A survey on ontology techniques deployed in the biomedical domain

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Abstract. The number of studies in big data aspects of biomedical domain are tremendously increasing because of the growing technical knowledge, need for reduced computation costs and the availability of internet facilities almost over everywhere. A considerable amount of data in the biomedical domain are stored across platforms that are semantically, structurally and semantically different. With this heterogeneity, it becomes extremely difficult to access and derive meaningful insights from data. Data Integration plays a significant role in merging the data and making access to these data faster and easier. Ontology, a form of knowledge representation, is widely used in data integration to denote the semantic relationship between the data stored in heterogeneous data sources and aid in easier retrieval. This paper surveys the ontology engineering methods used in various biomedical domains like cardiology, nephrology, diabetes, Covid-19, traditional medicine and the recent advancements in ontology development.

Keywords: Biomedical domain, Ontology engineering, Semantic data retrieval, Data Heterogeneity, Recommendation Systems.

1 Introduction

Ontology is a knowledge representation technique that symbolizes knowledge as a collection of concepts within the domain. Ontologies usually contain a shared lexicon that describes the type, behavior and associations between the concepts in the domain. They are most commonly used in extracting meaningful insights from heterogeneous data. Hence, they have profound applications in domains like Artificial Intelligence, Semantic Web, Big Data Analytics, Biomedical domain, Library Management, etc. This paper surveys a variety of ontology engineering methods that are used in Biomedical Domain.

Digitization of patient records has led to the generation and will further generate a profuse amount of data. These patient records are generated by many sources like X-rays, scans, temperature sensors, lab results, prescriptions, monitoring devices, etc.; this big data has three main characteristics, variety, velocity and volume. Variety denotes the heterogeneity encountered in the data generated by the above sources. Velocity refers to the speed at which the data is generated, processed, analyzed and stored across various platforms. Volume refers to the quantity of data that are generated by the data sources. Ontology serves as an important tool for managing the big data in all the stages of biomedical data management like Data Acquisition, Data Integration and Data Storage [1].

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The three major phases of ontology engineering are ontology construction, ontology mapping and ontology integration. Many manual methods of the above three phases are proposed. More emphasis is now laid on automating the three major phases of ontology engineering. One such automated ontology matching technique was devised based on Domain Specific Word embeddings [2]. In this method, the semantic meaning of the entities was extracted by training the word vectors on the biomedical corpus. The word embedding was further implemented on the existing systems and the results showed great accuracy. This method addressed the semantic problems that arise in the biomedical domain.

Based on the outlook of the application, ontologies can be classified into three major types [3]. The first type is called an upper ontology. This ontology aids in providing a basic framework for determining and organizing the terms and associations in a particular domain. The second type is a reference ontology that represents the objects and relationships in a specific domain. The final type is application ontology that can be used for a specific scenario and provides a minimal dictionary to fit the required need. An ontology-based solution devised to solve a heterogeneity problem can fall under any of the above three types based on the scenario considered for development.

To solve heterogeneity problems, data integration can be done by either Data Translation or Query Translation. The entire data residing in a database is translated when the data translation approach is used. Whereas in query translation technique, the query from the user application is converted through appropriate software to access the data residing in various data sources.

Among the two techniques discussed, query translation is efficient because the process is fast and has less overhead. On the other hand, the data translation technique suffers from the limitation of acquiring huge time for translating data and is less efficient when new data is added. The data has to be translated to match the predefined rule and then accessed. Results from an ontology model can be effectively retrieved using a query language based on an ontology model, called SPARQL.

Another challenging issue in the field of data integration is data consolidation. When several data sources are merged, there are high chances that the data will be redundant, transitively dependent, and have multi valued attributes. Hence, it is necessary to normalize the data before ontology construction and mapping, as the presence of unnormalized data can lead to deriving less efficient conclusions. The normalization in data integration can be applied on the three types of granularities: record-level, field-level, and value-level components.

