Ontologies related to animals or livestock for the GBADs programme: a review

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Summary

The Global Burden of Animal Diseases (GBADs) programme aims to assess the impact of animal health on agricultural animals, livestock production systems, and associated communities worldwide. As part of the Animal Health Ontology theme's objectives, the programme reviewed conceptual frameworks, ontologies, and classification systems in biomedical science. The focus was on data requirements in animal health and its connections with human and environmental health. In May 2023, the team conducted searches on recognised repositories of biomedical ontologies, including BioPortal, Open Biological and Biomedical Ontology (OBO) Foundry, and Ontology Lookup Service (OLS), to identify animal and livestock ontologies and those containing relevant concepts. Sixteen ontologies were found, covering topics such as surveillance, anatomy, and genetics. Notable examples include 'Animal Trait Ontology for Livestock', 'Animal Health Surveillance Ontology' (in progress), 'NCBITaxon', and 'Uberon'. However, some ontologies lacked class definitions for a significant portion of their classes. The review highlights the need for domain evidence to support proposed models, critical appraisal of external ontologies before reuse, and external expert reviews along with statistical

tests of agreements. The findings from this review informed the structural framework, concepts, and rationales of the Animal Health Ontology (AHO) for GBADs. The AHO aims to increase the interoperability and transparency of GBADs data, thereby estimating the impacts of animal diseases on agriculture, livestock production systems, and associated communities globally.

Keywords

Animals – Health – Information science – Livestock – Ontology.

Introduction

Animal health is closely linked to humans' economic activities, food sources, fuel, and general health and well-being. The Global Burden of Animal Diseases (GBADs) programme aims to measure the impacts of animal disease burden on agricultural animal and livestock production systems as well as human health worldwide [1]. The primary goals of GBADs is to assess livestock disease burden, correlating with economic impact due to infectious, non-infectious, and external causes. With the extensive domain knowledge, the existing biomedical classification systems like ontologies, taxonomies, and catalogues must be identified and integrated to address data needs in animal health and its links to human and environmental health.

In philosophy, ontology studies concepts such as existence, being, becoming and reality. It probes the ways in which entities are categorised and the most fundamental existence of such entities [2]. In computer science, it refers to a structured framework that categorises and represents knowledge about specific topics, defining relationships between terms and enabling automated reasoning. An animal health ontology in the context of computer science should offer representations, formal naming, and clear definitions of the categories, properties, and relations between the concepts, data, and entities that underlie the domains of animal health [3].

Numerous biomedical ontologies developed for a range of purposes such as disease modelling, gene clustering, and surveillance, etc. For example, an ontology could be produced for disease vector surveillance and management, focusing on vectors and vector-borne pathogens relating to animals [4]. With extensive literature review and observations, substantial gaps in existing ontologies might be identified regarding concepts, processes, and physical entities such as vector species, pathogen species, and vector surveillance and management equipment in the domain of animal health and vector control [5]. Some ontology-like taxonomies such as the 11th and 10th revisions of

the International Statistical Classification of Diseases and Related Health Problems (ICDs) were widely adopted globally and could be helpful. They were well-recognised in terms of the sharing codes for diseases, signs and symptoms, and abnormal findings, etc. [6].

An ontology of infectious diseases in animals might play multiple key roles for the modelling of infectious organism community by providing a backbone of disease concepts represented among the model organism databases; a development of subsets of the ontology representative of diseases annotated to animal models; and some disease curation services within the databases to researchers and resource providers [7]. Ontologies could be used to capture facts about a disease and map them to disease codes. Animal health ontologies have the potential to improve disease understanding if effectively integrated into existing research [8]. This facilitates analysis of ontologies and domain annotations in biomedical databases.

