REVIEW ARTICLE



Deep Learning Applications to Combat Novel Coronavirus (COVID-19) Pandemic

Amanullah Asraf¹ · Md. Zabirul Islam¹ · Md. Rezwanul Haque¹ · Md. Milon Islam¹

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Abstract

During this global pandemic, researchers around the world are trying to find out innovative technology for a smart healthcare system to combat coronavirus. The evidence of deep learning applications on the past epidemic inspires the experts by giving a new direction to control this outbreak. The aim of this paper is to discuss the contributions of deep learning at several scales including medical imaging, disease tracing, analysis of protein structure, drug discovery, and virus severity and infectivity to control the ongoing outbreak. A progressive search of the database related to the applications of deep learning was executed on COVID-19. Further, a comprehensive review is done using selective information by assessing the different perspectives of deep learning. This paper attempts to explore and discuss the overall applications of deep learning on multiple dimensions to control novel coronavirus (COVID-19). Though various studies are conducted using deep learning algorithms, there are still some constraints and challenges while applying for real-world problems. The ongoing progress in deep learning contributes to handle coronavirus infection and plays an effective role to develop appropriate solutions. It is expected that this paper would be a great help for the researchers who would like to contribute to the development of remedies for this current pandemic in this area.

Keywords Novel coronavirus · COVID-19 · Pandemic · Deep learning · Diagnosis

Introduction

The novel coronavirus was first detected in December 2019 and spread around the globe rapidly. Now, it has affected almost every country with forty million confirmed cases and more than a million deaths on 18th October 2020 [1]. It has

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Md. Milon Islam milonislam@cse.kuet.ac.bd

> Amanullah Asraf amanullahoasraf@gmail.com

Md. Zabirul Islam zabir.kuet.cse@gmail.com

Md. Rezwanul Haque rezwanh001@gmail.com

¹ Department of Computer Science and Engineering, Khulna University of Engineering & Technology, Khulna 9203, Bangladesh created a tremendous impact on healthcare facilities as well as an economic crisis. To prevent the spread of COVID-19, several national governments have introduced 'lockdown' to measure 'social distancing' and 'isolation' guidelines that limit the movement of people [2]. The coronavirus symptoms can range from cold to fever, as well as acute respiratory illness [3]. The infection of coronavirus is transmitted predominantly via droplets [4].

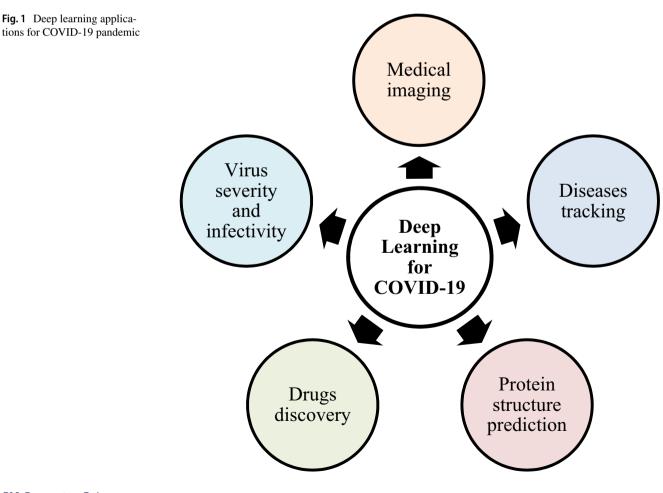
From the time of civilization, several diseases like heart disease [5], diabetes [6], liver disorder [7], breast cancer [8–10], COVID-19 [11–13], etc. caused severe and acute actions on human health, and artificial intelligencebased systems show better performance to identify those diseases. Fighting against COVID-19, modern technologies are playing significant roles in the development of a smart healthcare system [14, 15]. For example, a facial recognition system is used to trace the infected patients, and robots are used to deliver food and medicine in hospital and drones are applied to disinfect streets [16, 17]. Besides, the researchers around the globe are looking for emerging technologies to monitor and control this virus. Deep learning is such a technology that can be able to diagnose COVID-19 infected patients using radiological images and also used to discover new drugs and medicine so that it can recover infected patients and also utilized to produce a vaccine.

This paper focuses on the contributions of deep learning techniques to fight against the global pandemic. It provides a comprehensive review of deep learning applications that support the world healthcare system by reducing and suppressing the epidemic's impact. The most recent applications are described throughout the study. The current challenges of existing systems with potential future directions are also outlined in this paper.