The key integrity issues faced in the biomedical domain during heterogeneous data integration are surveyed by many researchers and the possible methods of rectifying the issues are suggested [4]. The paper discussesdata integrity techniques used in the biomedical domain and explores their most important data integrity method. An intensive Systematic Literature Review in the biomedical industry is performed. The major goal of the Systematic Literature Review (SLR) is to determine the current data integrity techniques that are used by the researchers to secure the data in biomedical domain.

This SLR has been done in two stages. In the first stage, the SLR provides detailed information about the past data integrity attacks linked with biomedical industry. The Data Breaches in Various Healthcare Industries are discussed in this stage.

In the second stage, the SLR provides a detailed review of past research initiatives related to biomedical data integrity that help in securing the healthcare systems. Only the standard papers from the biomedical domain were considered as a part of the research.

Various integration techniques like the blockchain approach and Masked Authenticated Messaging Extension are explored, and the appropriate integrity method for each healthcare domain were postulated. The research suggested that Secure BSN and authentication based access can be used in healthcare systems. Blockchain Approach, Masked Authenticated Messaging Extension can be used in data transfer, Blockchain, Secure cloud, Slepian wolf coding based secret sharing can be used for data sharing, Cryptography, Merkle Tree based Approach can be used for patient data access and finally Secure cloud and Blockchain can be used for data Storage.

The above mentioned survey provided a descriptive analysis of previous publications through various analysis methods. It also summarized the data integrity techniques in all the methods. Ranking assessment shows that researchers must pay attention to blockchain techniques for ensuring data integrity. The number of studies reviewed and databases accessed by the authors are limited in this paper. Though many databases are accessible by the researchers, some studies and databases could not be incorporated in the proposed SLR.Therefore, data integrity techniques and methods based on Fuzzy AHP (Analytical Hierarchical Process) can further be explored.

A Privacy-free Data Fusion and Mining (PFDM) approach was used to integrate data in the healthcare domain using time efficient and privacy preserving manner [5].

The major contribution of this model was divided into three parts.

i) The LSH (Locality-Sensitive Hashing) was introduced into multi-source Internet of Health (IoH) data fusion and integration to secure the sensitive information of patients that are not explicitly available in the previous IoH data.

ii) For the Internet of Health data without having any sensitive information about the patient after LSH process, a similar IoH data record search method for consequent IoH data mining and canvas is designed

iii) Based on a data set collected by real-world users, the advantages of the PFDM work are validated through a set of experiments that were designed prior.

First, the sensitive IoH information is projected based on LSH functions. Then, a set of hash tables is created according to the IoH data record and its corresponding hash values obtained after hash projection. Finally, similar IoH data search and mining are made according to the traced hash tables.

This method was comparedwith User Based Collaborative filtering (UCF) and Item Based Collaborative Filtering PDFM. It was shown that LSH returned IoH data records with a small response time, decreased Mean Absolute Error rate and higher similarity index. Only a simple IoH data of continuous type without considering the possible data type diversity (e.g., continuous data, discrete data, Boolean data) and data structure diversity is considered.

The capability of securing sensitive patient information is still not introduced in PDFM. There is often an integral trade-off between data privacy and data availability. Data Availability is not always guaranteed. The suggested PDFM method can be updated by considering the possible diversity of data types and data structure. Fusing multiple existing privacy solutions for better performances is still an open problem that requires intensive and continuous study. Ontologies can be used efficiently to secure patient details based on security recommendation systems.

This paper is divided into five sections. The first four sections deal with the ontology-based solution in biomedical fields like cardiology, nephrology, diabetes and Covid-19. The fifth section represents the ontological solutions developed for traditional medicines in India, Persia and China. Finally, the approaches are discussed along with the advantages, limitations and future enhancements in the respective areas.

2 Ontology-based solutions in Biomedical Domain.

Biomedical Domain includes sciences, a group of disciplines that use elements of natural science, formal science, or both to generate information, therapies, or technology for healthcare and public health. Biomedical sciences include fields like medical microbiology, clinical virology, clinical epidemiology, genetic epidemiology, and biomedical engineering.

