Machine learning applications to Covid-19: a state-of-the-art survey

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***Abstract*—There exists a large and rapidly growing body of literature related to applications of machine learning to Covid-19. Given the substantial volume of research, there is a need to organize and categorize the literature. In this paper, we provide the most up-to-date review as of the beginning of 2022. We propose an application-based taxonomy to group the existing literature and provide an analysis of the research in each category. We discuss the progress as well as the pitfalls of the existing research, and propose keys for improvement.**

***Index Terms*—machine learning; Covid-19; deep learning; LSTM; CNN; review**

I. Introduction

The Covid-19 pandemic has had a devastating effect on the social and economic lives of people around the world. In response to the pandemic, the scientific community has focused its energy to create solutions against the virus. In particular, there has been a considerable effort to apply machine learning and artificial intelligence to issues related to Covid-19 [2]. There are currently over 500 related research articles discoverable through Google Scholar. Given the large amount of research, there is a need to organize and summarize the existing body of literature.

Our goal in this paper is to review and analyze the existing research related to applications of machine learning to Covid-19. The Covid-19 research is ongoing with dozens of new articles published on a weekly basis. Researchers are continuously improving on the existing results. Our review differs from others in that we provide the most up-to-date coverage as well as a new taxonomy of the literature.

We divide the existing literature into three major groups: i) detection, ii) forecast, and iii) drug discovery. Each major category is further divided into subgroups. Detection and diagnosis is by far the largest category of machine learning research in Covid-19. The recent advances in computer vision have allowed researchers to detect the presence of the disease based on chest X-ray images and CT scans. It has been a productive research avenue with some studies achieving close to 100% accuracy in classifying patients based on lung imaging. Forecasting the number of new cases has also received considerable attention. Researchers have applied various deep learning techniques such as long short-term memory and graph neural network to build forecasting models. Finally, AI-powered search for new drugs against Covid-19 has been undertaken albeit with limited success. It is the newest research avenue with promising outcomes.

The analysis of the literature reveals several promising research avenues. In particular, the AI-based detection methods have achieved impressive results. Despite the encouraging results produced by many studies, machine learning algorithms are not yet ready for deployment due to limited test data. Furthermore, rigorous clinical trials are required before approving the use of machine learning methods in practice.

Our paper is structured as follows. Section 2 describes the proposed taxonomy for organizing the existing research. In Section 3, we review the machine learning research related to detection and diagnosis. In Section 4, we review the research related to forecasting. Section 5 discusses the research related to drug discovery. Section 6 concludes the paper with a discussion of challenges and potential solutions.

II. Literature taxonomy

There exists a large volume of literature related to machine learning and AI applications to Covid-19. There is a need to organize and categorize the existing research in order to facilitate its understanding. To this end, we propose application-based taxonomy. In particular, Covid-19 related research can be grouped into three major categories according to the field of application:

1) Detection and diagnosis of the disease
2) Forecasting the number of cases and deaths
3) Search and discovery of potential cures

The three categories of research given above are listed according to the level of activity. Detection and diagnosis comprises by far the largest portion of the research related to Covid-19, while forecasting and drug discovery are the second and third active fields, respectively. The main reason for the popularity of the detection methods is the recent advances in computer vision which allow for highly accurate X-ray and CT scan image classification. Forecasting the number of new cases and deaths has also garnered considerable attention from researchers. In general, machine learning-based forecasting is an active area of research and it is not surprising to find its applications to Covid-19. Finally, AI-based drug discovery is an emerging field of research.

As shown in Figure 1, detection and forecasting categories can be further divided into subgroups. The research related to Covid-19 detection is divided into imaged-based and symptom-based approaches. The image-based approaches employ X-ray and CT scan images of patients' lungs to identify the presence of the disease, while the symptom-based approaches rely on clinical assessment results to identify Covid-19 cases. Forecasting methods are grouped according to the models: long short-term memory (LSTM), convolutional neural networks (CNN), and graph neural networks (GNN). Drug discovery research is not sufficiently advanced to warrant additional categorization.

