and interconnected genetic, protein, metabolic, and cellular components using biology, mathematics, biophysics, biochemistry, bioinformatics, and computer science. Systems biology is the key concept underlying Physiome, a mathematical measure of how an organism functions in normal and pathologic states which is based on morphome. The simulation models based on mathematical expressions and physics can aid in the interpretation and encapsulation of biological phenomena in a computable and repeatable manner. Researchers have created tools and standards to allow the reproducibility and reuse of mathematical models of biological systems, as well as tools and guidelines to promote semantic representation of computational models and repositories where models can be archived, shared, and discovered.

Keywords: Bioinformatics, Database, Genomics, Physiome project, Reductionism, System biology.

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INTRODUCTION

Living systems are complex yet well-organized and structured entities showing a definite hierarchy in the organizational structure that includes atomic, molecular, cellular, tissue, organ, and organ systems of the organism. Since the beginning of time, man has endeavoured to comprehend the workings of life for a variety of reasons, ranging from efforts focusing on improving human health, such as gaining insights into disease processes that allow the development of novel therapeutics and innovative medical devices, to an understanding of the interrelationship with the environment and other living species. Scientists have followed different approaches to understanding and exploring living systems, notable ones being reductionist, mechanistic and holistic approaches. The next few paragraphs describe the principles underlying reductionism, molecular biology from the perspective of reductionism, and limitations of reductionism that led to the emergence and widespread acceptance of concepts of systems biology [1]. The physiome is well compiled of the observations and studies in a database that help to develop integrated descriptive, quantitative, and logical modelling. The developed models remove contradictions that further illustrate emergent features of the system, such as structure/functional behaviour. These keen observations are not possible from their component elements through iteration and experimentation.

The proposed book chapter also focuses on the relationship between systems biology and Physiome project and mathematical models and how it will help to understand livestock system biology.

From Reductionism to Systems Biology

The principle underlying most research is to analyze and understand the fundamental constituents to get an insight into complex systems. Accordingly, physicists focus on the study of the basic particles and forces, chemists explore the chemical bonds, and biologists, to understand organisms, explore the DNA sequences and molecular structures focusing on a particular gene or a protein. This approach of “divide and conquer” is termed reductionism [2, 3].

The concept of reductionism dates back to as early as the 16th century when Rene Descartes (1596-1650) put forth the notion that complex entities can be analyzed by breaking them into constituent parts, studying the behaviour of individual parts and finally putting them back together to understand the whole [4]. Reductionism attempts to explain all biology in terms of physics and chemistry, based on the premise that all biological systems are made up of molecules and atoms, and so their physiochemical qualities should be able to describe biological systems [5]. Thus, reductionism is based on the premise that isolated molecules and their structures may give insight into the entire system. Reductionism is analogous to a jigsaw puzzle, in which a whole image may be created by assembling separate parts, each of which contains a component of the picture [6].

It is difficult to understand how any process other than a reductionistic approach might have produced many significant scientific breakthroughs. Avery, Macleod, and McCarty could not have shown that DNA alone was responsible for the pneumococcus transformation without isolating it from other cellular constituents. Similarly, the power of reductionism was demonstrated when a single *Yersinia* gene conferred the capacity to invade eukaryotic cells in tissue culture to *Escherichia coli* K-12 or when the human equivalent of murine E-cadherin made transgenic mice vulnerable to oral challenge with *Listeria* [7].

Molecular Biology from a Reductionist Perspective

The study of metabolomic processes within cells, such as DNA replication, RNA transcription, and protein translation, is known as molecular biology. It can be said that reductionism is the heart of molecular biology evolution. The aim of this discipline, which combines physics and chemistry with biochemistry, biophysics and genetics, is to get to the most fundamental level of explanation possible [8].

Reductionist molecular biology overlooks the dynamic interactions between the parts of a cell and views them as static and in isolation. Molecular biology that epitomizes reductionism considers the components of a cell as static and in isolation, overlooking the dynamic interactions between them. However, the positive side of the reductionist approach is that it influenced the creation of a wide range of molecular techniques, without which the discovery of different genes, molecules, and processes, as well as the human genome project, would not have been possible. Hence, the systems of molecular biology would not exist. The lack of holistic and integrative awareness of biological processes was cited as a disadvantage of the reductionist molecular approach.

Limitations of the Reductionist Approach

The reductionist approach has been successful in detailing the chemical basis of several living processes. Despite the several ground breaking accomplishments attached to reductionism, reactions against this approach began in the early part of the 20th century [9]. This is due to the fact that biological systems are complex and have emergent features. As a result, understanding the functioning of biological systems and forecasting their behaviour is difficult unless the interactions between system components are recognised. This intricacy is ignored by the reductionist approach. As a result, it has a negative impact on several fields of scientific research, including drug discovery and vaccine development [10].

CHAPTER 4

A Systems Biology Approach in Fisheries Science

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Abstract: Systems biology is concerned with complex interactions in biological systems, employing a holistic manner in addition to classical reductionism. Systems biology uses statistics, computational biology, and mathematical modelling to integrate and analyse vast data sets to obtain a better knowledge of biology and predict the behaviour of biological systems. It has gained attention in fisheries because of its ability to uncover novel processes. It can generate a panorama of events that occur within fish. In a systems biology approach, data from fish genomics, transcriptomics, proteomics, and metabolomics are integrated, allowing for a comprehensive understanding of dynamic systems with varying degrees of biological organisation. Protein-protein interactions help us understand the systematic mechanisms underlying overall growth, development, physiology, and disease in fish. Systems biology and omics techniques are being applied in a variety of fisheries studies such as species identification, understanding the processes of infection and stress tolerance, fish-pathogen interactions, fish disease diagnostics and disease control, the impact of environmental factors on fish, and determining the fish's response to these, identification of gene sequences and biomarkers. Except for a few pioneering applications of system biology to Fisheries, this approach to fisheries research is still in its infancy stage. Systems biology has the potential to provide solutions to the diverse issues of fisheries.

Keywords: Aquaculture, Biomarkers, Fish health, Genomics, Holistic approach, Metabolomics, MetaFishNet, Microarray, Modal organism, Protein-protein interaction, Proteomics, Sex determination, Toxicology, Transcriptomics.

INTRODUCTION

For many years, there has been a conflict between the two philosophies of reductionism and holism. The reductionist perspective understands the nature of

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complex things by reducing them to a simple level, whereas the holistic approach, analyses all components and interactions within and between organisms. It is probably time to integrate these two ideas into a more open and flexible strategy. This is what systems biology is all about. The term "Systems biology" has many definitions and encompasses a wide range of concepts and areas. Systems biology is defined as a data integration method that takes into account information from all relevant domains, such as biology, pharmacology, engineering, chemistry, computation, mathematics, and physics [1]. Instead of investigating individual system components, systems biology focuses on understanding or analyzing system dynamics as a whole. It can also be defined as an interdisciplinary and integrated approach to understand biological aspects, such as genes, proteins, and cellular and biochemical components, using mathematical and computational systems [2]. Omics technologies are being utilised to examine the entire genome, transcriptome, proteome and metabolome to achieve this goal as depicted in Fig. (**1**). While the scientific community has embraced the complexities and discoveries of system biology, their translational utility has been hampered by a perceived disconnect with fisheries science.

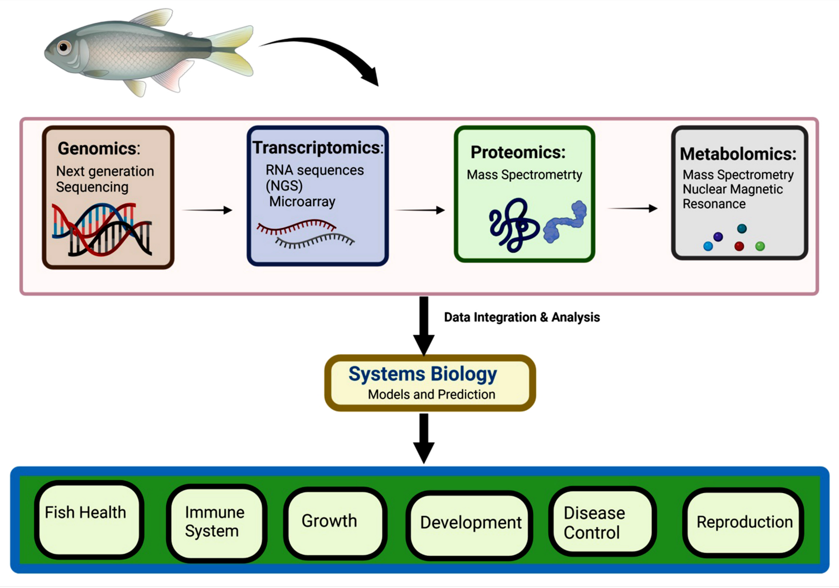

Fig. (1). An overview of Integrated Omics approaches to understand the Systems biology in fish.

