Machine and Deep Learning Towards COVID-19 Diagnosis and Treatment: Survey, Challenges, and Future Directions

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Abstract—Machine Learning (ML) and Deep Learning (DL) have been widely used in our daily lives in a variety of ways with many effective stories. Also, they have been instrumental in tackling the Coronavirus (COVID-19) epidemic, which has been occurring around the world. The COVID-19 epidemic caused by the SARS-CoV-2 virus has spread rapidly around the world, leading to global outbreaks. Most governments, businesses, and scientific research institutions are taking part in the COVID-19 struggle to stem the spread of the disease. In this survey, we investigate the Artificial Intelligence (AI) based ML and DL towards COVID-19 diagnosis and treatment. In addition, we summarize the AI-based ML and DL methods and available datasets, resources, and results in the fight against COVID-19. This survey provides the ML and DL researchers and the wider health community a comprehensive overview of the current state-of-the-art methodologies and applications with details of how ML and DL and data can improve the status of COVID-19, and further studies to stop the COVID-19 outbreak. Challenges and future directions details are also provided.

Index Terms—COVID-19, diagnosis, treatment, artificial intelligence, machine learning, deep learning.

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1 INTRODUCTION

SEVERE Acute Respiratory Syndrome Corona-Virus 2 (SARS-CoV-2) is currently a serious infectious global disease. As of December 2019, Coronavirus 2019 (COVID-19) caused by SARS-CoV-2 was first reported in China and later in many countries around the world. The World Health Organization (WHO) announced on January 30, 2020, that the disease is a Public Health Emergency of International Concern (PHEIC), and confirmed COVID-19 as a pandemic on March 11, 2020 [85]. From May 16, 2020, this disease has been reported in 216 countries or regions around the world. The disease has spread and led to serious side effects involving 31,668,942 cases confirming COVID-19 cases and 972,437 deaths in September 22, 2020.

In this global health crisis, the medical industry seeks new technologies to monitor and control the spread of the COVID19 (Coronavirus) epidemic. Artificial Intelligence (AI) is one of such technologies that can easily track the spread of the virus, identify high-risk patients, and help control the disease in real time. It can also predict the risk of death by adequately analyzing previous patient data. AI can help us fight the virus by testing people, medical help, information, and suggestions about infection control.

AI is a big umbrella that consist of several sub-areas to solve complex problems in our lives. These sub-areas include learning, planning, reasoning, knowledge representation, and searching. Machine Learning (ML) and Deep Learning (DL) are a subset area of AI which consists of many algorithms that imitate human brains and behaviors to classify or cluster specific tasks based on the supervisory of data.

ML is a subset of AI area which is a traditional type of learning that requires only a small number of data to learn to solve problems. ML methods include Logistic Regression (LR), Decision Tree (DT), Random Forest (RF), K-nearest Neighbor (KNN), Adaboost, K-means clustering (KC), Density clustering (DC), Hidden Markov Models (HMM), Support vector machine (SVM), Naive Bayes (NB), and Multilayer Neural Network (NN) or the so called Artificial Neural Network (ANN).

On the other hand, DL is a subset of ML area which is focused on building deep structural NN models that learn from data using feedforward and backprobagation algorithms. The DL appeared after ML and outperformed it in many tasks in the past two decades. However, it requires a large number of data to train. Transfer learning and generative models have been exceptional cases from DL where a large-scale data is not required to train. Typically, DL algorithms include Deep Belief Networks (DBN), Deep Neural Network (DNN), Convolutional Neural Networks (CNN), Restricted Boltzmann Machines (RBM), Recurrent Neural Networks (RNN) including Long-short-term-memory (LSTM), Autoencoder (AE), and Generative Adversarial Network (GAN).

Encouragingly, in the short time since the outbreak of COVID-19, research in the industry, the medical, scientific, and military sectors have successfully implemented advanced AI-based ML and DL methods in the COVID-19 war and achieved significant progress. For example, ML and DL supports COVID-19 diagnosis through medical image inspection and provides non-invasive detection solutions