The remaining parts of the paper are arranged as follows. "Deep Learning Applications for COVID-19" described the most recent applications of deep learning techniques to combat ongoing pandemic in detail. The summary of the reviewed works is depicted in "Discussions". In addition, the challenges of existing systems with possible future trends are demonstrated in "Discussions". Lastly, "Conclusion" concludes the paper.

Deep Learning Applications for COVID-19

Deep learning is a subset of artificial intelligence that contains multiple layers to analyze data. In this model, data are filtered through several layers, where each successive layer using the output of the previous one to produce its output. The analysis of biomedical and healthcare problems helps medical professionals and researchers to find out the new scope for serving the healthcare communities. The detection of COVID-19 at an early stage and isolation of the affected people from others is the most crucial step in controlling this pandemic due to high transmissibility. The reverse polymerase chain reaction (RT-PCR) is considered as a key indicator [18] to diagnose COVID-19 cases; however, it is a time-consuming process with a high false-negative rate. Deep learning focuses on medical imaging, disease tracking, protein structure analysis, drug discovery, and virus severity and infectivity to combat coronavirus. Figure 1 shows several applications of deep learning for the COVID-19 pandemic. In recent studies, several works are found that used deep learning techniques to control COVID-19. The recent applications of deep learning are outlined as follows.



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Medical Imaging for Diagnosis

With the rapid spread of COVID-19, there is growing interest in alternative methods for diagnosing coronavirus infection using medical imaging. Deep learning techniques have been used to process and analyze X-rays as well as computed tomography (CT) to help the doctor to predict COVID-19 infection [19, 20]. Several works are introduced, focusing on the detection of coronavirus using deep learning. Wang and Wong [21] proposed a convolutional neural network-based system named COVID-Net to distinguish COVID-19 cases from others by analyzing lung conditions from X-ray images. A modified Inception model is introduced for extracting the feature of COVID-19 using CT scans with 89.5% accuracy [22]. A 3D deep learning system based on the location-attention mechanism is developed to identify infected regions of COVID-19 patients utilizing CT scans. The system achieved 86.7% accuracy for differentiating COVID-19 pneumonia from Influenza-A viral pneumonia [23]. For the detection of coronavirus, a deep neural network is trained on CT images to distinguish infected parts from other lung diseases [24]. Song et al. [25] developed a ResNet architecture to extract complex features from CT samples and merged a feature pyramid network with an attention module for the classification of COVID-19. A diagnosis system is introduced to identify coronavirus symptoms utilizing CT scans to separate COVID-19 cases [26]. Islam et al. [27] proposed a combined Convolutional Neural Network (CNN) and Long Short-Term Memory (LSTM) architecture to identify coronavirus infected patients from chest X-rays. The deep learning applications for medical imaging-based COVID-19 diagnosis are summarized in Table 1.

Disease Tracking

Deep learning techniques are frequently applied to track the spread of COVID-19 infection over time and space. Instead of medical imaging, depth camera footage can be used to analyze respiratory patterns to predict tachypnea [28]. The researchers applied bidirectional Gated recurrent unit (GRU) and attentional techniques to forecast tachypnea that could be a first-order diagnostic feature to contribute large-scale screening of COVID-19 patients. Smartphone sensors are utilized to find COVID-19 symptoms based on a deep learning algorithm to track the COVID-19 pandemic [29]. Ye et al. [30] introduced α -satellite to identify geographical risk assessment at community levels. The large-scale real-time data are applied to deep neural networks to learn the public perceptions and estimated the risk level. A forecast model based on LSTM networks is developed to predict the trend of the COVID-19 outbreak in Canada [31]. Dutta et al. [32] presented a combined LSTM and GRU model to measure positive, negative, death, and release cases of COVID-19 for estimating the position of the current epidemic. This information can be used to take appropriate steps to control the virus infection.