Some Fish Species as a Model Organism for Systems Biology

Fish are among the earliest and most diverse vertebrate classes that have been used in scientific research. Fish species like *Danio rerio* (Zebrafish), *Oryzias melastigma* (Medaka), *Gasterosteus aculeatus (*Stickleback), *Platichthys flesus*

*(*European flounder), *Ictalurus punctatus (*Channel catfish), *Cyprinodon variegates (*Sheepshead minnow), *Fundulus heteroclitus (*Mummichog), Atlantic cod *(Gadus morhua)*, *Salmo salar (*Atlantic salmon), *Cyprinus carpio (*Common carp), *Oncorhynchus mykiss (*Rainbow trout), *Tetraodon nigroviridis (*Pufferfish), *Paralichthys olivaceus* (Japanese flounder), Fugu (*Takifugu rubripes*) and *Xiphophorus hellerii (*Swordtail) are widely used as a model organism for research purposes in various ecological, reproductive biology, evolutionary biology, developmental biology, toxicological, genetical and human disease research [3]. Each of these fish species fulfills a distinct role as a research tool. For example, *Danio rerio* have been considered to be especially useful in developmental biology, genetics and human disease modeling [4, 5]. Zebrafish can also be used as a model for Systemic inflammation [6]. Swordtail (*Xiphophorus* spp.) are among the oldest animal models used in cancer research to study melanoma [7]. Medaka *(Oryzias melastigma*) is a suitable organism model in aquatic ecotoxicology and toxicogenomics [8]. *Paralichthys olivaceus* (Japanese flounder) was also employed as a model species for immunological investigations [9].

OMICS IN FISHERIES SCIENCE

Fish Genomics

Fish genomics has rapidly evolved and now provides a roadmap for spectacular findings. Whole genome sequences (WGS) are available for Zebrafish, Atlantic cod, Atlantic salmon, Medaka, Rainbow trout, Common carp, Fugu, Pufferfish, and Three-spined stickleback [10 - 12]. Zhang *et al.* (2020) assembled the genome of *Ancherythroculter nigrocauda* [13]. Li *et al.* (2010) constructed MetaFishNet, a genome-wide fish metabolic network model based on fish gene sequences. This model was used to analyse high throughput gene expression data and this model also provides a glance at the resemblance between fish and human metabolism. Metafishnet was found to be a climax to the broader application of fish system biology [3]. Medaka and Zebrafish are well-known genetic model organisms in which large-scale mutagenesis has been accomplished. The Targeting Induced Local Lesions in Genome (TILLING) platform provides a viable research tool for analyzing medaka and zebrafish functional genomics. Pufferfish and Medaka are in a phylogenetic position that allows them to locate orthologous genes in the genomic sequence [14].

The increased rate of sequencing of fish genomes over the last decade has improved comparative and evolutionary genomics, illuminating vertebrate genome evolution in unique ways. Over the last three years, advances in NGS technology have significantly boosted the availability of fish genomes in publicly

CHAPTER 5

System Biology and Livestock Gut Microbiome

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Abstract: With the recent advances in high throughput next-generation sequencing technologies and bioinformatics approach, gut microbiome research, especially in livestock species, has expanded immensely, elucidating the greatest potential to investigate the unacknowledged understanding of rumen microbiota in host physiology at the molecular level. The association of a complex aggregated community of microbes to host metabolism is of great importance due to their crucial participation in metabolic, immunological, and physiological tasks. The knowledge of this sophisticated network of a symbiotic association of gut microbiota to host organisms may lead to novel insights for improving health, enhancing production, and reducing the risk of disease progression in livestock species necessary to meet the demands of the human race. The full picture of microorganisms present in a particular area can be achieved with the help of culture-independent omics-based approaches. The integration of metagenomics, metatranscriptomics, metaproteomics, and meta-metabolomics technologies with systems biology emphasizes the taxonomic composition, identification, functional characterization, gene abundance, metabolic profiling, and phylogenetic information of microbial population along with the underlying mechanism for pathological processes and their involvement as probiotic. The rumen secretions or partially digested feed particles, as well as fecal samples, are generally employed for gut microbiome investigation. The 16S rRNA gene sequencing amplicon-based technology is the most employed technique for microbiome profiling in livestock species to date. The use of software and biological databases in the field of gut microbiome research gives an accurate in-depth analysis of the microbial population greatly.

Keywords: 16S rRNA gene sequencing, Archaea, Bacteria, Biomarker, BLAST, Databases, Fungi, Gut microbiome, Goat, KEGG, Livestock, Metagenomics, Meta-metabolomics, Metaproteomics, Metatranscriptomics, Next-generation sequencing, Ruminants, Sheep, Shotgun sequencing, Swine.

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INTRODUCTION

The aggregated complex communities of microbes colonizing the gastrointestinal tract, also known as the gut microbiome, are of great importance to the host animal due to their remarkable contribution as commensal, pathogen, or mutualistic organisms to host physiology. Thousands of bacteria, archaea, protozoa, and other eukaryotic microbes populated in the digestive tract of livestock species play a crucial role in maintaining the homeostasis of the host animal by participating in the conversion of feed particles into essential nutrients necessary for growth and survival [1, 2]. They also influence energy as well as fat metabolism and are even associated with obesity and diabetes in humans and animals. Due to the ability of a gut microbial population to ferment plant polysaccharides to short-chain fatty acid (SCFA) molecules, their participation in greenhouse production, and their ubiquitous role in biofuel production, they are collectively regarded as a separate biological system within the biological system and termed as ‘super organisms’ [3]. On the other hand, about 125 million tons of greenhouse gas, methane is released into the atmosphere by ruminants alone as a result of enteric fermentation. The term ‘gut microbiota’ was initially introduced by Joshua Lederberg, who defined it as ‘the ecological community of commensal, symbiotic, and pathogenic microorganisms that literally share our body space and have been all but ignored as determinants of health and disease’ [3, 4, 5]. A healthy gut contains a healthy gut microbial pool, protects the intestine from potentially harmful exogenous and indigenous microorganisms, and maintains immune homeostasis [1, 6, 7]. The gut microbiota, primarily responsible for the conversion of plant materials to energy in livestock, start colonizing after 24 hours of birth in ruminants, continue to grow and colonize, influenced by nutrition and diet type, which in turn impact the development, physiological changes, and mass yield of animals [5]. The presence of symbiotic association of diversity of microbial life forms in the digestive tract of higher vertebrates and livestock species requires an emphasis on the molecular level to analyze their mechanism of interaction both in the defensive pathway as well as in disease progression. The knowledge is also required for increasing the productivity of farmed animals as well as for reducing agricultural carbon emission along with biofuel formation from lignocelluloses degradation [8].

Omics-approaches and bioinformatics tools are extensively used in the field of microbial research in farmed animals to investigate the complex diversity and functional characterization of microbial gut inhabitants of livestock. With the increasing advances of omics science and high throughput next-generation sequencing (NGS) technologies coupling with systems biology, gut microbiome research has received new perspective and additional interest in the last 15 years to address the unrevealed role of gut microbiota that may lead to novel strategies for increasing productivity in farmed animals [9]. Metagenomics, Metatranscriptomics, Metaproteomics, and meta-metabolomics-based technologies provide insights into molecular changes, in response to the change in internal and external environment necessary to improve health and nutrition and susceptibility to the disease without isolation and cultivation of microbes [4, 5]. The study of interrelationship and characterization of the interaction within and between microbial communities is essential to investigate the contribution of gut flora to growth and development concerning susceptibility to disease progression or their input in the production of healthy phenotypes. Microbial community profiling methods such as the 16S ribosomal RNA gene-based technique is an important tool to analyze the microbial communities present in the gut, reveal molecular interactions and determine the evolutionary relationships among the species. Several other techniques have been used to reveal the taxonomic profile, microbial abundance, taxonomic and functional composition, gene abundance, expression of genes, protein profile, metabolite profile, and expression of proteins of gut microbiota, including amplicon-based sequencing, metagenome, metatranscriptome, metaproteome, and meta-metabolome approaches by using 16S rRNA gene, genomic DNA, RNA, Protein, and metabolites respectively [7, 10 - 14].