There are large repositories of biomedical ontologies being operated nowadays. For example, the Open Biological and Biomedical Ontology (OBO) Foundry comprises over a hundred ontologies and candidate ontologies of diseases, parasites and vectors such as the National Center for Biotechnology Information (NCBI) organismal classification ontology, Mosquito Insecticide Resistance Ontology, Infectious Disease Ontology, Infectious Disease Ontology-MALaria (IDOMAL) ontology, and ontologies for mosquito gross anatomy and tick gross anatomy [4]. The development of new ontologies will support the creation of the disease atlas, which aims to provide a comprehensive molecular, cellular and anatomical map of the animal diseases [9]. However, it remains a big challenge to properly identify, define, retrieve, analyse, and validate the required concepts and their potential relationships from textual and numerical data.

Aim

Our aim was to conduct a synthesis review and create a technical report of classification systems, main categories, and proposed terms in biomedical sciences (i.e. animal health-related ontologies, with the focus on data needs in animal health and its links with human and environmental health).

Materials and methods

Between April and May 2023, we conducted a search for ontologies related to animals or livestock, or any ontologies that included animal concepts, in well-recognised

repositories of biomedical ontologies such as BioPortal, OBO Foundry, and Ontology Lookup Service (OLS).

BioPortal [10,11] is a web portal that provides access to a library of biomedical ontologies and terminologies via the Web services of the US National Center for Biomedical Ontology (NCBO). NCBO strives to disseminate biomedical knowledge and data on the Internet using principled ontologies which allow semantically interoperable and useful data analysis for furthering biomedical science and clinical care. The OBO Foundry [12] is a well-known repository that has operational rules based on the FAIR principles [13] to ensure data is Findable, Accessible, Interoperable, and Reusable. These principles require ontologies to be based on well working ontology models and adhere to several criteria like logical coherence, accuracy, non-overlapping scopes, open collaboration, and the use of common syntax and relations.

The OLS [14,15] is a repository developed and maintained by the Samples, Phenotypes and Ontologies Team (SPOT) at the European Bioinformatics Institute, European Molecular Biology Laboratory. It provides a range of means to query, browse, and navigate biomedical ontologies and controlled vocabularies via its API.

We searched on BioPortal for ontologies with the terms 'animal' or 'livestock' in the names of ontologies. On OBO Foundry, we performed searches with these terms in the ontology descriptions. Moreover, we conducted searches of these terms in their names and descriptions on OLS. That means ontologies which focus on animal and/or livestock were included. The data extracted included ontology name, URL, publication, explanation, file format, classes, number of definitions, properties and parents.

Results

Animal Health Ontology for Livestock (AHOL)

AHOL [16] characterised health issues of livestock in their environments linked to their phenotypes (Table I). It aimed to provide a reference of health traits of farm animals for the farmers, industries, scientific and educational communities, etc.; to represent generic traits for livestock vertebrates; and to be operational as a measurement tool. AHOL described production diseases. It is organised according to disease groups such as communicable, non-communicable, genetic, metabolic, physical or psychological. The disease properties include associated symptoms, phenotypical character, the organism, livestock type, poultry, mammals, fishes or the pathogen, virus, bacteria, fungus, or parasite. The potential uses of AHOL include decision-making for integrated health

management, potential health status severity assessment, or as an additional way of supporting diagnostics.

Animal Health Surveillance Ontology (AHSO)

AHSO [17] is an ontology for health surveillance, assuming that surveillance data is recorded for the sample collected, the observations on some samples, as well as the context in which observations were taken. In this ontology, a health event is an event that occurs in a particular time period, space and population units on which observations were taken. Data can be recorded in different databases or sources as well.

Health Surveillance Ontology (HSO)

HSO [18] focuses on surveillance data on the system level, i.e. data outputs from surveillance activities, such as number of samples collected, cases observed, to name a few. Surveillance is defined as any activity that collects information which is analysed to inform disease control. HSO aims to support the One Health vision, covering surveillance about animal health, public health and food safety, and for example, the investigation of foodborne zoonotic outbreaks.

