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Deep Learning Techniques in Personalization of Medicines and Treatments

[1]Merin Meleet, [2]G.N.Srinivasan, [3]Nagaraj G.Cholli

[1]Assistant Professor, [2]Professor, [3]Associate Professor
[1]Department of Information Science and Engineering,
[1]RVCE, Bangalore,India

Abstract : Modern machine learning tools and techniques are playing a pivot role in the advancements in the area of Personalized medicine because of its ability in dealing with huge amount of unstructured data that is complex and heterogeneous in nature. Personalized medicine refers to providing customised or tailored medication or treatment to individuals by identifying and considering the features like their genomic structure, lifestyle, symptoms, vital statistics etc. A lot of researches are going on in this area in the past few years . This paper intends to provide an overview of the research works happening in this area as applications of deep learning techniques. Main focus has been on major applications like development of new drugs, prediction of therapeutic drugs and identification of disease characteristics. The more popular deep learning techniques that are commonly applied in this domain for specific tasks are also analysed. Successful research works and the research challenges that this area is facing is also discussed which will provide a clarity for future research directions.

***IndexTerms* – Personalised Medicine, Deep learning, Drug discovery and development, Adverse drug reaction, Recurrent Neural Network, Electronic Health records, Long-Short Term Memory**

I. Introduction

Personalised medicine or Precision medicine refers to providing customised, individual treatment plan , given a patient's clinical history, genomic data etc. Personalise medicine is gaining more and more importance over the tradition medicine which follows a "one-fit-for-all" approach with the increasing size of clinical and medical data that characterises a patient's response and genetics. Precision medicine finds widespread application in the treatment of diseases that has a lot of dependency on medical history, genetics and environment like cancer[1], cardiac diseases[2], psychiatric diseases[3] and diabetes[4].

Personalised Medicine includes a huge amount of data from heterogeneous sources and forms – each of these which are unique for every patient. Dealing with huge amount of data like this to finalise an optimal treatment plan is tedious from a physician's point of view. All such data is fed into the system and will reflect the patient's current status .

In recent years, substantial clinical breakthroughs that used machine learning applications have been made that includes disease diagnosis, prognosis, prevention, drug discovery and clinical trial design. One of the most important development in the area of intelligent algorithm is that of Deep Neural Networks. Latest advances in DNNs has made possible the automatic identification of relevant features for prediction and training of large dataset possible. Traditional machine learning have proved to be less efficient than DNNs in handling data that are multidimensional and possessing a higher level of complexity. This paper discusses the different deep learning algorithms, major application areas of research and challenges that are faced.

II. OVERVIEW OF DEEP LEARNING TECHNIQUES

There are a lot of Deep learning algorithms that are being used in the domain of personalization of medicine there days. A few important ones are described below

2.1 Convolutional Neural Networks

In the recent years , CNNs or Convolutional Neural Network based techniques have gained popularity in image processing applications, especially in the area of healthcare. Multilevel hierarchical feature learning is made possible by the suitable architecture of CNN. The initial layers of the network fetches the low level features and the deeper layers extracts the high level semantic features which are put together to find the location of the key points precisely. The CNN architecture comprises of an Input layer, followed by a convolutional layer, pooling layer, a fully connected layer, rectified linear unit (ReLu), and an output layer. The CNN model is built by stacking these layers. Convolutional, ReLu and the pooling layers are responsible for performing feature extraction. The fully connected layer is responsible for the task of classification. Designing an end to end model of this kind improves the recognition of the relationship between the layers[5].

2.2 Recurrent Neural Networks

One good choice of deep neural network to be used when the data is sequentially ordered (like time series data)is Recurrent Neural Network. Sharing of parameters across different time steps and self-loop connections are permitted in RNNs. As shown in Figure 2, an RNN maps a sequence to a sequence. As shown in the figure, if 3 is the length of the input sequence, there are 3 hidden units and single output.

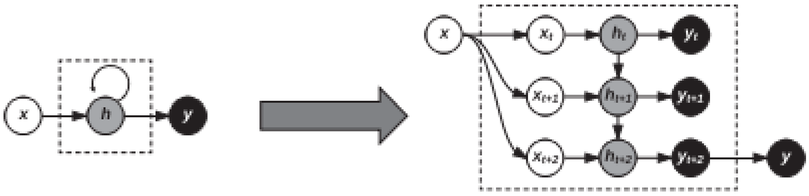

Figure 1: A representation of RNN and expanded representation.

The information cycles through a loop in RNN . Hence the previously received inputs and current input determines the output. Multiple hidden layers with their weights, biases and activation functions constitute the middle layer. For the determination of the gradient, RNNS use back-propagation through time algorithms . This algorithm sums the error at each time the network shares parameters across each layer.