DIVERSITY OF MICROBIOMES IN LIVESTOCK/FARM ANIMALS

The increasing interest of researchers in the gut microbiome is due to their significant role in the gut maturation and growth of farmed animals. The colonization of gut microbiota is essential in newborns to start the processes of metabolism efficiently, also responsible for animal resilience against the pathogen in later life. Modulating the gut microbiome with specific dietary components shows significant results to increase productivity and reduce the risk of diseases in farmed animals [3]. Therefore, understanding the mechanism of the interplay of microbiome interactions with the host or within the microbial community is crucial for the treatment of certain diseases, improvement of health, enhancing the production of livestock organisms which are often poorly understood. The structure and activity of the gut microbiome differ based on breed, diet, age, health, and environment of the animal, also known as microbial succession [1, 2, 11].

Microbiota of Ruminants

Ruminants were the first domesticated animals, including cattle, sheep, and goats, presently with over 3.5 billion population worldwide, in demand as a good source of high-quality meat and milk products to meet the needs of the increasing human population. The microbiota of ruminants play an essential role in the fermentation

CHAPTER 6

Omics in Livestock Animals: Improving Health, Well-being and Production

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Abstract: India has an extensive livestock wealth with a growing rate of 6% per annum with a crucial role in the Indian economy. The livestock sector is one of the important subsectors of agriculture, which contributes 25.6% of total agriculture GDP. The arrival of deep sequencing technologies such as Next Generation Sequencing (NGS) and Single Cell Sequencing (SCS) has produced huge sequence data that can be exploited to advance well being, health, reproduction and yield of livestocks by employment of integrated *omics* strategies. The current era of *omics*, *i.e.*, genomics, transcriptomics, proteomics, metabolomics, translatomics and single-cell sequencing, has considerably improved researcher's understanding of livestock research at the gene level and opened new avenues in terms of single-cell studies, which need to be carried out in the near future. NGS plays a crucial role in understanding the genetic mechanism of animal's functions and its interaction with the environment. Furthermore, the SCS will provide insight into the functions of cell types in livestock species. The data generated using NGS and SCS approaches may help to discover novel molecular markers from the complete genome and develop global diagnostic methods for the detection of infectious diseases and their agents.

Keywords: Animal health, Livestock, NGS, *Omics*, Systems biology.

INTRODUCTION

In India, Uttar Pradesh has the highest population of livestock, followed by Rajasthan, Madhya Pradesh, West Bengal and Bihar [20th Livestock Census, 2019]. Livestock is an important component of livelihood for at least 50% of

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India,s poor rural population and contributes to the national economy. Farm and agricultural animals have an important role in providing food and fiber to humans, and different byproducts of animals are used in cosmetic and pharmaceutical industries. Indigenous cattle, buffalo and crossbred are the chief animals which provide different types of livelihood support [1, 2].

Progress in cellular biology paved the way for the creation of "*omics*" technologies. Each "*omics*" technique (genomics, transcriptomics, proteomics and metabolomics) aims to measure the most important elements at work in cells [3]. The emergence of *omics* technologies has greatly improved our understanding of livestock and animal science research (Fig. **1**). Integration of genomics with other "*omics*" research disciplines and computational tools may help researchers better understand the molecular underpinnings underlying animal morphological characteristics or phenotypes. Genomics facilitates the discovery of genes linked to a particular attribute. Furthermore, combining these technologies allows for a comprehensive analysis of an animal's, tissue's, or cell's metabolism [4].

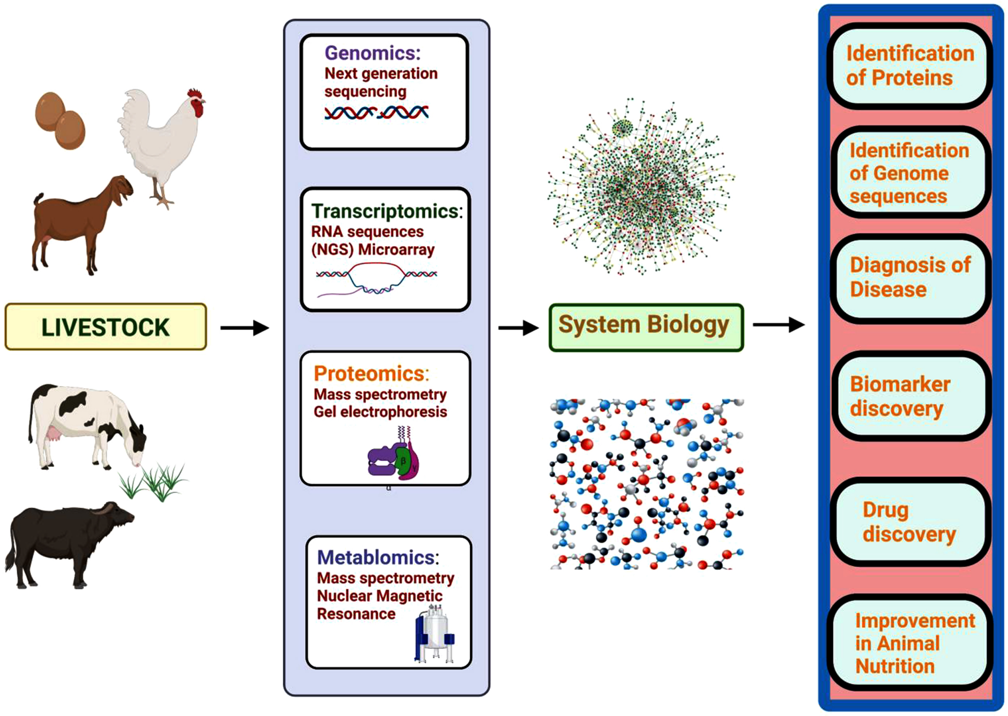

Fig. (1). The description of *omics* approaches in livestock research. The systems biology with *omics* approaches has applications in disease diagnosis, drug discovery, and improving animal nutrition and breeding.

There has been a tremendous development in the application of *omics* in livestock in India. The genomic regions which are responsible for multiple functions were identified with genome wide association mapping studies [5]. The RNA sequencing of mammary epithelial cells of Kashmiri and Jerser cattle breeds unveiled probable single nucleotide polymorphism (SNP) responsible for variations in milk quality production [6]. *Omics* technologies give molecular insight into resilience mechanisms and product quality.

System biology refers to the study of composite biological systems interactions and the properties which emerge from these interactions. It is considered a holistic approach which studies the whole biological system as a unit [7]. Systems Biology establishes a balanced approach for understanding different mechanisms involved in health, nutrition, production (milk, meat and wool) and disease. The systems biology observes infection by quantitative and qualitative analysis of the relationships between different components of biological systems [8]. The deep sequencing or massive parallel sequencing approaches in combination with advanced computational tools, transformed the perception of researchers to generate and analyze the transcriptomic and genomic data. These NGS technologies are gradually employed in the field of host-pathogen interactions, evolution and animal infectious diseases, which directly have an impact on livestock health [9].

OMICS TECHNOLOGIES AND ANIMAL GENOME

The first genome sequencing took about 15 years and more than 3 billion dollars. Presently, it takes a maximum of one day for 500 to 1000 dollars to sequence a complete genome. The advancement in genomics has induced various innovative research concepts in animal and livestock sciences. *Omics* is an advanced field which is still in the development mode and has made expeditious growth with immense biotechnological applications. *Omics* is the multidisciplinary approach by which one can study and analyze the complete central dogma of an organism. It is one of the efficacious methods to select animal breeds for the production of milk, meat and wool [10].