Animal Trait Ontology for Livestock (ATOL)

ATOL [19] defines and organises livestock phenotypical traits, developed in response to recent biological data influx. It comprehends phenotypes resulting from genotypic and environmental interplay. To further contextualise this, the Environment Ontology for Livestock (EOL) was introduced, detailing livestock rearing conditions across four categories: farming systems, structures, environment, and feeding. These ontologies aim to provide an internationally recognised framework for livestock conditions, standardise language for computer applications, encompass prevalent livestock traits, align closely with measurement techniques, and focus on animal production.

Animal Natural History and Life History Ontology (ADW)

ADW [20] is an ontology for animal life history and natural history characteristics about populations and higher taxonomic entities. It was last uploaded onto BioPortal in 2010 and is labelled as obsolete on OBO Foundry.

Livestock Breed Ontology (LBO)

LBO [21] simply described itself as an unambiguous controlled vocabulary for the breeds of buffalo, cattle, chicken, goat, horse, pig and sheep. It claimed its utility was the identification of the sources of inherited variation from the genetics/genomic studies.

Livestock Product Trait (LPT) Ontology

LPT Ontology [22] introduced itself as a controlled vocabulary for the concepts of traits i.e. measurable or observable characteristics, regarding the products of agricultural animals such as proteins in terms of meat and milk or products maintained for future use and profit making. LPT is developed based on morphological, physiological, and developmental traits in vertebrates, aiming at enhancing the ability to standardise phenotype nomenclature across species.

Environment Ontology for Livestock (EOL)

EOL [23] aimed to form an authoritative ontology to describe rearing conditions of livestock, which can be shared by the scientific, industrial and educational community. It also set to include the most common livestock traits possible; to make it as useful as measurement techniques; to structure the foundation towards animal production. EOL contains concepts of environmental conditions of livestock farms, the feeding modalities, the environment, the structure of livestock farms and rearing systems, as well as the main functions of life (epigenome, transcriptome, proteome, metabolome, etc.) Nowadays, big data contributes to an extensive knowledge of the characteristics of each individual, such as phenotype, the result of the expression and regulation of its genome, which came from the shared action of one's genotype and one's environment. Therefore, EOL characterise, generically, husbandry systems and rearing conditions, as well as livestock farming system, structures, environment, and livestock feeding.

Cell Ontology (CL)

CL [24,25] is designed as a structured controlled vocabulary for cell types in animals. CL was created for use by the model organism and other bioinformatics databases, where there is a need for a controlled vocabulary of cell types. CL is not organism specific as it covers animal cell types from mammals to prokaryotes excluding plant cells.

Histopathology Ontology (HO)

HO [26] is an ontology of histopathological morphologies used by pathologists to classify or categorise animal lesions observed histologically during regulatory toxicology studies. The ontology was developed using real data from over 6,000 regulatory toxicology studies donated by thirteen companies spanning nine species.

Uber Multi-Species Anatomy Ontology (UBERON)

UBERON [27] is an integrated cross-species anatomy ontology covering animals and bridging multiple species-specific ontologies. It consists of over 6,500 classes of anatomical structures in animals and is organised according to traditional anatomical classification criteria. UBERON represents the structures in a species-neutral way and includes extensive associations to existing species-centric anatomical ontologies, allowing integration of model organism and human data, as well as translational phenotype analyses. Therefore, it provides a necessary bridge between anatomical structures about taxonomic variation, and different taxa for cross-species inference.

Biological Spatial Ontology (BSPO)

BSPO [28] is an ontology for representing spatial concepts, anatomical axes, gradients, regions, planes, sides and surfaces. These concepts can be used at multiple biological scales and in a diversity of taxa, including plants, animals, and fungi. BSPO is used to provide a source of anatomical location descriptors for logically defining anatomical entity classes in anatomy ontologies.

