Machines and Networks: How Graphs Bridge Machines with Analytical Processes Towards –Omics Studies

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ABSTRACT

Machine learning algorithm has made its appeal throughout the years as a powerful tool to analyze, develop, and predict how a specific subset of data can function and behave. By implementing other relevant algorithms, such as graph theory, it has made significant improvements, both in algorithms as well as its implementation in the biological field, computational processing, and even business and social studies. The objective of this paper is to give a brief overview of how machine learning implementations work side by side with graph-based learning algorithms to improve and resolve challenges in the mentioned fields.

Keywords: Machine Learning, Graph Theory, Omics, Network-based Learning, Graph-based Algorithms

INTRODUCTION

Scientific and technological advancements throughout the year have aided mankind in terms of life sciences, business, to even social studies. Each progress in the development of related subjects has paved its way towards the new era and phenomenon people known as Big Data. Adapting to the spike of data has pushed the creation of new tools which are equipped especially for the specific task of making sense of all the information and using them for the better good. Such tools revolve around many artificial intelligence (AI) techniques, in particular, machine learning (ML) algorithms (Mahmud, 2018).

Machine learning is defined as the act of giving computers, or machines, the ability to learn without relying on being programmed (Cuperlovic-Culf, 2018). This technique uses experimental data to "train" the machine in clustering or classifying the features extracted from the data for prediction based properties of the system. This is important to handle concerns with the Big Data explosions or when there is a lack of understanding of the data by the expertise at hand (Chicco, 2017). With such complex task, machine learning algorithms need other learning-based methods to achieve its full analytical potentials. Throughout different types of available machine learning algorithms, one method is by implementing graph theory to create graph-based learning methods, which are involved in general and more specific machine learning area (Qiao, 2018).

Graph theory is an algorithm based network and behavioural analysis, consisting of a set of elements called nodes that are linked with an interaction or connections (nodes) (Mijalkov et al., 2017). By doing so, interactions between a wide range of systems in life, such as social interactions to biological networks, can be illustrated and better understood (Mijalkov et al., 2017). Graph processed data analysis uses the presence of significant similarity measurements between two graphs (Yu et al., 2016). This graph-based learning

method is a class techniques applicable in several categories of machine learning, but mainly in two broad range of tasks: supervised and unsupervised learning (Feng et al., 2017).

In this review, the interaction between machine learning algorithm and graph-based learning algorithms is evaluated further in varying aspects of daily life, ranging from omics field and computational field.

METHOD

This study was conducted by literature research on the National Center for Biotechnology Information (NCBI) hosted PubMed database and ScienceDirect database. The relevancy of the paper was maintained by specifying the published date from 2008 to 2018. Pairs or lone keywords are used in the search forms such as ("Machine Learning" "Graph Theory"), "Machine Learning", "Graph Theory", "Graph-based Learning". Constraints used in this study include the lack of each keyword in either title and abstracts of the papers, thus deemed irrelevant towards the study.

MACHINE LEARNING APPROACHES

In this section, the progress and overall approaches of machine learning algorithms and its basic implementation are reviewed. Two conventional studies of machine learning supervised and unsupervised algorithms with a hybrid model of semi-supervised learning will be briefly explained below. As an algorithm, machine learning is tasked with specific objectives revolving around the prediction, modelling, forecasting, and evaluation of the data (Guégan & Hassani, 2018). There are some implementations of this model, which are:

- Regression analysis (Guégan & Hassani, 2018): A regression model aimed to analyze categorical data. Iterative approaches improve the model relationships between the features and labels using error measures (Cuperlovic-Culf, 2018).
- Decision Tree Algorithms (Cuperlovic-Culf, 2018): A model which trains the datasets for classification and regression analyses towards a flowchart-like model to predict the outcomes of the data.
- Bayesian Algorithms (Cuperlovic-Culf, 2018): The use of Bayes' theorem for the probability of classification and regressions.
- Artificial Neural Networks (Prieto et al., 2016): A model based on the human brain first created to understand the nervous system and construct information by mimicking the natural biology of the brain.
- Support Vector Machines (SVM) Classifications (Sacchet et al., 2015): Supervised learning models which focus on specific patterns analysis, combined with classification and regression analysis.