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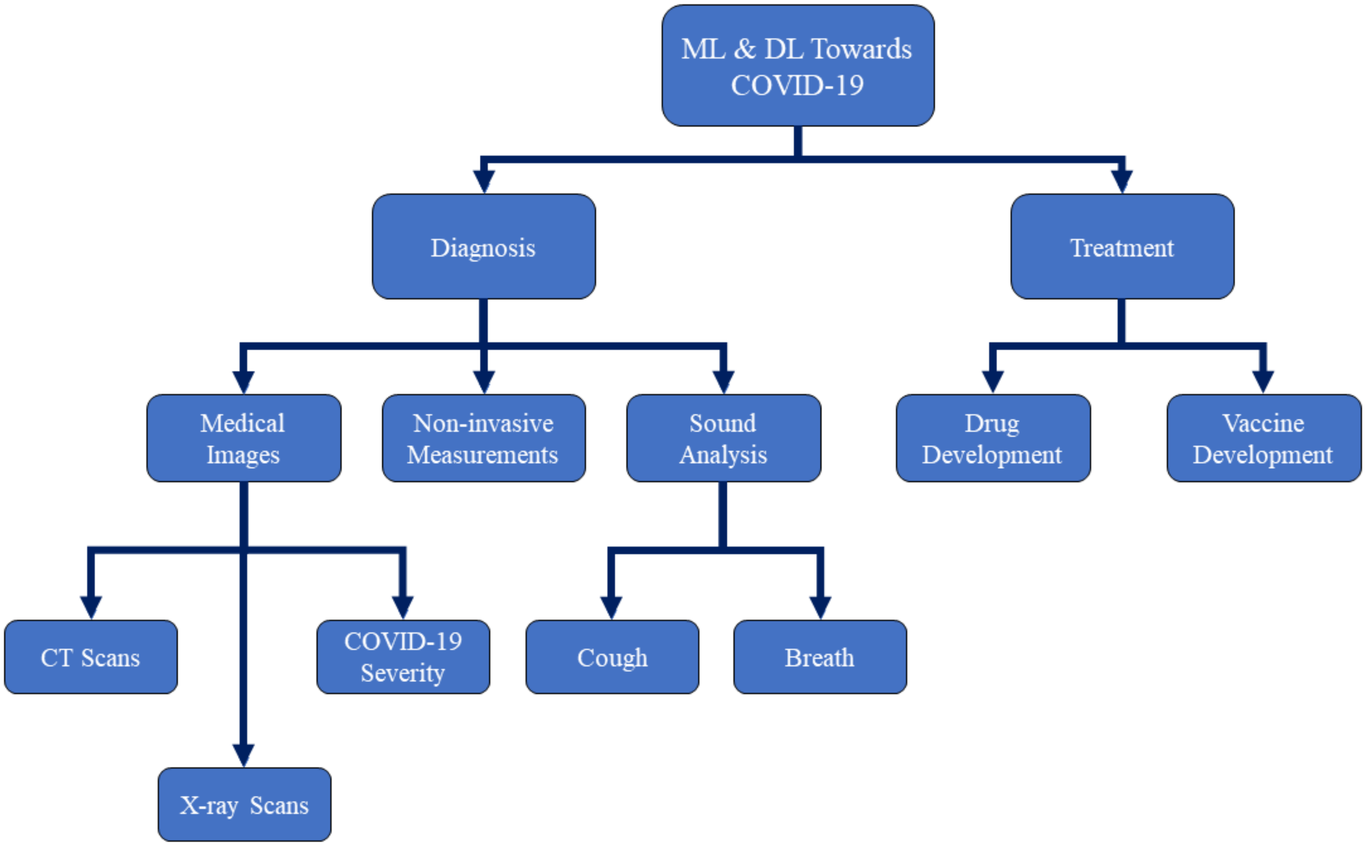


Fig. 1. A taxonomy of our survey on ML and DL research works towards COVID-19 diagnosis and treatment.

to prevent medical personnel from contracting infections and also provide severity score of the patient for further treatment. The ML and DL are used in virology research to analyze genetics related to SARS-CoV-2 proteins and predict new chemicals that can be used for drug development and vaccination. Moreover, AI intelligent models based on ML and DL learn on a large scale COVID-19 case data and social media data to create epidemic transmission models accurately predicting outbreaks, transmission route, transmission list, and impact. ML and DL are also widely used in epidemic protection and public control, such as airport security check-ups, patient tracking, and epidemic detection.

In this survey, we present the main scope of AI focusing on ML and DL towards COVID-19 research incorporates the aspects of disease detection and diagnosis and drug and vaccine development. Note that due to the fast development of the COVID-19 epidemic, we have quoted many published research works before a thorough investigation, where these works actually should be surveyed for their precision and quality in peer review. A taxonomy of our survey on ML and DL research works towards COVID-19 diagnosis and treatment is shown in Figure 1.