Epidemiological Modelling and Medicines

Computational biologists are helping to battle against COVID-19 by disease modeling and identifying effective drugs in this pandemic. It has been used to understand the protein structure of coronavirus to discover drugs for potential treatment. The dynamic modeling of the disease can contribute to identify the essential parameters that are responsible for the spread of infection and the impact of mediation to control this pandemic [33]. The ground-glass opacities are

Table 1 Summarization of deep learning applications for medical imaging-based COVID-19 diagnosis

Authors	Sample size	Methods	Results
Khan et al. [19]	1300 chest X-rays including 290 COVID-19 cases	CoroNet: Xception architecture	Accuracy = 89.6%
Wu et al. [20]	495 CT images consisting of 368 COVID-19 cases	Multi-view fusion model using deep learning techniques	Accuracy = 70.0% AUC = 73.2%
Wang and Wong [21]	13,975 X-ray images from 13,870 patients	COVID-Net: deep CNN architecture	Accuracy=92.4%
Wang et al. [22]	325 CT scans of COVID-19 and 740 of pneumo- nia	Deep transfer learning using modified Inception	Accuracy = 79.3% Specificity = 83.0%
Butt et al. [23]	618 CT images including 219 COVID-19 cases	3D deep learning with location-attention mechanism	Accuracy = 86.7%
Jin et al. [24]	970 CT images from 496 patients	Deep neural network	Accuracy = 94.98% Specificity = 95.47%
Song et al. [25]	275 CT scans comprising of 88 COVID-19 cases	DeepPneumonia: ResNet architecture	AUC=99.0% Sensitivity=93.0%
Islam et al. [27]	421 X-ray images including 141 COVID-19 cases	Combined deep CNN-LSTM architecture	Accuracy = 97% Specificity = 91%

found in both lungs when the virus increases in the body. Drug repurposing is proposed to identify the patient's illness that can be treated using existing medications.

Protein Structure Prediction

While entering the RNA genome into a cell, it combines with the host's protein production to duplicate RNA molecules by utilizing it. This is called "polymerase" that is used for a target in treatments [34]. Three-dimensional (3D) protein structure is determined by their genetically encoded amino acid sequence that impacts the function of the protein. Template modeling and template-free modeling are two approaches for the prediction task. For template sequence, template modeling predicts similar protein structures, and template-free modeling predicts unknown related structures [35]. Senior et al. [36] proposed an architecture called AlphaFold based on extended ResNet network [37] that used amino acid sequences and also extracted features using several sequences alignment from its to find out the distance and dispersal of angles between amino acid residues. This system is applied to predict several proteins structure related to COVID-19 [38]. Though these predictions still need to be verified experimentally, it would be helpful to perceive the functionality of coronavirus as well as medicine development for COVID-19.

Drug Discovery

In this COVID-19 pandemic, the crucial step is to identify the right drugs that can be committed for better treatment. There are some researches that are trying to discover effective drugs using deep learning architecture for COVID-19. Zhavoronkov et al. [39] utilized a pipeline to detect inhibitors for the 3C-like protease. The system used three types of information, such as crystal protein structure, co-crystallized ligands, and the homology model of the protein. For every case, several networks, including Generative Auto-encoders (GAs) and Generative Adversarial Networks (GANs), are used [40]. The system analyzed the potential candidate to incorporate factors like novelty, diversity, and medication measurement. Moreover, the author ensured that the detected candidate molecules are different from the existing compound. Tang et al. [41] used reinforcement learning techniques to discover the compounds that inhibit COVID-19. The system generated 284 molecules and broke down the protein into 316 fragments, which later combined using a deep Q-learning network to design a fragment-based drug. Beck et al. [42] applied a deep learning-based system to identify the available drugs that could act against COVID-19 infection. The result showed that the existing drug named atazanavir could be potentially repurposed to treat coronavirus. Patankar et al. [43] generated new molecules using deep learning techniques to discover drugs for COVID-19. An atom of error could be occurred in the training phase of the system using limited data. Zhang et al. [44] used a deep learning method to predict suitable antivirals that might be helpful for COVID-19 patients. The system applied a modified DenseNet network to identify protein–ligand interaction and then used an RNA sequence of coronavirus with chemical compounds to develop an effective drug.

Virus Severity and Infectivity

Viral host prediction is a crucial task to assure biosafety for evolving viruses rapidly. It is difficult to detect humaninfecting viruses using bioinformatics systems. Bartoszewicz et al. [45] proposed an approach to predict whether a virus can infect the human-body directly utilizing next-generation sequence. The system showed that CNN and LSTMbased architecture outperformed the other machine learning algorithms and generalized to taxonomic units with a half error rate from those that are presented in the training phase. The visualization of nucleotide data is done in convolutional filters. Finally, GWPA plots are used to insight the behavior of the system to analyze the COVID-19 virus. Guo et al. [46] introduced virus-host prediction technique based on a deep learning algorithm to identify what types of a viral host can infect a human with DNA input sequence. The prediction result showed that various vertebrate infectious coronavirus has good strength for infecting humans. This system is also effective for virus analysis and prevention in an early stage.