Biomedical data is data that is related to (or could be fairly understood to be related to) human health. In general, such knowledge should be backed up by a respectable biomedical source, such as peer-reviewed publications, advanced medical textbooks, and professional reference works. Hence the biomedical data includes symptoms or characteristics of an illness or condition, characteristics of a treatment or medicine, medical choices, any considerable effects on health, Epidemiology and population data, Studies in bio-medicine.

Research in Biomedical ontology spans over a wide range of things and processes (from biological product dictionaries to regulated vocabularies to principled knowledge systems), acquisition of ontological relations, heterogeneous databases integration and biological knowledge reasoning using ontology.

Biologists will keep up with an expanding amount of information by the useful applications enabled by biomedical ontologies. They will also be freed from the less exciting activities that can be handled automatically by using ontologies. The application of ontologies in specializations like cardiology, nephrology, diabetes, covid-19 and traditional medicine are explained further in the paper.

Cardiology

Cardiology is a discipline of medicine that focuses on problems with the heart and other components of the circulatory system. Congenital heart defects, coronary artery disease, heart failure, valvular heart disease, and electrophysiology are all included in this field.Cardiovascular diseases (CVD) remain one of the major causes of mortality worldwide. The number of people affected by CVD increases daily because of the sedentary nature of work, lack of healthy exercise, and increased consumption of food rich in bad cholesterol.

A cardio ontology [6] was implemented using the exiting datasets like SNOMED CT, RxNorm and GO, to prescribe medicine to patients. This model allows us to search for a specific CVD, medicine or gene and retrieve the related encoding and other externally identified information regarding the symptoms, reactions to medicine taken and the major elements of the medicine to be prescribed with respect to the search made. The semantic information was extracted from nearly twenty-five books belonging to the cardiology domain.

The model effectively gave information related to the analysis, diagnosis and prescription of the patients. The ontology construction was based on OWL and RDF. The work's limitations involve considering a limited vocabulary and the difficulty of incorporating the changes in the priorly designed networks because of the updates. The future enhancements include expanding the considered library and updating the presented dataset according to the recent changes.

Being physically fit is an important aspect for the patients with CVD. Another ontology called OPTImAL [7] was designed to check if the CVD patients strictly adhere to physical activities, yoga and exercises. The ontology was developed by following the Ontology Development 101 methodology and modified based on the NeOn framework. It was implemented using OWL2 language, Protégé, WEBVOWL and Ontograph with OAF plugin. OPTImAL includes one hundred and forty-two classes, ten object properties and three hundred and seventy-one individuals to denote the patient profile factors. The constructed model was evaluated by a cardiologist and three Cardiac Rehabilitation trainers for its appropriateness and usefulness.

The ontology of human cardiovascular system can be used to improve the classification of microscopic images of the affected tissues [8]. The model involved describing the histological image into small regions of images called blocks, by using a Local Binary Pattern (LBP). A cascade Support Vector Machine (SVM) was used to identify which part of the cardiovascular tissue was present. The Resource Description Framework (RDF) triples were built for every discriminant class occurrence. Using these triples a Histological Ontology was constructed to identify the 'not possible' situations. The tools used for ontology construction were Protégé API, SPARQL and reasoners based on FaCT++, Pellet, Java and C++. Classification of human tissues can be done effectively by using Computer Vision Techniques. But this fails when the image has insufficient visual information. Since Ontology is a domain-based Knowledge representation technique, it can clearly detect the issues in classification of microscopic images

. The major advantage of this method, was that this ontology-based classification could detect the epithelial tissues, which was not done by any other computer vision Techniques. Even a CNN based model called HistoResNet failed in detecting the epithelial tissue. The future work of this model includes exploration of an apt image block size to reduce the edge misclassification and the use of Convolutional Neural Network (CNN) in the place of cascade SVM.

Nephrology

Nephrology is a specialization that is concerned with the study of kidneys. The kidneys filter the blood, removing waste and extra fluid. Waste accumulates as the kidneys fail. Symptoms appear gradually and aren't unique to the disease. Some show no symptoms and are diagnosed through a blood test. Medications aid in the management of symptoms. Filtering the blood with a device (dialysis) or a transplant may be required at a later point in time.