The remainder of this paper is organized as follows. In **Section 2**, we provide details on the current AI-based ML and DL approaches for classifying and detecting COVID-19 from Chest CT and X-ray scans in addition to non-invasive COVID-19 measurements. We also show the COVID-19 severity detection using the DL-based methods. In **Section 3**, we provide details on the current AI-based ML and DL approaches for drug and vaccines development. In **Section 4**, challenges and future work directions using AI-based ML and DL approaches for tackling the problem of COVID-19 are provided in details. Finally, our conclusion is provided in **Section 5**.

2 MEDICAL IMAGE INCEPTION USING AI-BASED ML AND DL FOR THE DETECTION OF COVID-19

The Coronavirus (COVID-19) epidemic is spreading worldwide. Medical imaging, for example, X-ray and Computed Tomography (CT) play an important role in the global fight against COVID-19, and the latest AI technologies continue to strengthen the power of imaging tools and assist medical professionals.

Clinical imaging testing is widely used by clinicians to detect and diagnose COVID-19. COVID-19 clinical imaging studies mainly include chest X-ray and lung CT images. AI innovation assumes a significant part in medical imaging testing and has accomplished huge outcomes in image detection, organ recognition, regional classification of infection, and disease classification. Not only does it reduce the radiologist's image diagnostic time but it improves the precision and execution of the diagnosis. AI can improve work efficiency with precise diagnostic accuracy in X-ray

TABLE 1
A summary of highest performance AI-based ML and DL methods for COVID-19 diagnosis using radiology images.

Author	Data	ML/DL Method	Accuracy/AUC	Sensitivity	Specificity
Li et al. [45]	4,356 chest CT exams from 3,322 patients from 6 medical centers: 1,296 exams for COVID-19, 1,735 for CAP and 1,325 for non-pneumonia.	A 3D Convolutional ResNet-50, namely COVNet	96% AUC	87%	92%
Butt et al. [12]	618 CT samples: 219 from 110 COVID-19 patients, 224 CT samples from 224 patients with influenza-A viral pneumonia, and 175 CT samples from healthy people	Location-attention network and ResNet-18	86.7% Accuracy	N/A	N/A
Ghoshal and Tucker [23]	5,941 Posterior-anterior chest radiography images across 4 classes (normal: 1,583, bacterial pneumonia: 2,786, non-COVID-19 viral pneumonia: 1,504, and COVID-19: 68)	Drop-weights based Bayesian CNNs	89.92% Accuracy	N/A	N/A
Bai et al. [6]	Clinical data and a series of chest CT data collected at different times on 133 patients of which 54 patients progressed to severe/critical periods whilst the rest did not	Multilayer perceptron and LSTM	95% AUC	95%	95%
Jin et al. [39]	970 CT volumes of 496 patients with confirmed COVID-19 and 1,385 negative cases	2D deep CNN	97.17% AUC	90.19%	95.76%
Jin et al. [40]	CT images of 1,136 training cases (723 positives for COVID-19 from 5 hospitals	A combination of 3D UNet++ and ResNet-50	N/A	97%	92%
Narin et al. [56]	Chest X-ray images of 50 normal and 50 COVID-19 patients	Pre-trained ResNet-50	98% Accuracy	N/A	N/A
Wang and Wong [94]	16,756 chest radiography images across 13,645 patient cases from two open access data repositories	A deep CNN, namely COVID-Net	92.4% Accuracy	91.0%	N/A
Gozes et al. [24]	CT images obtained from 157 international patients from China and U.S.)	ResNet-50	97% AUC	98.2%	92.2%
Chowdhury et al. [15]	1,579 normal, 1,485 viral pneumonia, and 423 COVID-19 chest X-ray images	AlexNet, ResNet-18, DenseNet201, SqueezeNet	99.7% Accuracy	99.7%	99.5%
Maghdid et al. [47]	170 X-ray images and 361 CT images of COVID-19 from 5 different sources	A new CNN and pre-trained AlexNet with transfer learning	Accuracy of 98% on X-ray images and 94.1% on CT images	100% on X-ray images and 90% on CT images	N/A
Apostolopoulos and Mpesiana [5]	Chest X-ray Images of 224 COVID-19 positive, 700 pneumonia patient, and 504 healthy	VGG-19	93.48% Accuracy	92.85%	98.75%
Sethy and Behera [80]	Chest X-ray Images of 25 COVID-19 positive and 25 negative	ResNet-50 and SVM	93.28% Accuracy	97%	93%
Hemdan et al. [27]	Chest X-ray Images 25 COVID-19 positive and 25 Normal patient	COVIDX-Net	90% Accuracy	N/A	N/A
Wang et al. [95]	Chest CT images of 195 COVID-19 positive and 258 COVID-19 negative patient	M-Inception	89.5% Accuracy	87%	88%
Zheng et al. [104]	Chest CT images of 313 COVID-19 positive and 229 COVID-19 negative patient	UNet and a 3D Deep Network	90% Accuracy	95%	95%
Hall et al. [25]	135 chest X-rays of COVID-19 and 320 chest X-rays of viral and bacterial pneumonia	Deep CNN (ResNet-50)	89.2% Accuracy and 95% AUC	N/A	N/A
Ni et al. [58]	CT images of 96 confirmed COVID-19 patients in three hospitals across China	Deep CNN	73% Accuracy	95%	95%
Apostolopoulos et al. [4]	3905 X-ray images, corresponding to 6 diseases	CNN MobileNet v2	99.18% Accuracy	97.36%	99.42%
Shi et al. [82]	CT images of 2,685 collected from three hospitals, 1,658 COVID-19 cases diagnosed by positive nucleic acid testing with conformation by national CDC, and 1,027 cases were CAP patients	RF	87.9% Accuracy	90.7%	83.3%
Loey et al. [46]	X-ray images of 307 for COVID-19, normal, pneumonia, becterial, and pneumonia virus	GAN with transfer learning pre-trained CNN models: AlexNet, GoogLeNet, and ResNet18	100% Accuracy for two classes, 85.19% for three classes, and 80.56% for the four classes	N/A	N/A