NGS is one of the hottest topics in the field of biology and genomics research. With the advancement of the new *omics* era, deep sequencing technologies have shifted the focus to process and evaluate huge "*omics*" data, *i.e.*, genomic, epigenomics, metagenomics, transcriptomic, proteomic, translatomic and single cell genomic/transcriptomic data [11]. The multi *omics* approaches are helpful in the identification of genomic sequences, RNA expression, lncRNA, microRNA and the discovery of metabolite and protein markers in animal research (Fig. **2**). In recent years, genomes for various agricultural animals (cow, sheep, chicken,

CHAPTER 7

Livestock Viral Diseases and Insights into Systems Biology

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Abstract: With the increasing human population, livestock farming has been intensified over the years to support different products from farm animals. Hence, the requirement to monitor livestock diseases becomes critical. In particular, outbreaks due to viral diseases are a major concern for the livestock industry worldwide. It has been observed that close interaction of humans-livestock could lead to transboundary diseases. Hence detection of potential viral pathogens requires a deeper understanding of the livestock virome. The rapid development of bioinformatics and computational tools, as well as advances in Next-Generation Sequencing (NGS) technologies, has opened up new options for infectious disease surveillance in terms of both quality and scale. The phrase "systems biology" has just been recently adopted to define cutting-edge cross-disciplinary biology research. Synthetic biology, integrative biology, systems biomedicine, and metagenomics are some of the growing post-genomic domains that intersect with systems biology. Systems biology represents a paradigm shift in biology and medicine from many perspectives by incorporating a new culture that acknowledges the dynamic and interdependent interactions of the complex network of genes and their associated proteins in order to gain a systematic understanding of biology, health, and disease. By enhancing our understanding of viral disease development, diagnosis, prevention, and therapy, the application of systems biology to human and veterinary medicine has the potential to transform healthcare. The current chapter focuses on examples of various viral diseases associated with livestock animals and the role of systems biology approaches to understand them.

Keywords: Animal viruses, African swine fever, Avian influenza, Bovine respiratory disease, Bovine herpesvirus-1, Co-expression, Global virome project, Livestock diseases, NGS, Newcastle disease virus, RNA-seq, Systems biology.

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INTRODUCTION

Viruses are sub-microscopic, infectious agents that can enter and replicate within a living cell of a susceptible host. They can infect virtually all living organisms, namely animals, plants, fungi, bacteria and archaea [1, 2]. The typical structure of a virion consists of a protein coat or capsid which shields the information molecule (Ribonucleic acid or deoxyribonucleic acid). Viral genome encodes all information required for its replication and together with the hijacked host cell machinery, it ensures rapid multiplication. Based on pathogenicity, structural organization, genomic content and size, viruses are quite diverse in nature [3]. Viruses are omnipresent, since an average human being encounters billions of virus particles on a daily basis. Our intestinal, respiratory, and urinary tracts also serve as reservoirs for several viruses, however, does not show any negative impact on our growth and development, despite such intimate association [4]. Every animal virus has a specific host range, but sometimes due to several factors, they can spill over to humans and cause debilitating or fatal diseases. A recent outbreak of swine influenza is an excellent example which involved pigs [5]. Epidemic causing viruses like Influenza and severe acute respiratory syndrome (SARS) are highly infectious in nature and can rapidly spread in a given population within a very short time. Epidemic viruses are gaining more attention in terms of research and public concern because of their high spreading capacity as compared to endemic viruses in a given population. Viruses are obligate parasites, meaning they are completely dependent on the host for replication and survival. This property of a virus serves as an important tool to study cellular functions and biology [6]. Adenovirus is an example of a DNA virus that invades the host's nucleus but remains isolated from the host's genome while using the host cell's machinery to replicate it [7]. Influenza is an RNA virus that carries its own enzymatic system to replicate its genome while its proteins are synthesized through host cell mechanisms [8]. RNA viruses provide high zoonotic hazards because they can develop and spread quickly. According to a statistical analysis of 146 livestock viruses [9], a virus's ability to replicate in the cytoplasm is the biggest predictor of cross-species transmission and human infection.

The livestock disease load is expected to increase as a result of climate change, antibiotic resistance, agricultural changes, and population shifts. The proliferation of viral infections poses a significant threat to the sustainable operation of high-yield animal production over the long term. The management of viral infections is essential for the maintenance of healthy agricultural systems, the promotion of national and international food security, and the alleviation of poverty in less developed countries [10]. This chapter will cover a variety of significant livestock viruses, as well as provide examples of systems biology approaches that can be used to tackle the viruses that affect livestock.

VIRUSES AFFECTING LIVESTOCK

With introductions from wildlife and livestock reservoirs, animal-borne epidemics of severe acute respiratory syndrome (SARS), Nipah sickness, avian influenza, Rift Valley fever, and swine influenza have occurred in recent decades. Infectious disease transmission can be facilitated by livestock animals living in close proximity to humans *via* the wildlife-livestock-human interface [11]. A few of the important animal viruses are discussed below.

Avian Influenza Virus (AIV)

Avian Influenza Virus (AIV) belongs to the genera within the *Orthomyxoviridae* family and is known to have several subtypes based on differences in a combination of the two surface antigens hemagglutinin (HA) and neuraminidase (NA) [12]. The primary reservoir is aquatic birds which include ducks, geese, swans and others; however, AIV is also known to infect poultry animals like chickens [13, 14]. Strains that usually cause more than 75% mortality (H5 and H7 subtypes) within 10 days in a defined population of chickens are referred to as Highly Pathogenic Avian Influenza Virus (HPAIV) [15]. Over the years, outbreaks have been reported in several countries worldwide [15, 16]. Importantly, a systematic study by Chatziprodromidou *et al.* showed that between 2010-2016, a majority of the outbreaks were reported in countries like China (13.6%), Vietnam (8.2%), Egypt (4.9%), Germany (4.5%), India (4.2%) and the United States (3.5%) [15]. The dominant subtype identified was H5N1 (38.2%) whereas 82.5% were HPAIVs. The source of these outbreaks was often found to be commercial poultry farms [15]. Europe is currently experiencing the worst HPAIV driven epidemic in its history. Since 2020, a total of 3555 HPAI detections and ~22,400,000 poultry birds have been affected, spanning 28 countries [16]. Symptoms of AIV infection are dependent upon several factors like species infected, age, sex, and virus strain/subtype and can vary widely. Typically, it is characterized by disorders of the gastrointestinal tract, nervous system and/or the reproductive system. Infection can also be asymptomatic followed by sudden death [17]. Structurally, AIV is an enveloped virus which can be either spherical (80-120 nm) or filamentous (~300 nm) [18]. The genome contains 8 negative sense segmented single stranded RNAs, which encode a total of 10 viral proteins (PB2, PB1, PA, HA, NP, NA, M1, M2, NS1, NEP/NS2) [18]. The virus enters a susceptible host cell *via* endocytosis [18]. Although humans are susceptible to AIV infection and inter-species crossover does happen occasionally, resulting in high mortality [12], and human-human transmissions are not yet reported.

CHAPTER 8

Proteomics in Livestock Health and Diseases

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Abstract: Proteomics is a branch of science that allows us to study a whole expressed protein pool from a cell or tissue. This has been helpful for many years in studying microbial makeup, but in animals, this field has not been explored much due to factors like the complexity and variation in genes of every cell depending upon their specialized function and tissue organization. However, in recent years many new techniques have been introduced in this area, which has added to the plethora of knowledge about animal proteins and has made it easy to understand the diseases and health-related aspects of livestock science. In this chapter, we will discuss the new advancements in animal proteomics to discover the protein pool from the different animal species of interest, branches of proteomics, and their role in livestock health and diseases.

Keywords: Animal diseases, Bioinformatics, Biomarkers, Disease diagnosis, Expression profile, Gel electrophoresis, Livestock, Mass spectroscopy, Proteomics, Proteome, Post-translational modifications, Quantification, Samples.

INTRODUCTION

Proteomics is a term coined to describe the study of the structural and functional aspects of proteins on a large scale. The term proteome was coined by Marc Wilkins in 1994 and is a blend of two words, “protein+genome”. It has allowed us to explore a large pool of data by analyzing thousands of expressed proteins. The technique includes the identification and characterization of a whole set of expressed proteins within a cell, including their structure, function, and post-translational modification [1]. In the last few decades, proteomics has evolved strongly due to technological and bioinformatic advancements. In the case of

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animals, the proteomic technique is more complex than the genomics as they have a complex system with a large number of cells which may vary in their protein expression from cell to cell due to specialized functioning, environmental factors, and various post-translational modifications (PTMs) resulting in a dynamic proteome [2]. Proteomics includes various sub-branches like quantitative proteomics, computational analysis, analysis of posttranslational modifications, and clinical proteomics (Fig. **1**).