Kidney diseases are most commonly classified as Acute Kidney Injuries and Chronic Kidney Diseases. These terms used for representation, indicate the decreased functionality of kidney but doesn't provide any insights on the diagnosis part. Computer readable representations of the interested entities are provided by ontologies. This computer readable information can be easily understood by humans through encoding techniques that represent data in a way that both computers and humans recognize.

A broad survey of ontologies in the nephrology domain [9] has been done to aid the researches and nephrology clinicians. This article discusses the roles of ontology in biomedical sciences and the inevitable role of data integration in accessing big data. The existing ontologies in the nephrology domain and the role of Kidney Precision Medical Project (KPMP) ontologies in filling the gaps of kidney specific data representation were explored.The application of the designed ontologies to help in data harmonization of terms related to kidney disease were analyzed. A huge emphasis was laid on the concepts of two ontology resources namely, Kidney Tissue Atlas Ontology (KTAO) and Ontology of Precision Medicine and Investigation (OPMI), that can be used to analyze KPMP data .

The neglection of important information from the clinical data reduces the efficiency of the healthcare industry. A study [10] was done to evaluate the important chronic kidney disease-based information that was neglected by the non-nephrology clinicians. A patient specific data model was constructed from the Electronic Data Records (EHR) using the ontology structure of knowledge graph to identify the unused information identified in EHR. The knowledge graph was constructed using a two-level ontology model based on the Observational Medical Outcomes Partnership (OMOP) common data model (CDM).

The ontology construction was done using OWL API, Jena API, and RDF type triples. The model has five major phases. The first phase involves a semantic consistency check from the patient Information Model, followed by the entity classification and abnormality detection. Then the unconsidered CKD reasoning is done followed by the system response that alerts the risk factors. This system allows clinicians to take appropriate decisions through explainable Artificial Intelligence. The work can be further extended to cancer risk detection in colorectal and pancreatic areas.

Chronic Kidney Disease (CKD) problems are identified only in the later advanced stages. A model to predict the CKD was designed based on ontology modelling techniques like RDF/OWL combined with Linear Support Vector Machines (SVM) [11]. The model's architecture contained three major layers: Context Provider Layer, Context Reasoning Engine, and Semantic Learning Engine. The context provider layer gathers the attributes related to the contextual behaviors (patient profile information relating to the kidney) from various sources. The context reasoning engine contains the context model to analyze the contextual information from the previous layer and an inference engine to check the semantic consistency. Finally, the semantic learning engine performs the preprocessing, learning and evaluation of the patient profiles.

The model then predicts if a patient profile is susceptible to CKD or not using a linear SVM model. The future work of this model can include logistic regression or Median Gaussian SVM to increase the system efficiency.

Diabetes

Diabetes Mellitus (DM) is an alteration of metabolism that occurs due to the increased glucose level in the blood. Many ontologies were developed to diagnose diabetes. Only a few recent models were considered as a part of the study.

An Ontology Network [12] for Diabetes has been constructed by using three major resources namely the medicine catalog of patients having diabetes, the medical history and notes of the patient and the previous five years epidemiological hints of T2DM (Type 2 Diabetes Mellitus). From the details above, six ontologies related to the diabetes domain was built, followed by the Ontology reuse and Integration.

The network was developed in RDF language and was further enhanced by including Semantic Web Rule Language (SWRL). SPARQL queries were used for the data retrieval from ontology. Few non ontological data like the notes about the patient in natural language were also considered part of the network. Future enhancements of this network can include generating alerts for high glucose and cholesterol values.

The presence of semantic inconsistencies is a major constraint for developing ontology-based solution for the detection of diabetes. An Ontology Based Model for Diabetic Patients (OMDP) [13], was developed by considering seven hundred and sixty-six records of patients from the medical environment to enhance the process of diagnosis by using Semantic Web Rule Language (SWRL). A Basic Formal Ontology and Ontology for Generating Medical Sciences (OGMS) were considered the top layer ontology in this model. The model was developed using Protégé, OWL2 Language and Pellet. The data in relational databases were translated into RDF by using D2RQ. The reasoning is done based on the SWRL.