Discussions

This paper introduced a survey of deep learning applications to reduce the crisis of humanity that are faced due to COVID-19 and control strategies of this pandemic. In particular, we highlighted emerging applications such as medical imaging for diagnosis, disease tracking, protein structure analysis, drug discovery, and virus severity and infectivity which are summarized in Table 2. To classify COVID-19 cases, the system developed in [19, 27] used a different number of X-ray images and achieved 97% and 89.6% accuracy, respectively. On the contrary, the schemes introduced in [20, 22-25] applied a various range of CT scans and obtained the highest 94.98% accuracy to distinguish coronavirus symptoms. To track the outbreak of COVID-19, the proposed systems in [29–31] applied a deep learning algorithm on real-time data to take appropriate steps. In the field of epidemiological modeling and medicines, deep learning is used to explore and analyze the protein structure of the virus to identify the essential components for the vaccine [36]. For the development of effective drugs, the systems demonstrated in [39] trained

Table 2 Summarization of deep learning applications to combat COVID-19 pandemic

Sl. no.	Applications	Descriptions
1	Diagnosis using medical imaging	Deep learning architecture is used to extract complex features from radiological images for proper diagnosis
		Early prediction of COVID-19 infection using different CNN architecture from an increasing number of samples
		CoroNet is based on Xception architecture used for the diagnosis of coronavirus infection from X-ray images
		COVID-Net used a deep CNN architecture to distinguish COVID-19 cases from pneumonia and normal cases
		DeepPneumonia used ResNet architecture for the classification of COVID-19 symptoms from CT scans
2	Disease tracking	Bidirectional GRU and attentional techniques are used for the analysis of respiratory patterns to contribute large scale COVID-19 screening
		A dynamic neural network is applied to identify the geographical spread of coronavirus pandemic AI-driven system used deep learning algorithms to identify geographical risk at community levels
3	Protein structure prediction	Critical assessment of techniques for protein structure prediction based on a deep neural network to identify protein characteristics
		CNN architecture is utilized to examine dense predictions
		The deeper ResNet network is applied to ease the training of models to recognize infected images
4	Drug discovery	GANs and GAs are utilized as a pipeline that generates essential drug compounds
		Reinforcement learning techniques are implemented to discover the compounds that inhibit COVID- 19
		Deep learning techniques are focused on generating new molecules to treat coronavirus
5	Virus severity and infectivity	CNN and LSTM-based systems showed the better performance to predict virus infectivity in the human body
		Virus-host prediction techniques used deep learning algorithms to analyze virus and early prevention

GAs and GANs, [41] used reinforcement learning techniques, and [43] applied LSTM networks. The humaninfecting virus can be identified using deep learning-based architectures utilizing its next-generation sequence shown in [45].

In recent years, many researchers are employing deep learning for COVID-19 cases, but the data about COVID-19 are still limited. Among them, the use of deep learning for the diagnosis of COVID-19 from medical imaging data seems to be dominant from others, but few systems still have some lack of transparency and interpretability. This means it is still unknown which imaging feature is responsible for generating output. Hence, it is necessary to explain the features of the medical image with the performance of the developed architecture that are responsible for differentiating COVID-19 cases from others, and it would be helpful to doctor to gain insights about the virus. The data of COVID-19 on case reporting are varying from country to country that may not represent the true transmission rate and also can create an issue for disease tracking. To discover drugs, some systems need longer length peptides against coronavirus protease on virtual screening and also need to develop a scoring function to redesign the antibodies of COVID-19. However, the number of deep learning applications would be significantly increased when more data would be available.

Conclusion

COVID-19 outbreak is still now an ongoing pandemic and outperforming the previous records of all communicable diseases in terms of infection and death cases. The researchers investigate all the potential steps to combat the COVID-19 pandemic that are reviewed in this paper. Deep learning has a significant impact on identifying coronavirus infection at an early stage for the proper treatment. It also tries to track the COVID-19 crisis at different scales, such as medical, molecular, and epidemiological, to enhance public healthcare systems. Deep learning-based system is also helpful in facilitating virus analysis for proper drugs and vaccine development. Although the impact of deep learning is so far limited, it would provide a better outcome to handle this crisis. Hopefully, this deep learning-based application will be helpful in developing appropriate solutions to combat the current pandemic.

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Compliance with Ethical Standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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