Supervised Learning

Features selection in the supervised learning algorithms uses data or training sets which have been previously labelled for the machines to learn, classify, and test the given data. This method of the algorithm is often oriented to classify the problems and correlates the features of the data class for its fundamental proposition (Schrider et al., 2018), aiming to find the optimal data or subset feature that maximize the classification accuracy (Cai et al., 2017).

One model of machine learning which uses this method is the Support Vector Machines (SVM) model. This model has been popular in the reconstruction of biological

imaging data such as MRI images (Wang & Fernandez-Gonzalez, 2017). Out of the other supervised machine learning models, SVM is relatively easy to implement due to a number of programming libraries available which facilitates this method (Wang & Fernandez-Gonzalez, 2017).

Unsupervised Learning

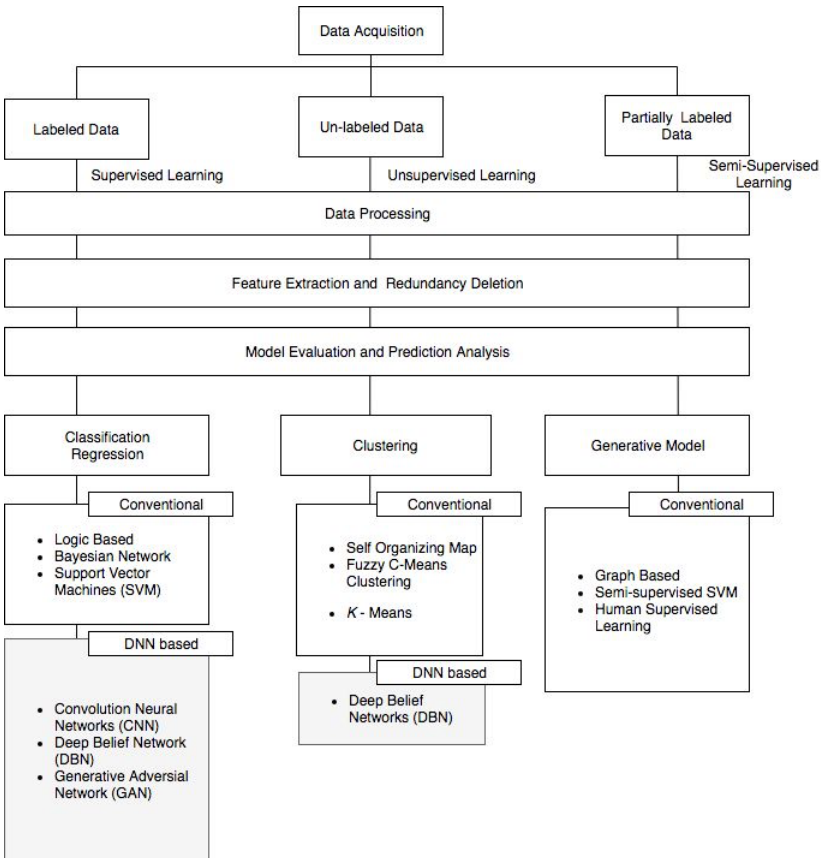
Compared to supervised machine learning algorithms, unsupervised learning tries to identify features in the data without the use of testing inputs from the users. Unsupervised learning organizes and clusters the data by the statistically independent group without a previous understanding of information of the data (Bowd et al., 2014).