and CT imaging, making it easier to measure the following. In addition, the computer-aided platforms help radiologists make clinical decisions, i.e., for disease detection, tracking, and prognosis. We will discuss in detail the contributions of AI methods to chest X-ray and lung CT imaging.

2.0.1 Chest CT Image Detection

Chest CT image is a treasured aspect in the evaluation of patients with suspected SARS-CoV-2 infection. There is an increasing interest in the role of imaging for diagnosis of COVID-19. The infection causes a wide assortment of imaging discoveries on CT scans, most regularly ground-glass opacities and consolidations in the periphery of the lungs. The sensitivity of chest CT to diagnose COVID-19 has been reported as high and can originate before a positive viral lab test. Therefore, in endemic territories where the medical care framework is under pressure, hospitals with a high volume of admissions are utilizing CT for fast emergency of patients with conceivable COVID-19 disease. Chest CT has a significant part in the evaluation of COVID-19 patients with extreme and compounding respiratory indications. Based on imaging, it can be evaluated how severely the lungs are affected, and how the patient's disease is evolving, which is useful in making treatment decisions. There is an increasing awareness that lung abnormalities caused by COVID-19 can be found suddenly in CT assessments performed for other clinical indications, e.g. abdominal CT scans for bowel problems, or in patients without respiratory complaints [59]. In this pandemic the estimation of AI becomes possibly the most important factor, by diminishing the burden on clinicians. While a manual read of a CT scan can take up to 15 minutes, AI can analyze the images in 10 seconds [59]. Therefore, automated image analysis with artificial intelligence techniques has the potential to optimize the role of CT in the assessment of COVID-19 by permitting exact and quick finding of infection in a large number of patients.

The continuation of AI-based CT imaging tests usually includes the following steps: Region Of Interest (ROI) regional division, pulmonary tissue removal, regional infection detection, and COVID-19 classification.

The classification of lung organs and ROIs is a fundamental basis for examining AI-based imagery. Demonstrates ROI in lung CT imaging (such as lungs, lung lobes, bronchopulmonary segments, and regions with infection or ulcers) for additional testing and evaluation. Different types of DL networks, for example, U-Net, V-Net, and VB-Net, VNET-IR-RPN were used for CT image classification.