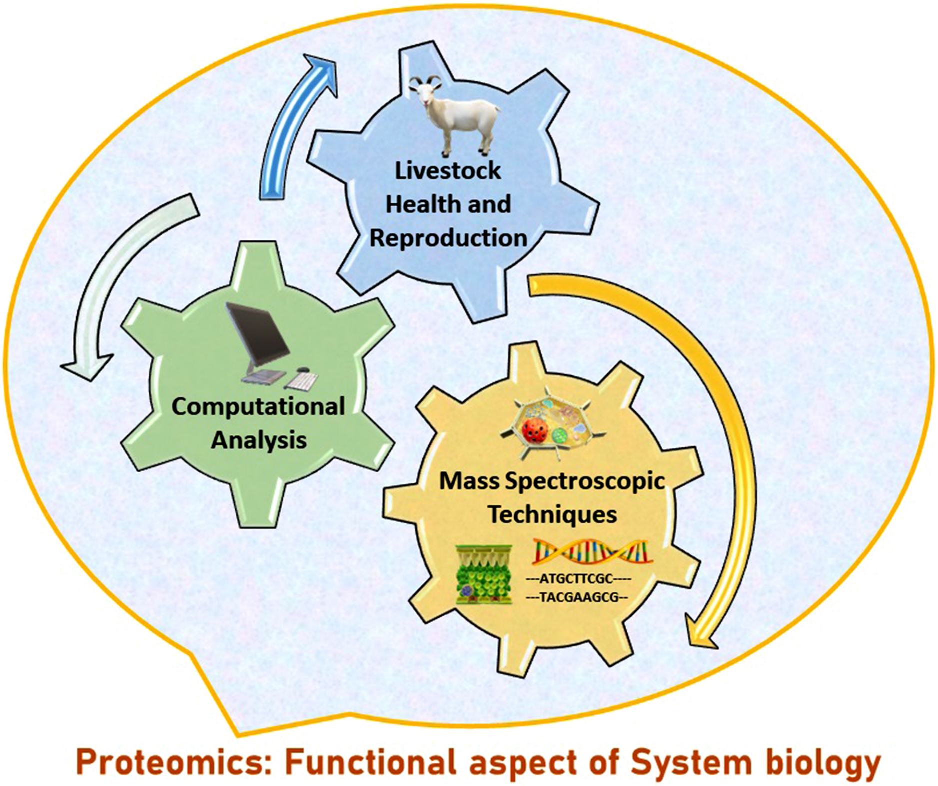

Fig. (1). The high-throughput MS-techniques and advancements in computational data analysis lead to the betterment of livestock health and reproduction.

The serum protein analysis is an essential part of livestock disease diagnosis, but it is only limited to methods like quantification of protein, globulin, and albumin, determining the ratio of globulin: albumin, and serum protein electrophoresis (SPE) [3]. The SPE method is used to separate serum into, multiple protein bands, which are further used to identify and characterize disease-related biomarkers. This makes proteomics to be a way to advance livestock pathology and diagnostics [4].

BRANCHES OF PROTEOMICS

Quantitative Proteomics

To understand the role of proteins in the physiology of organisms, it is necessary to quantify them in addition to their identification. Quantitative proteomics is a branch of proteomics that examine the relative abundance of different protein in healthy and diseased samples. This helps to avail the information about signaling pathways, interactions among the molecules, and biomarker identification. In addition to relative quantification, the absolute quantification of proteins [AQUA] is also carried out to determine the protein expression level and determination of PTMs within the cell [5]. The traditional protein quantification strategies are using gel-based approaches. However, the advancement of scientific methods has introduced the techniques like mass spectroscopy techniques for protein identification. These methods involve labeling using stable isotope and label-free [spectral count or peptide count] methods. In animal science, the quantitative proteomics approach has been used to quantify the protein pool of fluid from the female reproductive organs. It has helped to understand the reproductive processes and the identification of candidate proteins for artificial reproductive technologies in farm animals [6].

Clinical Proteomics

Proteomics enables us to identify a large number of proteins with high sensitivity and specificity and is therefore used for understanding and diagnosing important human diseases, in livestock sciences, the use of mass-spectroscopy is at its initial phase and has been applied to cattle (Bovine Genome Sequencing Analysis Consortium), horses, dogs, pigs, chickens, and sheep due to the availability of their whole genome sequence. Mass spectrometry techniques are used to measure proteins that are crucial to the regulation of physiology and metabolism. In addition to this, they are also being used for the detection and monitoring of subclinical infections and vaccine response. Biological samples like urine, saliva, cerebrospinal fluid (CSF), seminal fluid, tissue biopsies, meat products, milk, eggs, and serum or plasma [7].

Comparative Proteomics

Comparative proteomics aims to analyze the changes at the proteome level caused by diseases, development, and environmental conditions. The main goal of comparative proteomics is to identify the reason behind cellular changes by analyzing the changes in proteins. This involves two steps first is the fractionation of cellular extracts to reduce the sample complexity and in identification of proteins by mass spectrometry. The main challenge in comparative proteomics is

CHAPTER 9

Importance and Potential Applications of Nanobiotechnology and Systems Biology for Livestock Science

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Abstract: Nano-materials were utilized as therapeutics and diagnostics agents in the context of human medicine. However, the application of nanoparticles in the field of livestock animals is still at a nascent stage. The proper utilization of nanoparticles in livestock sciences, such as improvement in milk production, diagnosis of varied diseases, delivery of nutrients and/or in their reproduction, offers prospective outcomes which have direct implications to meet the ever-growing human populations. Further, with the advent of high throughput omics technologies, noteworthy development in the past decades has paved the way to advanced systems biology area. The high throughput data handling from diverse omics methodologies and making a holistic interpretation posed a challenge, moreover, to connect the dots and present a larger picture of the intricate network level data, systems biology comes to the rescue. The design and advancement in different algorithms of systems biology tools seldom help one to integrate multi-layered data. Systems biology is applied to livestock animals and poultry for their overall development and/or risk assessment for their diseases. In this chapter, we discussed the implementation of nanobiotechnology and systems biology approaches to livestock animals. We illustrated a few examples of how the application of nanotech and systems biology improved some desired qualities in livestock. This chapter summarizes the ongoing research and efforts of different groups, along with the future prospects of innovative technologies in the area of nanotech and systems biology.

Keywords: Diagnostics agents, Diseases, Human medicine, Intricate network, Livestock animals, Livestock poultry, Meat science, Milk production, Multi-omics, Nanobiotechnology, Nanomaterials, Nanoparticles, Nano vaccine, Network biology, Nutrients, Omics methodologies, Omics technologies, Reproduction, Systems biology, Therapeutics agent.

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INTRODUCTION

To produce supplies such as food (meat, milk, egg), labor, and fiber, for ever-growing human population, some animals are raised in an agricultural background. Such domesticated animals are known as livestock. The word "livestock" sometimes represents exclusively those animals that are raised for food and sometimes states only cattle and goats, which are farm ruminants. Livestock farms cover 30% of the planet's land area, except the ice zone, and contain critical global assets worth at least $1.4 trillion [1]. Animal production has become faster, cheaper, healthier, and more effective, with less environmental impact, as a result of genetic advancements. For example, between the 1970s and 2007, selective breeding resulted in the following improvements: the number of days it took chickens to gain 2 kilograms of mass decreased from 100 to 40, the proportion of breast meat rose from 12 to 20% [2], the ratio of feed conversion reduced by half, the number of eggs produced each year increased by 30%, the number of eggs produced per ton of feed rose by 80%; and, ultimately, the output of milk from cattle increased by 67 percent. This massive growth in the production of food reflects unbelievable progress in decades, even if the benefits spread predominately among developing nations [3]. In the last few decades, scientists from biological research have focused on recognizing the networks interacting in biological or physiological processes, identifying components involved in those networks using methods like high-throughput experimental technologies, computational models *etc*. and trying to connect molecules in different (*e.g.,* cells) and single biological scales to physiological purposes, organismic phenotype *etc*.