2.3 Long Short Term Memory

One of the advanced type of RNN is called the long short term memory or LSTM and falls under the category of gated RNNs. This was designed to prevent the exploding gradient problems and decaying problem from occurring. Gated RNNs are better at modelling longer term sequential dependencies than normal RNNs. The LSTM has 4 interacting layers that communicate with each other. The main idea behind the LSTM architecture is a memory cell . The cell has the ability to maintain its state over time . It also consists of non-linear gating units that regulate the flow of information into and out of the cell. Figure 2 shows an LSTM Cell.

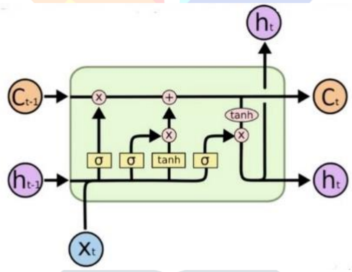

Figure 2: An LSTM Cell

2.4 Autoencoders

Autoencoders are one of the most important algorithms that demonstrates the idea of unsupervised representation learning. It has two components as shown in Figure 3 ,i.e., the encoder and decoder. The encoder is responsible for mapping input values to latent representations and the decoder does the reconstruction of inputs from latent representations.

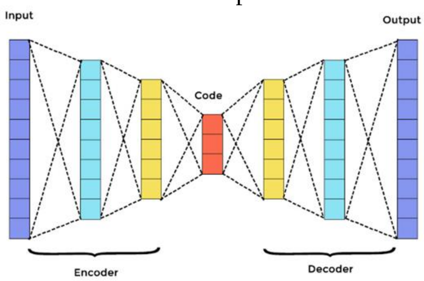

Figure 3: Structure of Autoencoder

Autoencoders are helpful at reducing the noise in data. By the process of compressing and encoding input data and then reconstructing it as output, they reduce the dimensionality and helps focus on areas with real values.

III. Applications in Personalised Medicine

3.1 Electronic health record (EHR) Analysis

The electronic health record data are highly unstructured and extracting information from such data is challenging. The subtasks involved in this task are concept extraction, extraction of temporal events, relation extraction and abbreviation expansion.

Concept Extraction: Jaganatha et al. in their work [6], consider the problem of concept extraction as a task of sequence labelling. The aim was assigning one of the 9 clinically appropriate tags to a word in the clinical text. They divided tags into categories like disease and drug . Each of these categories contained a relevant tag such as name of the drug , its dosage, adverse drug reaction, severity of disease and indication. In their experiments that made use of algorithms like LSTM,GRU, bidirectional LSTMs and several combinations of LSTMs with traditional conditional random field, they found that all the variants of RNNs outperformed the CRF baselines in detecting more restrained attributes like duration and frequency of drugs and severity of the disease.

Temporal Event Extraction: The assignment of notions of time to every concept that is extracted from EHR is the responsibility of this subtask. J.A.Fries [7] introduced a technique/framework that could extract clinical events and their respective times from medical text by means of a standard Recurrent Neural Network that is initialized with word2vec word vectors pre-trained on the inputted text.

Relation Extraction: The relation extraction is related to structured relationships that exist between clinical concepts in unstructured clinical text that includes relations like " a particular treatment can cause/worsen/improve another condition" or " a particular test can reveal a definite medical issue". Authors in [8] used UMLS-based word-to-concept mapping and normal text pre-processing methods combined with sparse autoencoders for the generation of features for input to a Conditional Random Field classifier, that outperformed the state-of-the-art techniques in relation extraction from the given clinical text.

Outcome Prediction: The most simple category of outcome prediction applications is the prediction of a particular outcome without the consideration of temporal constraints. Authors in[9] used the distributed representations in combination with Artificial neural networks and linear models for the prediction of cardiac failures. According to the authors , the best model was a standard Multilayer perceptron that was trained with the embedded patient vectors which outperformed all variants by the use

of raw categorical codes. Researchers in[10] made use of customised RBM architecture to derive patient vectors and then used a logistic Regression classifier for the stratification of suicide risks.

Clinical Data De-Identification : Clinical/Healthcare notes normally contain personal health information which are sensitive and hence it makes public release of such notes difficult. It is mandatory for the document to be made free from such information like patient names, address hospital names, dates etc. In the research work by [11], bidirectional LSTM network was used to create a framework for automatic de-identification of clinical text. This included both word level and character level embeddings.