Among a total of 905 patients tested with real-time RT - PCR assay and subsequent next generation RT - PCR, 419 (46.3%) were diagnosed with SARS-CoV-2 thorugh an AI system. The AI system consists on deep CNN to learn the images features and qualities of patients with SARS-CoV-2 on the initial CT scan. Then, SVM, RF, and MLP classifiers were used to classify patients with SARS-CoV-2 as per clinical information.The AI system works on radiological data and clinical information to anticipate COVID-19 status. In experimental set of 279 patients, the deep CNN-based AI system accomplished AUC of 0.92 and had a similar sensitivity compared to the senior thoracic radiologist. The Artificial intelligence framework additionally improved the detection of patients who hoped for COVID-19 with RT - PCR who presented with standard CT scans, which accurately identified 17 out of 25 patients (68%), and radiologists classified all of these patients as COVID-19 negative [50]. Also, The test set contained 25 patients positive for COVID-19 with a chest CT identified as normal by both of the reading radiologists at presentation. The CNN model identified 13 of 25 (52%) scans as COVID-19 positive, the clinical model classified 16 of 25 (64%) as disease positive and the joint model classified 17 of 25 (68%) as disease positive, whereas the senior thoracic radiologist and the thoracic radiology fellow identified 0 of 25 (0%) of these scans as disease positive [50] .

In order to find the answer that could deep-learning quickly break down images and identify features of COVID-19, Researchers develop many AI tools. To develop an AI tool to detect COVID-19, researchers led by Bo Xu of Tianjin Medical University Cancer Institute and Hospital took CT images of 180 people determined to have common viral pneumonia before the outbreak of COVID-19 and 79 patients with COVID-19 certified [66]. They Randomly provided images from patients to train or test a deep learning algorithm. In the results published in medRxiv [95], the researchers said that their model identified COVID-19 from CT images with 89.5% accuracy. Two radiologists who examined the images found an accuracy of about 55%. The team says the results show that AI can provide an exact analysis from a CT scan. Another algorithm named as RADLogics algorithm [38] that worked on detecting and help to incepting recovery of a COVID-19 patient.

Two studies, published in [50] and [102], advance this thought by utilizing DL trained on CT lung scans as a fast symptomatic tool to search for COVID-19 infection in sufferers who come to the hospitals and require medical image processing. In [102], researchers at Macau University of Science and Technology used 532,000 CT scans from 3,777 patients in China to train their AI models, focusing on the tell-tale lesions seen in COVID-19 patient lungs. In a pilot study in several Chinese hospitals the AI model successfully detected Coronavirus-induced pneumonia at least 85 percent of the when time it was used in a database of 417 patients in four different groups.

There is a major problem to distinguish whether the symptoms are of COVID-19 and pneumonia that radiologists found in CT images. A company, VIDA Diagnostics [93], has developed a product called LungPrint that uses AI to investigate CT scans to help diagnose respiratory conditions, including signs and symptoms of COVID-19. In [2] Investigators from NIH and NVIDIA set out to produce a deep learning algorithm to detect COVID-19 on chest CT using dataset from four hospitals across China, Italy, and Japan. In total, researchers used 2,724 scans from 2,619 patients in this study included two models (i.e. Full 3D, Hybrid 3D) used in series to come up with the COVID-19 final classification model. These two model work. The first model utilized the whole lung region with a fixed input size (full 3D). The second model utilized an average score for a couple of areas in each lung at fixed image resolution (hybrid 3D). When recognizing COVID-19 and other pneumonia, the hybrid 3D model achieved 92.4% validation accuracy, while the full 3D model achieved 91.7% accuracy.

In [14], Chen et al. built a DL model based on U-Net++ structure to extract ROIs from each CT image and to obtain a training curve for suspicious lesions. For model development and validation, 46,096 anonymous images from 106 patients already admitted, including 51 laboratory patients who confirmed COVID-19 pneumonia and 55 other disease control patients at Wuhan University's Renmin Hospital (Wuhan, Hubei province, China) were collected and processed. Twenty-seven sequential patients undergoing CT scan on February 5, 2020 at Wuhan University's Renmin Hospital were gathered to assess and compare the efficacy of radiologists compared with the model on 2019-CoV pneumonia. The model achieved an individual patient sensitivity of 100%, specificity of 93.55%, accuracy of 95.24%, a per-image sensitivity of 94.34%, specificity of 99.16%, accuracy of 98.85% in retrospective dataset. In [35], Huang et al. used the AI-based InferReadTM CT pneumonia tool to adequately assess changes in lung burden of patients with COVID-19. The tool incorporates three modules: pulmonary and lobe extraction, pneumonia classification, and quantitative analysis. Features of the CT image for COVID-19 pneumonia are divided into four types: mild, moderate, severe and critical. CT lung opacification level of the whole lung and five lobes were automatically measured by a commercial deep learning software, and compared over followups CT scans. A total of 126 patients with COVID-19 (age 52 years ± 15 years, 53.2% males) were evaluated, including 6 mild, 94 moderate, 20 severe and 6 critical cases. The percentage of CT-based opacification was altogether diverse between initial clinical groups, gradually progressing from mild to severe type (all $P < 1\%$).