Neuro Behavior Ontology (NBO)

NBO [29,30] is an ontology labelling human and animal behaviours and behavioural phenotypes. It consists of two sub-ontologies about the processes and phenotypes of behaviours respectively. The behavioural process is a classification which complements and extends Gene Ontology's process ontology. The behaviour phenotype is a classification of either normal or abnormal behavioural characteristics of the organisms concerned. Behavioural processes underpin physical, mental, and environmental influences which interact with genetic architecture. NBO facilitates the systematic representation of behaviour and behavioural phenotypes, as well as improvements in the unification and integration behavioural data.

National Center for Biotechnology Information Taxonomy (NCBITaxon)

The US NCBITaxon [31] is a curated classification and nomenclature for all organism names and classifications for every sequence in the nucleotide and protein sequence databases of the International Nucleotide Sequence Database Collaboration. It becomes a series of linked databases tied to NameBank which is a data framework, so that relations among data elements can be adjusted in more detail. It results in an expanded annotation of synonyms, an ability to flag names with specific nomenclatural properties, an enhanced tracking of publications tied to names, an improved annotation of scientific authorities and types, and the capability to explain terms peculiar to NCBITaxon.

Eagle-i Resource Ontology (ERO)

ERO [32,33] is developed by the eagle-i project which aimed to model research resources such as instruments, core facilities, protocols, reagents, animal models and biospecimens. Data collection and search tools are completely driven by ontologies in the eagle-i software. The software and ontologies model various biomedical research resources. It can also be integrated into other ontologies, which leverage and expand upon different ontologies to create a semantic framework that describes scientific resources, research activities and clinical activities.

Ontology of Laboratory Animal Medicine (OLAM)

OLAM [34] is a community-based biomedical ontology in the field of laboratory animal medicine. Its aim is to ontologically represent entities and the relations among the entities related to laboratory animal medicine. The OLAM is in an alpha status and is formatted in World Wide Web Consortium's (W3C) Web Ontology Language (OWL). It was last updated in February 2021. The ontology includes 209 classes, 25 individuals, and 51 properties. OLAM is a biomedical ontology for laboratory animal medicine. It helps standardise terminology, annotate and integrate data, generate and test hypotheses and mine literature. Its usefulness depends on the specific needs and how researcher use it.

Discussion

GBADs' initiative emphasises understanding the impacts of animal diseases on global agriculture, livestock systems, and human health. The vast domain knowledge, multifaceted data, and interconnectedness of animal, human, and environmental health necessitate advanced classification systems. Utilising ontologies allows the representation of intricate relationships and provides a logical foundation for automated

reasoning. Given the diverse biomedical ontologies in literature, it's clear that ontologies can bolster operational activities, offering clarity and standardisation in databases or decision-making systems. Moreover, ontologies can bridge gaps, like those in vector control and animal health. For GBADs, leveraging an ontology means a systematic framework to integrate diverse information, facilitating a more precise assessment of disease impacts. In essence, GBADs aims to harness the structured, integrative power of ontologies to enrich its understanding and management of animal diseases and their broader implications.

Summary of evidence

Potential use of existing ontologies

The cancer project of disease ontology mapped nearly four hundred cancer terms from six major sources including catalogue, atlas, consortium, programme, framework, and network, into a cohesive set of around two hundred disease ontology terms represented by over sixty top-level cancer terms [35]. This mapping facilitates pan-disease analysis across datasets generated from any of the terms' sources. Pan-disease means including or relating to multiple types of diseases concerned. On a genomic level, cell-based screening and computational analysis could be used to match gene expression signatures produced by natural products to those produced by small interfering RNA and synthetic microRNA libraries [36]. Statistical or computational prediction models can achieve excellent results in performance metrics such as large AUC, and high sensitivity and specificity. Thus, the application of ontology could have great potential in disease modelling and classification [37].