A fascinating and advanced area of life science is systems biology which entails the computational and mathematical analysis as well as the modeling of integrated data from the gene, protein, and pathway response monitoring that result in the formulation of a biological system's structure as well as its perturbation response. It is distinct from branches of bioinformatics, genomics, traditional molecular biology, or evolutionary genetics, and correspondingly older branches like medicine. Using a holistic approach to biological science, this biology-based interdisciplinary field focuses on the study of complex interactions between components of biological systems that describe how these interactions bring about the function and behavior of the system. For example, the interactions in metabolic pathways between various enzymes or metabolites, different interactions occur in cellular processes or cell signaling networks, and so on. Also, paying attention to a large area of genetics, applying principles in various system complexities and organizations from molecular to ecological level [4]. It is a discipline based on which we can design a blueprint of complex disease evolution or phenotype function to understand a biological organization by data/hypothesis-driven tactics.

Besides this, another quite prospective and prolific area of research is nanoscience which comes as a boon to solve unmatched challenges in diverse domains of science. In this chapter, we have deliberated upon a few prospective and noteworthy areas of livestock animals and summarized how applications of different nanoparticles/nanomaterials, along with the knowledge of systems biology, aided the scientific community to tackle the challenges in this area.

Nanotechnology in Livestock Animals

Nanoparticles (NP) are materials, structures, and systems of well-ordered size and shapes in the range of nanometers (nm), and they entail diverse physical and chemical, optical, and electronic properties compared to their bulk counterparts [5]. The term "nano" has arisen from Latin, which refers to the dwarf. Due to their tunability in size and shapes at the nm scale, they have shown promising applications in food, medical, materials and imaging areas. Depending upon the characteristics, the NPs are broadly classified as organic and inorganic. In recent times, almost every field of science and technology has been touched by NPs usage due to its beneficial role. It has been observed that the fields of livestock animals and poultry have also applied ample types of NPs to achieve different objectives. For example, organic NPs increase nutrient value by boosting feed functionality. Yet another organic NP is the nanocapsule, which delivers nutrients or drugs to livestock animals. The chief role is to increase the organic NP's availability compared to only nutrients/vitamins, as nutrients encapsulated with organic NPs enable their passage through the digestive tract into the bloodstream. NPs are known to be assimilated in feeds as liposomes and micelles and also utilized as shelf-life extenders, biosensors, and antimicrobials [6]. On the other hand, inorganic NPs comprise noble metals, semiconductors, and oxides of different elements. Inorganic NPs are nano-scaled inorganic constituents that have been recommended to be incorporated into feed. Silver NP is one of the most widely utilized NP, mainly as an antimicrobial [7, 8]. Examples of inorganic ones are gold NPs which have seen applications in vaccine delivery, as antigens carriers, or as a DNA vaccine adjuvant [9, 10].

Though NPs have huge benefits in the livestock and poultry sector, nevertheless, their applicability and significance have not scaled up for practical field utilization. Other apprehensions related to the synthesis, availability, toxicity levels, health hazards, conveyance challenges and incongruity of regulatory structure confine the comprehensive recognition and acceptance of adopting nanotechnology in livestock sciences.

CHAPTER 10

Single Cell RNA-Sequencing and Its Application in Livestock Animals

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Abstract: Single cell RNA sequencing (ScRNAseq) is in its infancy. There are limited studies in which this technique has been implemented to solve the scientific problem. ScRNAseq involves well facilitated labs and high end computing facilities. The ScRNAseq studies were mainly carried out in the clinical and biomedical areas. These studies are carried out in cancer research, which involves the role of immune genes or immunotherapy for cancer treatment. The human cell atlas programme is going on and atlases for different human cells are being released as it is completed. However, in the case of livestock animals, it has just started. In India, there are few ScRNAseq studies that have focused on the different developmental stages of buffalo. The experimental and bioinformatics analysis ScRNAseq involves various steps. Among this, the alignment of reads to reference genome/transcriptome is important. There is a need to develop a standardized reference genome/transcriptome for each type of cell present in different domestic/commercial livestock. Once we have all the valuable information from ScRNAseq, then this data can be integrated with system biology approaches to understand the cellular processes at a larger scale. This integration of interdisciplinary sciences will enhance the production, quality and health of the livestock animals and may help for sustainable management of livestock.

Keywords: Livestock, Single cell sequencing, Single cell atlas, Spatial biology, System biology.

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INTRODUCTION

The twenty first century has achieved lots of milestones in the fields of medicine and information technology; however, it is still at the edge of understanding the human body and livestock is lagging behind it. From the invention of microscopes in the late 16th century to the establishment of the Human genome in the 21st century, medical science has seen many curves throughout its way to date [1]. Genotypes and phenotypes mapping is one of the long-awaiting challenges in biology and medicine, which can be tackled by strategic transcriptomics. Although almost identical genotypes are shared in all cells, the transcriptome of any specific cell exhibits the activity of a particular set of genes [2]. The initiative to develop a human cell atlas was taken five years back [3]. Human cell atlas has involved the efforts of 2,000 scientists from >1,000 institutes across 76 countries from the globe to date to understand the different types of cells and their states [4]. Recently a database for the gut microbiome of livestock has been developed, *i.e.,* ADDAGMA: A database for domestic animal gut microbiome atlas to explore the gut microbiota and animal traits being affected by it can also be searched [5]. There are some studies on the cell atlas of rats, however, till now, there are few studies on the cell atlas of livestock animals. The chick retina has been studied by Single-cell RNA sequencing (ScRNAseq), which has developed its cell atlas and provided the evolutionary and developmental details of the cells [6]. scRNA-seq has enabled to obtain the overview of millions of cells at the transcriptomic levels [7]. The cell atlases are being established based on the data of ScRNAseq that explores the heterogeneity and diversity of the cells of different organisms and differential expression of the genes in the same cells (at the developmental stage or evolutionary stage or at different stages of disease) [8 - 11].

Sc RNAseq allows to analyse of multiple cell populations within a tissue sample, making it more dynamic and transient than conventional RNA sequencing. It provides a platform to determine the variation in gene expression levels of individual cells. Identification of cellular interaction has been improved by this sequencing technology which has made a noticeable transformation in organ rejection treatment [7]. Recently, this technology has been used in combination with organoid technology for disease modelling and treatment [12]. Various steps involved in the ScRNAseq are as follows:

Sample Preservation

Sample preservation is of utmost importance since the integrity of the sample is required for desirable results in Sc-RNA analysis. Cryopreservation has been established as one of the best methods for ScRNA sequencing [8]. The integrity of

RNA molecules and expression profile of samples (cell lines and tissue samples) that are stored at -80˚C for a year were found to be unchanged as compared to fresh samples. Snap-freezing should be avoided as it does not keep the outer membrane of the cell intact. However, nuclei sequencing can be done in case of snap-freezing samples if no other option is available [13].

The condition of the cells in both fresh and frozen is crucial for down streaming steps such as cell capture and sequencing. Minimum or judicial use of pipetting and centrifugation should be followed to prevent damage to cells. The speed, time and temperature can vary according to cell type. Similarly, clumping and aggregates of cells can be avoided by the optimized use of buffers, *e.g.,* PBS containing bovine serum albumin for washing and resuspension [14].

Sample processing is a crucial step in ScRNAseq. Sample processing might cause stress in the cell leading to the activation of genes and their expression. Incomplete digestion could result in incomplete analysis due to cell clumping. Some sensitive cell types might get destroyed during sample preparation [15]. Therefore, different strategies of optimization are required for successful ScRNAsq.

Tissue Dissociation

The primary step of single cell ScRNA-Seq is the dissociation of the tissue. There are two main types of tissues, *viz.,* fresh tissue and frozen archival tissues. Laser capture micro-dissection and enzymatic digestion are used to disintegrate fresh tissues. Frozen samples are treated differently to reduce the damage to the cells before tissue dissociation. Gradual freezing at 1˚C per minute till -80˚C has been found to maintain the transcriptional profiles for ScRNA-Seq [9]. The hypothermic strategy has also been proven as an alternative method for preservation up to 4 days [10]. However, in such cases, tissue disintegration will result in the loss of spatial and anatomical information of cells. RNA probes provide a good option for the identification of cellular transcriptional organization.