3.2 DRUG DISCOVERY AND DEVELOPMENT

The Prediction of effectiveness of a drug is one of the most important area of precision medicine. It is very crucial to administer a tailored medical treatment since the reaction of the patient to a drug differ based on different individual's profile. The work by [12] adopts VAE and a semisupervised version to predict the drug response through a comparison of a latent state of genetic representation. Logistic Regression was used to associate Disease and novel drug pair by ranking the accumulative evidence. Another major area of application is that of predicting and preventing adverse drug reactions(ADR). In their research work, [13] designed a Bayesian confidence propagation neural network for the identification of adverse drug reaction in the database. This improved the possibility of sequential and parallel computation, transparency and reproducibility.

3.3 CHARACTERIZATION OF DISEASES

A fast emerging application of personalised medicine is in predicting the recurrence, progression, chance of occurrence, susceptibility and phenotypes of a disease according to an individual's traits. Prediction of a person's susceptibility for a disease is critical since it can help in improving prognosis and can bring down the mortality rate. A study [14] adopted information from clinical data like lab test results, patient history and microarray data for the prediction of survivability in the case of breast cancer. An AUC(Area under ROC curve) of 0.85 was achieved in this work. Another work by [15] used a 3 layer stack of de-noising autoencoder for identifying hierarchical regularities and dependencies in EHR for the generation of patient phenotypes. The method was able to outperform traditional feature learning methods for the prediction of various cancers, schizophrenia.

3.4 THERAPEUTIC EFFECTS

The effect of a drug on a patient varies from individual to individual. Many a times, the most effective treatment plans apart from medication could be mapped to patients on the basis of the profile of the patient. An ensemble method based on the classification of ensembles were developed by [16]. The learning dataset was segregated on a random basis to an optimal number of categories and in each of them, a classification tree was run. The algorithm was used to analyse the genomic datasets on patients with lung cancer and lymphoma for distinguishing disease subtypes. This algorithm was able to perform better than traditional non-ensemble algorithms like random forest , Support Vector Machine, AdaBoost etc. Deep learning is also being applied in detecting patient subgroups, and a reasonable level of performance is being attained.

IV CHALLENGES

Regardless of the several possibilities of machine learning being used healthcare sector, there are several challenges that data scientists and researchers have to go through .For tackling healthcare tasks, there are factors that should be carefully considered during the design and evaluation of such applications. The main factors are discussed below.

4.1 Privacy And Security

Privacy and Security are important concerns in the area of medical domain. Some data cannot be made public due to the requirement of protection of privacy of the patients. The process of training of the model/learning system being built necessitates the distribution of data across patients, and this might breach the principle of security and privacy in the medical community, although sharing with anonymity is a possibility. Sensitive data needs to be masked before any clinical information is made accessible to general public or researchers.

4.2 Heterogeneity Of Data

The heterogeneous nature of the medical data elements and the high volume of unstructured data make clinical care and medical analytics studies difficult. Electronic health record data is available in different forms like handwritten text from the doctors , documents in digital format and printed documents. The deep learning techniques being employed needs to be capable of parsing and understanding such kind of data. There is also a lot of variations regarding the abbreviations and shorthand notations in the medical data that vary from one clinician to another.

4.3 Quality And Size Of Data

When compared to the data from other domains , medical/clinical data are highly heterogeneous, noisy, ambiguous, unstructured and incomplete. It is a challenging task to train a good deep learning model with such huge data sets . It also needs to take into consideration several issues like missing values, data sparsity as well as redundancy. With the wide spread application of EHR systems, more and more data are being stored and required to be properly incorporated to the model.

4.4 Complexity In Computation

Since Deep neural networks possess large depth and width and the data being huge, there is a high requirement on the computing power and computational time

4.5 Intellectual Property Rights

Another important concern in personalized medicine is considering the innovation in the area of medicine and interest. Nevertheless, there are many issues/ problems that are yet to be solved with regard to the patent protection for biomarkers, genes, diagnostic tools etc.

V. CONCLUSION

Recent Machine Learning algorithms, especially deep learning techniques have accelerated the development of personalized medicine in areas like EHR or Clinical record analysis , drug discovery and development, therapeutic effect prediction , disease characteristic identification etc. A variety of algorithms have been adopted by various data scientists and researchers like Artificial Neural Networks, Decision Trees, Ensemble methods MLP, logistic regression etc. As the performance of each algorithm highly depends reliant on the proper tuning of the relevant parameters, different research studies should adopt different processes of tuning that will result in different levels of performance. As the capability of the learning algorithms keeps on improving, with its capability to deal with more complex and unstructured data, we may assume that this domain is developing intensely towards the proper direction, and the multidisciplinary area of machine learning and precision medicine will bring out some excitement in the future.

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