One implementation of this model is the Independent Component Analysis (ICA) classification method which reveals a single set of random variables (Bowd et al., 2014). ICA algorithms managed to significantly reduce noise in a wide range of applications, from medical uses such as electroencephalographic data for the brain to even social study data such as social network analysis (Bowd et al., 2014). Frequently used ICA algorithms utilize "maximization of independence of non-Gaussianity (Fast ICA)" or "minimizing mutual information (InfoMax)" (Xie et al., 2018). The use of this specific unsupervised learning methods is usually implemented in functional MRI (fMRI imaging to better categorize brain networks (Ribeiro de Paula et al., 2017).

Semi-Supervised Learning

This algorithm is a combination of the two conventional algorithm model previously explained. This hybrid model uses both labelled datasets from supervised learning and unlabeled datasets from unsupervised learning for the training process to produce classifiers that out-performs unsupervised and supervised learning alone (Stanescu & Caragea, 2015).

The basic principle in semi-supervised learning is to leverage intrinsic features of the unlabeled data to strengthen the prediction ability of the supervised learning model, thereby giving advantages for the semi-supervised learning (Stanescu & Caragea, 2015). However, considering the limitations of both supervised and unsupervised learning, semi-supervised learning models may not always work as intended; it may even perform worse than supervised and unsupervised learning models under incorrect assumptions (Stanescu &



Caragea, 2015).

Fig.1: Diagram depicting the specification of each machine learning models.

GRAPH-BASED LEARNING APPROACHES

As explained before, graph theory is the study of behavioural analysis of networks (Mijalkov et al., 2017). This network-based interaction could indicate and visualize a wide range of natural or biological interactions in life ranging from computer science, engineering, social science, even understanding biological interaction networks (Pavlopoulos et al., 2011). The most important thing to consider when dealing with graph theory or graph-based learning is the relationships between the two objects interconnected with each other in the same networks (Yu et al., 2016).

There are two general methods to represent the relationships between two networks in the graph: graph edit distance (GED) and graph kernel (Yu et al., 2016). GED computes the distance between two graphs by considering the insertion, deletion, and substitution of vertices and edges that will transform the first graph into the second graph with minimum cost (Abu-Aisheh et al., 2017). On the other hand, the kernel is specialized in measuring the similarity between two available graphs by mapping the graph kernel to a higher dimensional vector (Yu et al., 2016).

In machine learning fields, graph-based learning is a popular approach for data mining activities especially in unsupervised clustering method, semi-supervised learning, and manifold learning (Wang et al., 2013). Conventional graphs, such as the *k*-nearest neighbours and fully-connected Gaussian Radial Basis Function (RBF) graphs, use Euclidean distance counting for the analysis of each edge, counting in data space (Feng et al., 2017). However, high-dimensional data and those with a significant amount of noise might result in a distorted graph, thus enabling it to be useless.

APPLICATIONS TO OMICS FIELD

As a comprehensive and powerful tool, machine learning algorithms based on graph theory excels at finding interactions between biological network systems such as those used in the integrated system biology in *Omics* (fields consisting of genomics, proteomics, or metabolomics). This section will give a brief progress of graph-based algorithms within machine learning in each *Omics* field.

Genomics

Large-scale genomics data and sequencing technologies have paved their way to revolutionize the way genomics is viewed in the world of research. These advancements have aided researchers in understanding clinically relevant diseases such as cancer biology for personalized medicine. More network-based tools are needed to understand the biological interactions of the cancer pathways or subnetworks by integrating various widely available genomics data (Zhang et al., 2017). Precision oncology treatment has then been lifted by the emergence of network-based machine learning methods, for example, for drug-drug similarities clustering pipeline, genomics profile of the patients, and drug disease phenotypes modelling in a network (Zhang et al., 2017) as seen in Figure 2.