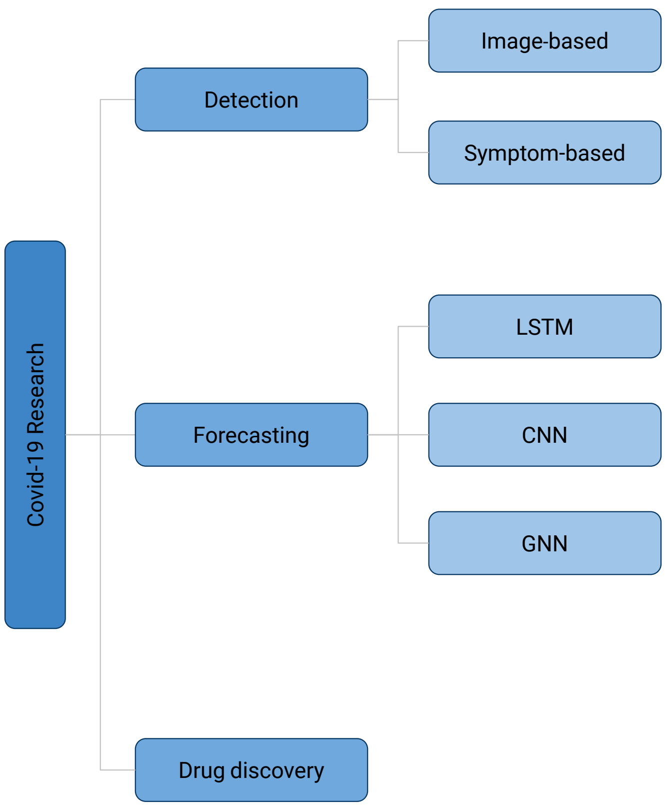

Fig. 1: Deep learning models.

Although there are also other avenues of machine learning research related Covid-19, we find them to be underdeveloped and too early to be considered. For instance, several researchers have proposed intelligent contact tracing albeit with limited success. It is possible that with time new fields of research related to Covid-19 will emerge and a new taxonomy will be required.

III. Detection and diagnosis

Covid-19 detection and diagnosis has been the most active area of research in machine learning. There are over 300 articles discoverable on Google Scholar related to this topic. As shown in Figure 1, detection methods are divided into image-based and symptom-based approaches. Image-based approaches utilize X-ray and CT scan images, while symptom-based approaches utilize the results of clinical observation.

A. *Image-based detection*

Image-based detection methods use X-ray and CT scan images of patient lungs to determine the presence of the Covid-19 virus. Since the images of affected lungs contain abnormal patterns, computer vision algorithms can automatically distinguish between positive and negative cases. Given the tremendous advances in computer vision over the last decade, the image-based detection methods have been able to achieve a high level of accuracy.

There are two main approaches to image-based detection based on the image preprocessing stage:

1) feature extraction
2) transfer learning

In the first approach, the relevant features are extracted from the image and passed on to the classifier. Feature extraction is performed either manually or via machine learning algorithms such as Isomap [19], [50] or principal component analysis In the second approach, a pretrained deep learning model is applied to images before further processing. The authors in [14], applied the first approach to identify Covid-19 cases based on the X-ray images. Their method employed Fractional Multichannel Exponent Moments together with a special optimization technique to select the optimal features. The proposed method achieved accuracy rates of 96.09% and 98.09% on two datasets. In [6], the authors utilized U-Net models, trained for segmentation of lung and Covid-19 lesions, to quantify CT scans in terms of lung volume, lesion volume, nonlesion lung volume, and fraction of nonlesion lung volume. The extracted features were used as inputs to the random forest classifier to assess the severity of the disease. The proposed model achieved area under the ROC curve (AUC) 0.927. The authors in [27] used dimensionality reduction to extract relevant features that were passed to a deep learning classifier to distinguish between Covid-19 and other types of pneumonia. Feature extraction in conjunction with several machine learning models was considered in [43]. The authors found that while k-NN and SVM attained high accuracy in detecting positive cases of Covid-19, K-ELM achieved the highest overall accuracy.