The model produced an accuracy of about ninety-five percent for disease prediction, ninety-eight percent for diabetes diagnosis and eighty-five percent for medicine recommendation. The limitation of the model is that it takes a little time to decide and hence might not be effective for patients with high severity of diabetes needing urgent medical attention. The model can be further enhanced by applying it to Internet of Medical Things (IoMT) based applications.

A balanced diet plays a very important role in the lives of diabetes patients. An ontology-based decision support system [14], was designed to recommend diets to patients with diabetes as a part of effective healthcare. Diabetes Mellitus Treatment Ontology (DMTO) and Semantic Web Rule Language (SWRL) rules were used to build the system's knowledge base. The patient details are imported from the database and are stored in the server in DMTO ontology model representation. When a diet suggestion is queried, the server contacts the reasoner, makes analysis from the knowledge base and gives the result.

The diet suggestion gives the appropriate amount of carbohydrates, fat, proteins and minerals that the patient can take. However, the model suffers from the disadvantage that it doesn’t consider the treatments and medicines that the patients take for diseases other than diabetes. The model can be further enhanced by providing a food menu that can be consumed by a patient, having the required nutrients.

3 Covid-19

Coronavirus, also known as COVID-19, has been declared a pandemic by the World Health Organization (WHO). Currently, over 220 million confirmed cases and more than 4.6 million have died due to it. In those who have already been infected, this extremely contagious respiratory disease manifests itself in both symptomatic and asymptomatic patterns, resulting in an exponential increase in the number of disease contractions and fatalities.

Bats, cats, and camels are all known to carry coronaviruses. The viruses reside in the animals but do not infect them. However, viruses can sometimes spread to other animal species. As the viruses spread to different species, they may change (mutate). The virus can eventually travel between animal species and infect people. The first person identified with COVID-19 was from Wuhan, China, was most likely to have contracted the virus at a food market that sold meat, fish, and live animals, but scientists are still looking into it. Although researchers aren't sure how people became infected, they know that the virus may be transmitted straight from person to person through intimate contact and immediate treatment is required to lower the effect of the virus.

A Coronavirus Infectious Disease Ontology (CIDO) [15], was devised to provide ontology-based solutions for the causation, transmission, pathogenesis, epidemiology, prevention, diagnosis, and treatment in the domain of coronavirus illnesses. CIDO follows the Open Biomedical and Biological Ontologies (OBO) principles and follows its compatible ontology development techniques. Future work of this model can be applied to vaccinology to develop and analyse the vaccines that eradicate Covid-19.

The Suspected COPD coviDOlogy ontology model was developed from five major ontologies [16] for detecting the patients who have higher chances of being susceptible to Covid-19. The ontologies use the specifications from vital signs, symptoms, service providing mechanisms, alerts and symptom questionnaires.

The generic detection method in this model uses a Semantic Web Rule Language (SWRL) in the Protégé platform for checking any abnormalities in patient data. The model first identifies the vital signs like the presence of fever, temperature and oxygen levels. Suppose the patient has high temperature, fever and low oxygen levels. In that case, the system provides a questionnaire for the patients regarding the other symptoms they are facing to know about their current health state.

The Vital Sign Ontology identifies the major terms like fever, SpO2 levels, sensor data and the medical profile of the patients and defines relationships between them. The Questionnaire Ontology is constructed from the seven questions asked to the patients, like cough, extreme tiredness, lost in taste & smell, diarrhoea, etc. The Symptom Ontology extracts the answers given by the patients for the questionnaire, which is excel data submitted through google forms. The excel data is then stored in the SQL database. The Alert Ontology alerts the healthcare staffs using email/SMS alerts based on the symptom details collected from the patient. The Service Ontology facilitates interaction between the patients to keep the suspected symptoms in control.