It is necessary to avoid cell clumps, dead cells, non-cellular nucleic acids and reverse transcription inhibitors through standardization. Once the washing of cells is done, the isolation of single cells from the suspensions is needed. In suspensions such as blood, density centrifugation using Ficoll paque or Histopaque-1077 is used for the separation of cells [11]. In tissues, including fresh or frozen tissues, mechanical and enzymatic dissociation is implemented. Mechanical dissociation is achieved *via* chopping or mincing of tissues. Enzymatic dissociation includes the use of various enzymes like accutase, collagenase, liberase, papain, depending upon the specific tissue used for ScRNA

CHAPTER 11

AI-ML and System Biology for Drug Discovery in Livestock

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Abstract: Advanced research methods have enhanced the productivity and problem solving abilities of scientific development in the field of drug designing and discovery. Various diseases have been problematic for the survival of human civilisation and livestock. Available methods that can provide results for diseases include; computer aided drug designing, system biology, and machine learning. Due to the diversity of livestock and multiple disease types, robust methods are required for drug discovery. Artificial intelligence has paved the way for faster problem solving innovations and discoveries in multiple aspects, such as economics, engineering, and healthcare. Systems biology plays a pivotal role in the biological evaluation of living beings. System-level understanding of livestock animals is the need of the hour for effective drug discovery, which includes genomic, proteomic, enzymatic, and metabolic pathways involved in a biological system. Livestock deaths due to diseases are reported worldwide, which creates a demand for drug discovery solutions. Multiple diseases for various livestock have been investigated, and drug discovery has been a great relief for those specific diseases. In this context, we have communicated about the integration of all the above mentioned aspects (artificial intelligence, machine learning, systems biology, drug discovery) to come up with a better resolution for the livestock in terms of drug development.

Keywords: Drug discovery, Livestock, Machine learning, Systems biology.

INTRODUCTION

The bonafide foundational value of civilization lies with the development of technology. The twenty-first century have witnessed tremendous flaw in evolution with advanced science. Different arena of research methodologies have undergone fast and specific inventions that can be defined from the emerging branches of

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science. In the last five decades, information technology has been a most valued field which enables interdisciplinary research. Computational sciences merged with the mathematical evaluation of biophysical and biochemical properties, to solve a biological problem is a boom. The invention of bioinformatics paved a way for decoding the building blocks of life in terms of multi-omics studies. Machine learning integrated with systems biology has the power to revolutionize future research.

SYSTEM BIOLOGY

System biology is the study of complex biological systems, including cells, organs, organisms and biomolecules. Systems biology provides insight into the complex biological system of animals to estimate the system-level understanding of the pathophysiology and manifestation of diseases by predicting the changes [1]. Different types of data in systems biology used to build models for understanding the complexity of the biological system are sequence, structure, molecular pathway, gene expression, multi-omics, experimental data, and biological network [2]. Biological network construction and analysis is one of the applications in systems biology, which represents the target genes, proteins, metabolites, drugs, and diseases as nodes, whereas the interactions are represented in edges [3]. Several measures, namely degree, shortest path, clustering coefficient, network diameter, network radius, mean path length, betweenness centrality, eccentricity, closeness centrality, radiality *etc*. calculated for centrality analysis of biological networks [4, 5]. Application of biological networks includes the prediction of protein-protein interaction, function, protein-drug interaction, drug-drug interaction, comparison of biological networks and metabolic pathways to estimate the system-level depiction of biological types of machinery [1].

Systems Biology in Drug Discovery

Traditional approaches in drug discovery has several steps, such as target identification, target validation, lead selection by high-throughput screening, lead optimization, pre-clinical and clinical trials. Integration of system biology in traditional drug discovery has changed the existing methods and given a broad aspect to look into the drug discovery method. The systems biology approach in drug discovery begins with the target genes or drugs to identify a network of diseases for therapeutic development [6]. Systems biology is a powerful platform to unravel the molecular mechanism, biological and metabolic network and molecular interactions between the drugs and targets in the network [7]. Systems biology approach deals with a pool of data that can be cleaned, filtered and analysed through data analytics tools and machine learning algorithms to get the list of genes or proteins involved in the disease progression. Further analysis of the phytochemicals, FDA-approved drugs and new chemical entities can be performed based on their molecular descriptors. The system biology approach can construct the network of protein-protein interactions, gene-gene interactions, drug-target interactions and drug-drug interactions for functional enrichment analysis, disease diagnosis and metabolic pathway-based analysis to predict the potential drug candidate for the disease. The selected chemical compounds, based on their properties, can further undergo high-throughput screening. Molecular compounds with significant binding energy and molecular interactions with the targets can be considered for further analysis. The dynamic behaviour of the complexes can be further analysed by molecular dynamics studies. Another approach which can also give better insight into the drug discovery and development process is the quantitative structure-activity relationship (QSAR). QSAR model can be constructed based on the molecular descriptors of the chemical compounds using many tools and software, namely CODESSA, 3D-QSAR, BioPPSy, McQSAR *etc*. The systems biology approach was used in 2020 for the analysis of the relationship between type 2 diabetes and co-morbidities [8].

AI, ML IN DRUG DISCOVERY

Different AI and ML algorithms used for drug discovery and development process are as follows:

Linear Regression

Linear regression is a supervised machine learning algorithm used for classification problems.Based on the independent variable data points, it tries to apply relations that will predict the outcome of an event. The relation is a straight line which fits the different data points as close as possible. This analysis identifies the relationship between multiple factors for risk prediction [9]. Different R packages, namely stats, MASS, caret, *etc*. and SPSS software used for linear regression analysis. In 1984, a regression approach was applied to develop a model for the prediction of coronary artery diseases in 4226 medically treated patients [10]. Linear regression was used to trace the death count prediction of COVID-19 infection in the 5th and 6th week based on the data from 100 cases to the number of cases till 14th March 2020 [11]. In 2013 it was proved that multiple regression analysis is the best classifier for the prediction of heart disease [12].

Logistic Regression

Logistic regression is a supervised machine learning algorithm used for classification problems. It is the appropriate regression analysis to conduct when the dependent variable has a binary solution, and it is also a type of predictive regression system. It is used to evaluate the relationship between one dependent

CHAPTER 12

Genomics to Systems Biology in Livestock Management: its Applications and Future Perspective

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Abstract: The recurrent and comprehensive study of biological systems as a single entity in response to stimuli is known as systems biology. The introduction of high-throughput technology for studying an animal's DNA, proteome, and metabolome was a blow to reductionism in livestock science. It is based on ideas formalized in models derived from global functional genomics investigations of the genome, transcriptome, proteome, metabolome, and other complex biological systems. The mapping of entire sets of genes, transcripts, proteins, and metabolites from a variety of organisms has driven the creation of novel '-omic' technologies for gathering and analyzing vast amounts of data. This widely defined systems approach is being used to address a wide range of issues and organizational scales, along with several elements of livestock research. It is well established that the tools that relate genetic variations to their cellular activities, pathways, and other biological roles will become even more essential in the future. For each animal genomics research issue, a vision, current state of the art, research needed to progress the field, expected outputs, and partnerships are required. Modern computational tools capable of finding functional implications and biologically meaningful networks complement the ever-increasing ability to generate massive molecular, microbial, and metabolite data sets. The intricate inter-tissue responses to physiological status and nutrition can now be seen at the same time. The knowledge acquired from the application of functional analysis of systems biology data sets to livestock management in order to improve productivity, quality, and yield.

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Keywords: Genomics, Host-pathogen interactions, HoxD genes, Livestock, Systems biology.

INTRODUCTION

Systems Biology is the holistic and integrated study of the sequence, structural and functional properties of all biological organism components, including their identity, correlations, and dynamic interactivity [1]. Understanding of a few but distinct units of biological systems, the reductionist approach advocated by molecular biology has made significant progress in explaining disease mechanisms, including specific host–agent interactions, finding targets for therapy, and disease prevention [2]. Still, it is not much advantageous to create a comprehensive learning of the entire biological system. In the context of animal breeding, the biology of systems has been significantly linked to today's genetics of systems, suitably titled “systems genetics” or “systems genomics” [3]. Approaches based on 'systems genetics' examine complex features evaluated by omic technologies such as genome/exome arrays, gene expression arrays, mass spectrometry, and next-generation sequencing (NGS) [4]. Human and veterinary science has a great future to grow by practicing entirely new concepts. It will significantly improve knowledge about illness and its causation, improving disease diagnosis, prevention, and therapy [5]. Systems and Genomics Biology is a field that is still evolving, with sub-disciplines that are only beginning to be defined. The research of genomic sequences and their molecular products is the backbone of genomic science.