The second approach, based on transfer learning, allows to overcome the issue of small training sets that is frequently encountered in Covid-19 datasets. Transfer learning can be implemented in two different ways: i) use a standalone pretrained model to extract features or ii) train the final layers of a pretrained model on new data. In the standalone approach, the images are passed through a pretrained model and the output is taken as the new dataset which is then used to train a separate classifier. In the built-in approach, the initial layers of a pretrained model are frozen, while the final layers are trained on the image data. Transfer learning together with a convolutional neural network (CNN) was utilized in [1] to classify X-ray images as positive or negative for Covid-19. In particular, the authors utilized a CNN that was pretrained on ImageNet dataset to train the new set of X-ray images. The proposed method achieved top accuracy, sensitivity, and specificity of 96.78%, 98.66%, and 96.46% respectively. In [24], the authors compared several combinations of pretrained models and classifiers. In particular, the authors considered pretrained models Xception, ResNet, and others for initial preprocessing of X-ray and CT scan images. Afterwards the processed images were fed into several classifiers to identify the best method. The combination of the DenseNet121 feature extractor with bagging tree classifier achieved the best performance with 99% classification accuracy. In a similar study by [47], the authors considered 5 pre-trained deep learning models for transfer learning of X-ray images. The results showed that the Xception pre-trained model together with the SVM classifier achieve the optimal accuracy in identifying the Covid-19 cases. It was shown in [42] that CNN-based ensemble methods are also capable of producing robust results.

Detection and diagnosis continues to be an active area of research as of the beginning of 2022 [5], [12], [36], [46]. In a recent study, the authors proposed a 3-step procedure to classify Covid-19 X-ray images [5]. The proposed method consists of image segmentation using a conditional generative model, followed by a key point extraction of the X-ray images, followed by various classifiers. The best performance was obtained using VGG-19 classifier achieving accuracy of 96.6%. In another recent comparative study, the authors employed transfer learning based on Alexnet. The processed X-ray images were then given to several machine learning to classify Covid-19 cases [46]. The results show that SVM produces the optimal results achieving accuracy of 86%.

Although image-based detection methods have achieved impressive performance, with up to 99% accuracy rates, they are rarely utilized in production. The main obstacle in their deployment is the insufficient sample size which makes the accuracy results unreliable [41]. To obtain deployment-ready methods, the machine learning models must undergo a more rigorous testing procedure. In addition, the cost of implementing image-based detection methods must be considered. While X-ray is usually a cheap procedure, CT-scan is more expensive. A cost-benefit analysis relative to other detection methods such as the polymerase chain reaction (PCR) test must also be performed in deciding whether to adopt new technologies.

B. Symptom-based detection

Symptom-based detection methods utilize clinical data to determine the presence of Covid-19 virus in patients. It has been shown that even such basic symptoms as loss of smell and taste can accurately predict Covid-19 using machine learning techniques [8]. The authors in [3] compared five machine learning algorithms - multilayer perceptron (MLP), random forest (RF), gradient boosting decision trees (GBDT), logistic regression and support vector machines (SVM) - to diagnose Covid-19 patients based on symptoms at the time of admission to the emergency clinic. The study found that the SVM classifier produced the highest accuracy with AUC of 0.85. A more extensive study - based on dataset consisting of 8 basic clinical features - was conducted in [52]. Using the gradient boosting algorithm the authors were able to achieve AUC of 0.90. As shown in [29], it is feasible to diagnose Covid-19 based on routine blood tests. The authors attained AUC of 0.97 using the XGBoost algorithm based on routine blood samples. The authors in [49] considered only three basic criteria - age, gender, and nationality - to classify Covid-19 patients. A comparison of four machine learning algorithms - MLP, RF, SVM, and GBDT - based on the above criteria showed that the RF algorithm achieves the highest AUC of 0.63. A combination of IoT technologies and machine learning was proposed in [38] for real time monitoring of the symptoms of Covid-19.