Proteomics

Numerous protein interaction happens simultaneously and continuously inside the biological system. Understanding the protein-protein interaction (PPI) networks helps us to understand how different proteins operate and coordinate with each other to enable fully functioning biological processes (Pavlopoulos et al., 2011). This interaction between proteins helps researchers understand molecular interactions of the cell. With the help of graph-theory-based algorithms and data mining machine learning techniques, the interaction of each protein can be visualized to give an understanding of more complex interaction such as the one in cancer (Shen & Guda, 2014). Two major group of graph-based algorithms for proteomic studies, more specifically the protein-protein interactions, are graph comparison and module detections (Shen & Guda, 2014).

Patterns in protein interactions can be approached with machine learning statistical analysis and graph-based network interactions to make prediction outside of the given training datasets such as the prediction algorithm used in protein-ligand binding predictions (Colwell, 2018).

Metabolomics

Metabolic functions in the cell vary and thus providing complex pathways which when irritated, could lead to the collapse of biological systems. Network-based analysis and computational methods can help to build, interpret, integrate, and even predict molecular network interactions inside a living biological host function (Chasman et al., 2016). Building network-based predictive models of complex phenotypic interaction are becoming a major goal in the study of metabolomics as a whole (Chasman et al., 2016).

Bayesian network classifiers in machine learning are one of the effective methods to create a prediction based on the dataset given for regulatory networks (Yin et al., 2015). Recently, a tree-like Bayesian network classifier was found and implemented for small sample size and modified to better understand how regulatory networks and biological datasets function with few observations (Yin et al., 2015).

APPLICATIONS TO BREAST CANCER PROGNOSIS

Breast cancer is the most common type of cancer in women and has contributed to the total number of women's death worldwide. Classification of the breast cancer tumor revolves around Benign cases (Non-cancerous) and Malignant (Cancerous), though both can possess the same danger to the patient (Nahid & Kong, 2017). Trained medical personnel commonly rely on technologies such as ultrasound, MRI, or X-ray to visualize cancer image which can be used to classify and find the cancer stage and status, however, the need for a more accurate image classification technique or simply act as a second opinion is needed to save time (Nahid & Kong, 2017).

Machine learning technique has always been known for its accuracy for classification such as this case. A number of widely used method for image classification includes Convolutional Neural Network (CNN), Neural Network (NN), Random Forest (RF), and newer semi-supervised learning methods. The semi-supervised learning method, as previously mentioned above, utilize both supervised and unsupervised learning method. Combining graph-based learning with semi-supervised learning as reported by Li et al (2011) has improved image classification of the Wisconsin Prognostic Breast Cancer (WPBC) dataset to up to more than 92% compared to other semi-supervised learning methods.

APPLICATIONS TO COMPUTATIONAL FIELDS

Security in the age of digital revolution is a concern especially if the data inside a network or server holds a sensitive information. However, sometimes people do not realize this risk. Take for example the internet. The Internet has become an essential tool in daily life today and connects people together for entertainments, business, education, etc. With that daily usage, risks of the networks being attacked and loss of data can and will happen.

Anomaly detection for any security risk is thus important to predict the probability of a network being attacked and intruded. Or, misuse of this pattern information can be used to detect weak points in a network for hackers to invade (Tsai et al., 2009). To help prevent this intrusion, machine learning-based methods and graph learning methods can be implemented to predict and find patterns for intrusions (Tsai et al., 2009).

Neural networks are used in this example due to its similarity in computer networks and how it functions and interact with one another throughout. Other method includes the *Naïve Bayes networks* model. This model is important especially for instances where probabilistic relationship among the variables is difficult to be expressed (Tsai et al., 2009). This model uses a graph like structure called the directed acyclic graph (DAG) to represent the interaction between each node as a system variable and how they influence one another inside a network overall (Tsai et al., 2009)

CONCLUSION

Machine learning as a field holds promising future prospects towards a wide range of field applications. The implementation of graph-based learning and graph theory into the algorithm of machine learning has made machine learning a more powerful and versatile tool in analyzing, clustering, and prediction of data itself. Due to their numerous uses, machine learning and graph-based learning implementations are evolving and expanding even more to provide better and more versatile application for data feature.

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