The use of ontology allows comparisons of data from diverse sources, can facilitate comparisons across species, assists in identifying appropriate experimental disease models, and aids in the discovery of candidate disease characteristics on demographical, biological and molecular levels [38]. Some national collaborative efforts were working towards these goals through the collection and integration of large, disparate clinical, biological and imaging data of diseases. Both forward and reverse genetic screens can be used to identify molecular mechanisms for phenotypes and diseases, resulting in numerous genotype-phenotype associations in animals and model organisms [39]. Ontologies are crucial for analysing big data in precision medicine, combining diverse clinical, imaging, and biopsy data to define animal phenotypes [40].

Recent studies discovered that genes involved in phenotypically similar diseases are often functionally related on the molecular level. Machine learning methods such as ontology-based classifier for hierarchical classification can predict phenotypes resulting from loss-of-function in single genes [41]. In addition, the use of ontology allows comparisons of data from heterogenous sources or species, which helps to recognise appropriate disease models or concepts for experiments [41,42]. The semantic similarity of ontology terms can be used to improve disease concepts prioritisation. Also, ontology about functional signature can be used to identify mechanisms of action for natural products. Since many hereditary diseases are polygenic, an ontology can be used in vector surveillance and management in terms of data analysis [43]. Ontology can also address shortcomings of existing coding systems such as the ICDs which are difficult to decode. The aim of building computational ontology can be developing an ontology-based literature mining system to identify concepts of interest, so as to understand the effects of classes of key concepts on animal diseases [44].

Ontologies have great potential in diverse applications. For instance, by using ontological classification as a segmentation guide, regional changes in organ volume in animals could be tracked between baseline on day zero and the end of the observation period and could demonstrate differential growth rates in axial versus paraxial organ regions [45]. Ontologies could also be used to guide machine learning on disease data. For example, dimensionality reduction by certain algorithms such as t-distributed stochastic neighbour embedding (t-SNE) could be implemented to tissue architectures for the study of disease evolution by superimposing key features such as size and grade vectors [46]. Disease models could be refined through empirical analyses of directed evolution of disease characteristics as determined by experiments and external validations with the use of ontology [47].

Limitations of existing ontologies

Among the sixteen ontologies identified, only half had been published in a journal or in conference proceedings. The greatest limitations of the existing ontologies are that there is a lack of rule-based methods in determining the hierarchical structure of the classes, super classes and subclasses, which are often not well explained. For some concepts such as anatomical parts or biological structures, it is easy to group them by regions, structures or functions. However, for diseases, they comprise multi-dimensional features that more could be done than grouping diseases by body systems or pathogens only. The purpose of building the hierarchical structure for the classes should be enabling efficient mapping between new data and the classes to answer a question. For example,

diseases might be categorised based on body systems, pathogens and treatments, so that new patient's data mapped to the probable classes can tell the potential treatments.

A rigorously developed hierarchical structure for the classes is preferable, or a list of research evidence-based object properties e.g. labelled relationships between classes should be provided. Among the sixteen ontologies, six only presented 0–3 properties despite that they have around five hundred to two million classes. And six had no class definitions for over 98% of their classes, five had no definitions for around 30–60% of their classes, which added uncertainty about the validity of the classes structure and relationships labelled. In ontologies, clear definitions are essential for all concepts or constructs which should be grouped, and relationships should be labelled according to definitions (associated information).

Some key goals of building an ontology are to 1) establish conceptual clarity by providing clear and concise definitions of each concept and defining relationships between concepts in an unambiguous manner, 2) improve interoperability by using shared vocabularies, 3) facilitate in search and discovery, and 4) enable knowledge sharing. However, existing ontologies often do not achieve these goals. Firstly, the naming inconsistency of ontologies, like Uberon, Biological Spatial Ontology, or Eagle-i Research Resource Ontology, across different repositories creates confusion. Secondly, the lack of mandatory class reuse results in inconsistency. For instance, the term 'animal' from Semantic Types Ontology is reused in thirty ontologies but not in another 45 ontologies. Therefore, concepts carrying the same semantics across databases can be mapped to different IRIs, some labelled relationships might not be found, and the ontologies are not linked up, although classes can be searched on the website of the repository such as BioPortal. This review suggests establishing a globally recognised authority for reporting ontology development protocols with submissions and publication undergoing peer review. Funding bodies are encouraged to support data-ontology mapping with an emphasis on reducing mapping efforts through standardisation.