In a recent study, the authors employed an ensemble classifier to construct a model based on patient symptoms [31]. The proposed model achieved 97.88% overall accuracy in predicting the occurrence of disease. In another recent study, the authors compared the performance of several machine learning models to identify Covid-19 based on the patient symptoms [34]. The study found that Naive Bayes and decision tree classifiers produced the best performance with accuracy of 93.70%, while SVM, k-nearest neighbors, and logistic regression, achieved accuracy of 93.60%, 93.50%, and 92.80% respectively.

Although symptom-based approaches have attained impressive results, there is still room for improvement. As study by [7], showed that symptom-based approaches do not always perform well in diagnosing Covid-19.

IV. Forecasting

Forecasting the number of Covid-19 cases is an important avenue for research. Accurate forecasting helps public health officials to enhance their policies to manage the pandemic. As a result, a significant amount of research has been dedicated to forecasting [23], [40]. There are several machine learning techniques that have been utilized to construct forecasting models. As shown in Figure 1, the three main deep learning forecasting models are

1) Long short-term memory networks (LSTM)
2) Convolutional neural networks (CNN)
3) Graph neural networks (GNN)

LSTM has been the most popular forecasting framework for the number of Covid-19 cases. The LSTM design was originally proposed by Hochreiter et al. [17]. It is designed specifically to handle sequential data. In LSTM, predictions from the previous time steps are used together with the current inputs to make the prediction for the current time step. LSTM has been used successfully for various sequential tasks such as speech and handwritten data. Therefore, it is not surprising to see its application in forecasting the number of Covid-19 cases.

The LSTM forecasting model was used as the primary approach in several studies [15]. LSTM and its variants have also performed well in several comparative studies [9], [11], [20], [45]. The authors in [35], demonstrated that LSTM produced greater accuracy than CNN and MLP in forecasting Covid-19 in Egypt. The study used data over the period 14/02/2020 - 15/08/2020 and utilized the window size of 20.

Similarly, a large scale study by [48] compared LSTM with MLP and ARIMA using 12-month data for 171 countries. The study found that in the majority of cases LSTM outperforms other models.

CNN is another traditional deep learning model that has been utilized in Covid-19 forecasting. In CNN, a sliding array of values is used to convolute with the input sequence. It is akin to calculating the weighted mean of segment of the sequence. The goal is to capture local relationships between the values in the sequence. Although CNNs are used primarily in image recognition [13], they have also been utilized in forecasting. While the CNN-based models were able to achieve high accuracy rates in some studies, they still lag behind the LSTM models. The author in [18] compared the performance of several forecasting models based on a large dataset of 266 countries over the period of 22/01/2020 - 30/06/2020 and found that CNN achieves the optimal results. Similarly, the authors in [37], compared CNN, LSTM, MCNN, and GRU models on data from Russia, Brazil, and the UK over the time period 01/01/2020 - 18/11/2020 and found the CNN to be the most accurate forecasting model.

GNN is a relatively new architecture that is used for data with graph structure [44]. Graphs consist of nodes connected by edges. As such, geographical distribution of Covid-19 cases can be modeled as a graph. One approach is to model the cities as the graph nodes and assign the edges between the cities based on the pairwise distances. Since the spread of the infection has a geographical component, utilizing the graph structure on the data provides additional information. The graph structure has potential to provide a better model than simply using the raw data. Indeed, the most accurate current forecasting models are based on GNN. A research team from Google used GNNs together with spatio-temporal data to forecast the pandemic in the US during 02/2020 - 05/2020 [25]. In the proposed model, the graph nodes represent the region-level human mobility. There are also two types of edges: spatial and temporal. The spatial edges represent the mobility based inter-region connectivity, while the temporal edges represent node features through time. The study showed that the proposed GNN forecasting model outperformed LSTM achieving 0.9981 correlation between the true and forecasted values of the time series. In another spatiotemporal approach [33], the authors captured the spread of the disease in time and space based on the weekly number of new positive cases as temporal input, and hand-engineered spatial features from Facebook movement and connectedness datasets. The US county-level predictions using the model over 1 to 4 week horizons outperformed the existing state-of-the-art models.