Complete genomic sequences of one or more species are the starting point for studies in functional and evolutionary genomics. Such techniques use high-throughput experimental and integrative computational tools to uncover gene functions and create genetic network design, as well as how these change during development, illness, and within/between organisms. Biology methods combine many forms of genome-scale data to create gene network prediction models that may be used to generate testable hypotheses regarding the emergent characteristics, functions, disease progression/transmission and dynamics of organismal systems. All of these methodologies have been used by faculty to identify the characteristics, function, and evolutionary aspects of biological networks in a range of experimental systems, including bacteria, invertebrates, vertebrates, mammals, and plants.

Systems biology is a current integrative research area that incorporates biology, mathematics, biophysics, and computational science to build models for system components' dynamic interactions. Such models make it easier to estimate how a biological system will respond to specific environmental stimulation. The field of animal sciences is already on the threshold of a genomics data explosion. The integration of previously acquired knowledge about the structure, variation, and expression of animal genomes with current data will be of great use. Systems biology techniques would be applied to this genetic data in order to improve our comprehension of the biology behind animal behaviours. As a result, it will be possible to identify,-modify and refine animal characteristics. Systems biology methodologies need research alliances among a variety of relevant scientific groups ready to share resources, tools, and expertise, as well as integrate their data sets. The era of predictive theoretical biology for farm animals is rapidly arriving, thanks to the advent of systems biology methods [6].

Integral Systems Biology

Numerous systems biology experiments have divided and expanded the understanding of the organism level. Computational modelling of molecular systems and extensive interpretation of the ever postgenomic datasets are frequently seen with relevant and more useful components of biological study in a wide range of fields [7]. This variation reflects the field's young and integrative orientation, with the parent disciplines' objectives and methodologies still not being included in the form of a unique and uniform field. Knowing the threat of uncertainty and ambiguity, diversification is accepted and encouraged [8].

Many funding organizations, for example, use purposely imprecise definitions of systems biology, since a wide acceptance of current concepts is essential to provide conceptional skills and to support systems biology as a huge research field. Systems biologists have frequently attempted to design detailed descriptions in response to this issue. These efforts extend sound bites like “current form of biology” or “alternative cell biology” to in-depth analyses of ancient origins and philosophical implications [9]. It is an attempt during this initial perspective in Systems Biology to provision a quick distinct solution to challenge “What is Systems Biology?” besides highlighting the significance of fabricated biology as the field's most elementary approach area. Systems biology is a branch of science that lays the scientific groundwork for successfully fabricated biology. It was observed thorough examination of the molecular diverseness for natural and synthetic living systems, as well as the discovery of universal laws and designs which exist in both live and manufactured networks, and the inclusion of existing knowledge about biology into a composit approach towards governing systems [10].

Computational and Systems Biology

Computational and systems biology is a discipline that brings ideas and methodologies from the various branches of science together. Recent biological

CHAPTER 13

Applications and Future Perspectives of Computational Approaches in Livestock Animals

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Abstract: Livestock is regarded as a critical point of access for enhanced food and nutrition. With the population explosion, an increase in the successful fulfillment of livestock production, including meat and dairy products, is necessary in the most ethical way. Fundamentally keeping the overall nutrition intact along with the health of both human and livestock animals is vital. Although there is an increment in production, it contributes to rising greenhouse gas (methane) emissions, thus damaging the environment. Inheriting novel technologies will not only help in the surplus upliftment of livestock products but also the emission of greenhouse gases. Omics and Systems Biology are such approaches. Omics is a combination of different aspects dealing with complete molecular levels ranging from DNA to protein, protein to metabolites, whereas Systems Biology is the analysis of both mathematical and computational along with biological system modeling. Omics gives a broad overview of both pathways and traits controlling various characters. Thus, showing detailed links between genotype-phenotype. It can yield an enormous amount of data with incredible speed. In addition, Systems Biology lines up to give an overview of the complete biological system rather than just examining a single biological molecule. It combines mathematical modelling, statistics, and bioinformatics for a better grip and understanding of the enormous data sets. In this chapter, we discuss the latest cutting-edge technologies in the field of livestock and how omics can be implemented in creating disease resistant livestock animals without hampering the quality of the products. The chapter also discusses the various applications and future scopes involving computational approaches towards animal science.

Keywords: Dairy, Deep learning, Livestock, Meat, Metabolomics, Omics, Systems biology, Vaccines.

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INTRODUCTION

In the biological field, computational biology is one of the interdisciplinary sciences that originated in the 1960s, primarily with a background in biophysics and protein biochemistry. During the past few decades, biology has experienced new uprisings, lining up from storing the ever-expanding data to in-depth exploration of complete biological systems. The leading-edge techniques - Arrays, Next generation sequencing (whole-genome sequencing), Mass spectrometry, *etc.* unlocked large sample analysis, leading to an understanding of complete human genome sequences. Obtaining such colossal data is gradually expanding in leading-edge technologies. This leads to the requirement of new methodologies and improved analytics, with expertise from various scientific backgrounds, starting from biology to mathematical analytics, consequently expanding the computational tools. Thus, allowing us to handle complex data, leading to the integration of every stream as one, thereby improving various methodologies, including modeling, analysis of network, and systems biology. With the advancement, it indicated the new uprising of disciplines, in short, can be branched under omics [1]. Here we will discuss the impact of systems biology on livestock production using omics approaches.

Mostly, in tropical and subtropical regions, the products of animals are in increasing demand, along with maintaining optimum production despite climate change and the increase in population. Lack of proper novel technologies will not only elevate the demand for animal products but may also lead to a potential increase in the release of greenhouse gases [2, 3]. In temperate regions, the production of dairy and beef products is already in critical condition due to heat stress (HS) and scarcity of water [4]. Thus, adaptation and identification of suitable traits for animal sustainability and quality production are of prime interest.

Commonly, omics techniques are primarily used in sustainable animal production, followed by Systems Biology approaches [5, 6], named Genomics, Transcriptomics, Proteomics and Metabolomics. These techniques help to analyze the metabolism of an animal that is sustained under certain environmental conditions. Further, the in-depth study would reveal the impact of certain conditions on physiology at the molecular level [7, 8]. In the past few years, various omics techniques have been extensively utilized in livestock research [9 - 13]. However, omics approaches in animal production mostly remained confined to the temperate region itself; very little attention was taken into consideration for the tropical and subtropical regions. Based on the molecular level, some areas like heat stress and weight loss in bovine still need to be explored, thus benefiting the regions where the production is quite low.

Both theoretical, as well as experimental approaches, have been adopted for various livestock researches. In this chapter, we have discussed the various theoretical approaches, including the Omics and Systems Biology approaches, which are further subdivided into different levels.

COMPUTATIONAL APPROACHES

Omics

The word "Omics", was derived from a Greek word and added to the suffix of molecules, meaning studying of those molecules. Omics alone refers to the series of biomolecular techniques, methodologies, and protocols dealing with molecular level studies ranging from cells to organisms. It can be classified into five levels – Genomics (analysis of genes), Transcriptomics (analysis of the RNA constituent), Proteomics (analysis of protein constituent), metabolomics (analysis of the metabolite), as shown in Fig. (**1**). Utilizing these techniques, various complex mechanisms or pathways are being studied for better understanding at the molecular level, *i.e.,* from an expression of a gene to the phenotype of the product [9]. Omics allows the researcher to identify minute yet precise changes in cellular pathways.

Fig. (1). An overview of both omics technologies and Systems Biology.

Genomics

Genomics, a well-defined interdisciplinary area, deals with the various sequences and variants of DNA along with its functioning. The word *Genomics* was first coined in 1986 by Dr. Thomas H. Roderick. The foremost goal is to determine how DNA imparts traits and phenotypic expression in a particular organism [10]. Gene maps were considered an essential tool for gene sequencing. Initially, it was constructed using the somatic hybrid cells technique which is based on the enzyme marker segregation. Later on, denser genetic maps are constructed using

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