The implementation was carried out using Python, ONTYP platform for the considered databases and SQL server. The model was run on thirty patient profiles, out of which 3 were tested positive for Covid-19. The model can be extended for the diagnosis for other health ailments.

Another Ontology for collecting and analysing covid-19 data was developed and the model was termed as CODO (COviD-19 Ontology) [17]. The model facilitated the integration of data from heterogeneous data sources and followed the World Wide Web Consortium standards like SPARQL, RDF, OWL and SWRL. The implementation was made using a knowledge graph constructed based on FAIR Principles (Findable, Accessible, Interoperable, Reusable).

The data from the Indian Ministry of Health and Family Welfare (in an excel sheet) was integrated using the Cellfie Protégé plugin. By using the CODO Ontology, each row was converted into an instance of the Ontology classes. The SPARQL queries were then used to retrieve the people with higher chances of being susceptible to Covid-19.

Traditional Medicine

Traditional medicine encompasses various health practices, strategies, knowledge, and beliefs that include plant, animal, and mineral-related medicines, spiritual forms of treatment, home remedies, and workouts. They are used singly or in combination to cure, detect, and reduce the risk of infection, as well as to preserve health.

India has a very rich heritage in traditional medicine and includes Ayurveda, Siddha, Yoga, homeopathy and Unani. Ayurveda contains huge amount of information in an unstructured form and hence Ontology can play a vital role in helping to understand the information from the unstructured data. A model of Ontology based on Biomedical Text Mining (BTM) [18], [19] was created and was shown to have greater accuracy in classification of medical documents when compared to the machine learning solutions that exist to solve similar problems. The major activities in building the model included text gathering, processing and analysis. The data was gathered from Traditional knowledge digital Library (TKDL), and the medicinal plants taken into consideration were aloe vera, ginger, turmeric, tulsi, etc.,

The data processing was done based on the Natural Language Processing Techniques like tokenization, POS tagging and stemming methods. After data processing, an ontology was constructed using the knowledge base using protégé tool. The documents were then ranked using the tf-idf techniques to determine which medicinal plants can be consumed for the disease encountered. The system can be extended for other traditional medicine systems also.

The Persian Traditional Medicine has a history that goes back to nearly 1000 years. A mobile-based Methontology model [20] was constructed for Persian Traditional Medicine to help the medical specialists and researchers. The model was evaluated for its usefulness by traditional Persian medicine specialists. Two major phases of ontology development and application development were involved.

In the Ontology development Phase, the concepts related to diseases in Persian medicine were extracted from the text books and the conceptual hierarchies were defined.These concepts were then validated and a General Formal Ontology (GFO) based ontology model was implemented followed by the evaluation of accuracy and domain coverage. In the application development phase, a mobile-based application was developed using java, and its working was evaluated using a questionnaire. The limitation suffered by this model was the comparatively low accuracy. The model can be extended by adding more details to the diseases, ontology expansion, and healthcare decision support systems.

Integration of Traditional Chinese Medicine (TCM) to recommendation System [21] was developed based on ontology models. In TCM, each dish has a specific health effect. Therefore, a Dish Ontology Model was constructed to recommend dishes for the health ailment that occurred. The ontology is constructed by using the information like the dishes, current season, the body organs benefitted, taste, cuisine, cooking methods used etc., The rules are then formed based on the ontology model constructed. The recommendation system then returns the Top N dishes that can be considered for consumption by the user.

4 Conclusion

The role of ontology in the biomedical domain is indispensable. By means of ontology semantic meanings of the entities are explored. The data integration and retrieval across various sources becomes faster and easier, aiding in deriving meaningful insights from the data. The Ontology techniques are now effectively being implemented in prescribing personalized medicines to the patients [22], [23]. Many recent advancements in computer science like Virtual Reality, Neural Networks, IoT, etc., [24] – [26] are now combined with ontology engineering process to enhance its functioning. This work can be enhanced by exploring the usefulness of ontologies in domains other than biomedical domain like Enterprise management, semantic web and Artificial Intelligence.

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