V. Drug discovery

AI-powered search for novel drugs and chemicals is a relatively new yet active area of research in machine learning [16]. One approach is to model infected cells by changing the levels of sugar and oxygen exposure and track their lipid, metabolite, enzyme and protein profiles. The resulting biological and outcomes data is fed into an AI model to learn differences between diseased and healthy cells. Another approach is to employ an AI model to create a knowledge representation based on data from sources such as research papers, patents, clinical trials and patient records. Then the model can be queried to obtain the most salient information for drug-discovery scientists [32].

There have been several attempts to apply machine learning techniques to help find appropriate medicines for Covid-19 [2], [26], [51]. In [10], the authors employed molecular fingerprints together with gradient-boosted trees to identify the best repurposing candidates among FDA-approved drugs based on their predicted antiviral activity against Covid-19. The study found that Zafirlukast could be a potent drug against the Covid-19 virus. The authors in [4] used deep learning drug–target interaction model to identify commercially available drugs that can target SARS-CoV-2-related proteins. A deep learning algorithm to repurpose drug compounds named DeepCE was proposed in [39]. The authors showed that DeepCE can be used to identify potential leads for Covid-19 treatment. In another study, a machine learning model was constructed to determine new indications for existing drugs and herbal compounds based on 1330 positive drug-disease associations [28].

VI. Challenges and solutions

The main challenge in applying machine learning methods to Covid-19 is the lack of appropriate data. The issue of data availability is twofold: i) general scarcity and ii) imbalanced distribution. First, machine learning algorithms require large amounts of data for training which is problematic in case of patient health records. Second, the Covid-19 data is often skewed towards the negative cases creating an imbalanced dataset. Resolving the issue of data availability will have a significant positive effect on research.

Due to patient privacy concerns, there is a general lack of Covid-19 related data. The lack of data impedes efficient training of machine learning models. Machine learning algorithms, especially deep learning models, require large amounts of data to train their model parameters. Modern deep learning models contain millions of parameters which provides them with great flexibility to fit the data. Therefore, given a small dataset, a deep learning model will overfit the data and fail to generalize. To avoid overfitting, a large number of training samples is required. For instance, the ImageNet dataset employed in computer vision algorithms contains over 1 million training samples while the majority of Covid-19 X-ray images consist of only a few thousand images. Consequently, the efficacy of machine learning methods is significantly diminished.

The second major issue with the existing data is the imbalanced distribution of class labels. Since the vast majority of individuals are healthy (negative) only a small portion of data is positively labeled which leads to skewed class distribution of the patient data. Imbalanced data results in classification bias. Since the objective of a classifier is to maximize the overall accuracy, it will focus on learning the majority labels at the expense of the minority class. There exist several approaches to dealing with imbalanced data including sampling where the number of minority points is increased to the level of the majority points [21], [22]. The authors in [30], utilized SMOTE to balance a set of X-ray image data before analyzing it with a deep learning model. Nevertheless, it is difficult to completely eliminate the issues related to imbalanced data.

The issue of data availability must be addressed in order to improve applications of machine learning for combating pandemics in the future. The government plays an important role in facilitating the collection and dissemination of clinical data to the research community. A quick and easy access to the data will have a significant positive effect on the success of future research.

At the ground level, researchers can employ two basic techniques to deal with the lack of appropriate data. First, transfer learning can be utilized to mitigate the issue of small training set. In particular, a classifier that has already been trained on an external large dataset can be employed for training on the new, smaller dataset. Second, sampling algorithms can be applied to balance skewed class distributions.

Machine learning and artificial intelligence have potential to help fight the current and future pandemics. There are several research avenues related to the current pandemic including detection, forecasting, drug discovery, and others. Researchers have achieved impressive results. However, the proposed methods require further testing before deployment in production.

VII. Conclusion

In this paper, we presented a concise survey of the existing applications of machine learning related to Covid-19. We divided the literature into three major categories: detection, forecasting, and drug discovery. We discussed popular approaches in each field and the latest results. Our analysis highlights several issues in the existing research and provides potential remedies.

In the future, a more in-depth analysis of each category is warranted. Comparison of different studies within each field would provide a better understanding of the field. Furthermore, a more expanded search which includes articles from a wider range of sources will provide a better insight of the current advances.

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