Conclusions

By overcoming the limitations, ontologies can be useful in animal data query and integration for analysis. New ontologies should allow easier search of terms than old ones. For example, an ontology should enable cross-domain data integration through a common standard of disease terms and their etiological descriptions. As some diseases appeared to result from other diseases, this complexity needs to be reduced to a handful of pathological variables such as stage, grade and severity, but all variables have to

capture the breadth of the disease. Ideally disease databases store diagnosis and disease data using codes, the disease concepts should be browsed online and be downloaded from repositories. Expansion of term content and cross-references to disease vocabularies should also be included so the ontology can foster interoperability between biological and disease-related data. The functionality of known disease concepts should be annotated to assess the similarity of diseases as well as the disease relevance of candidate concepts. This is an important step to ensure that the knowledge contained in the ontology can be put into practical use, as the development process often yields lists of up to several hundred candidate concepts, which have to be prioritised and validated further. The absence of ontological frameworks in animal health has hampered the development of GBADs and strengthening this aspect of the animal health landscape will be a priority in the next phases of the programme.

Acknowledgements

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Table I

Ontologies related to animal or livestock and their characteristics

Ontology	Publication	BioPortal	OBO	OLS	Format	Classes	No definition	Properties	Parents
Animal Health Ontology for Livestock [16]	No	Yes	No	No	OWL	339	338	11	Multiple
Animal Health Surveillance Ontology [17]	Yes	Yes	No	No	OWL	38	38	38	Single
Health Surveillance Ontology [18]	No	Yes	Yes	Yes	OWL	426	178	269	Multiple
Animal Trait Ontology for Livestock [19]	Yes	Yes	No	Yes	OWL	2,352	2,352	0	Multiple
Animal Natural History and Life History Ontology [20]	No	Yes	Yes	No	OWL	364	179	81	Multiple
Livestock Breed Ontology [21]	No	Yes	No	Yes	OBO	1,101	1,083	0	Single
Livestock Product Trait Ontology [22]	No	Yes	No	No	OBO	502	24	2	Multiple
Environment Ontology for Livestock [23]	No	Yes	No	Yes	OWL	648	648	1	Multiple
Cell Ontology [24,25]	Yes	Yes	Yes	Yes	OWL	16,468	1,013	304	Multiple

Histopathology Ontology [26]	No	No	No	Yes	OWL	1,281	216	3	Multiple
Uber Anatomy Ontology [27]	Yes	Yes	Yes	Yes	OWL	20,772	6,708	253	Multiple
Biological Spatial Ontology [28]	Yes	Yes	Yes	Yes	OWL	173	12	158	Multiple
Neuro Behavior Ontology [29,30]	Yes	Yes	Yes	Yes	OWL	2,669	308	197	Multiple
NCBITaxon [31]	Yes	Yes	Yes	Yes	RDF/TTL	1,983,907	1,983,907	3	Multiple
Eagle-i Research Resource Ontology [32,33]	Yes	Yes	Yes	Yes	OWL	4,061	1,639	195	Multiple
Ontology of Laboratory Animal Medicine [34]	No	Yes	No	No	OWL	209	119	51	Multiple

NCBITaxon: National Center for Biotechnology Information Taxonomy
OBO: Open Biological and Biomedical Ontology Foundry
OLS: Ontology Lookup Service
OWL: World Wide Web Consortium's (W3C) Web Ontology Language
RDF: Resource Description Framework
TTL: Terse RDF Triple Language (Turtle)