In [68], Qi et al. gathered 71 CT scans from 52 patients with COVID-19 certified in 5 hospitals. They used Pyradiomics technique to extract 1,218 traits from each CT image. CT radiomics models based on logistic regression (LR) and RF developed on the extracts from pneumonia lesions in training and intermediate interactions. Predictability performance was also assessed in the experimental database at the lung lobe and at the patient level. CT radiomics types are based on 6 second order. They have been successful in discriminating short-term and long-term stay in patients with pneumonia associated with SARS-CoV-2 infection, with AUC of 97% and 92% by LR and RF, respectively, in the test dataset. The LR model showed sensitivity and specificity of 100% and 89%, and the RF model showed similar sensitivity and specificity of 75% and 100% in the test data. Short-term hospital stay is less or equal than 10 days while a long-term hospital stay is greater than 10 days.

2.0.2 Chest X-Ray Image Detection

Chest X-rays have been proposed as a potentially useful tool for assessing COVID-19 patients. Figure 3 shows representative architectures of DL-based CT image classification and COVID-19 inspection. Compared with CT images, chest X-ray (CXR) images are simpler to acquire in clinical radiology examinations. There are many available study [64] [7] that work on chest X-ray (CXR) images for the detection of corona virus. The CXR image testing measure dependent on AI strategies for the most part incorporates steps, for example data correction, DL model training, and COVID-19 segmentation. There are many deep learning methods (such as CNN, nCOVnet, U-Net++) that are used in the detection of cOVID-19 using CXR images to find better and fast detection.

As we know, X-ray machines offer less expensive and quicker results from scanning various human organs in hospitals. Interpretation of various X-ray images is usually done manually by radiologists. Radiologists are just ready to identify 69 percent of COVID-19 cases in x-rays [8]. Pre-trained models made the detection work much easier and faster. In [64], a dataset containing confirmed COVID-19 positive, common bacterial pneumonia and healthy cases (no infection) were used. A total of 1,428 X-ray images were used in this study. The authors used VGG-16 pre-trained model to model division function and perform the classification. The examiner accomplished an accuracy of 96% and 92.5% in two and three output class cases, respectively. Based on these findings, the medical community can access X-ray images as a potential symptomatic tool for rapid and quicker detection of COVID-19 to complement existing diagnostic and symptomatic strategies. Many more Novel algorithm is used for better result through CXR images against the battle with SARS-nCOV-2. In [7], Basu and Mitra presented domain transfer learning for alternative screening of COVID-19 by determining characteristic features from chest X-Ray images. In order to get an regarding about the COVID-19 detection transparency, the concept of Gradient Class Activation Map (Grad-CAM) are also employed on the dataset of 20,000 Chest X-rays. A 5-fold cross validation was performed to get an estimate of the feasibility of utilizing chest X-Rays which is tuned for classifying between four classes i.e. normal, other disease, pneumonia and COVID19 data were used to diagnose the disease. The overall accuracy was measured as 95.3% with 100% of the COVID-19 and normal cases being effectively characterized in each validation fold. There has been a misdiagnosis between pneumonia and other stages of disease.

Students Were also involved in the production of ML algorithm to identify novel COVID-19 patients. Students at Cranfield University proposed computer models with the help of AI that can detect COVID-19 in CXR images [89] [90]. The proposed models used ML and DL techniques to extract features and classify CXR images. It can distinguish information that would not normally be visible to the naked eye and assist with the diagnosis of COVID-19.

The first model is to analyze anomalies in an X-ray, dividing normal and pneumonia patients. Then, the second model work on those pneumonia patients to diagnose if the pneumonia is caused by the COVID-19 virus [89] [90]. Figure 3 shows our high level representation of proposed computation intelligent models used at Cranfield University.

Earlier Researchers at King's College London, Massachusetts General Hospital and health tech firm Zoe have meanwhile started trials of an AI-primarily based totally detection that try to expect COVID-19 infections via way of means of evaluating the signs with the consequences of conventional COVID-19 tests [88]. Another model [62] is proposed having an end to end architecture without using any feature extraction method with the help of Chest X-ray images for diagnoses COVID-19. This model is constructed

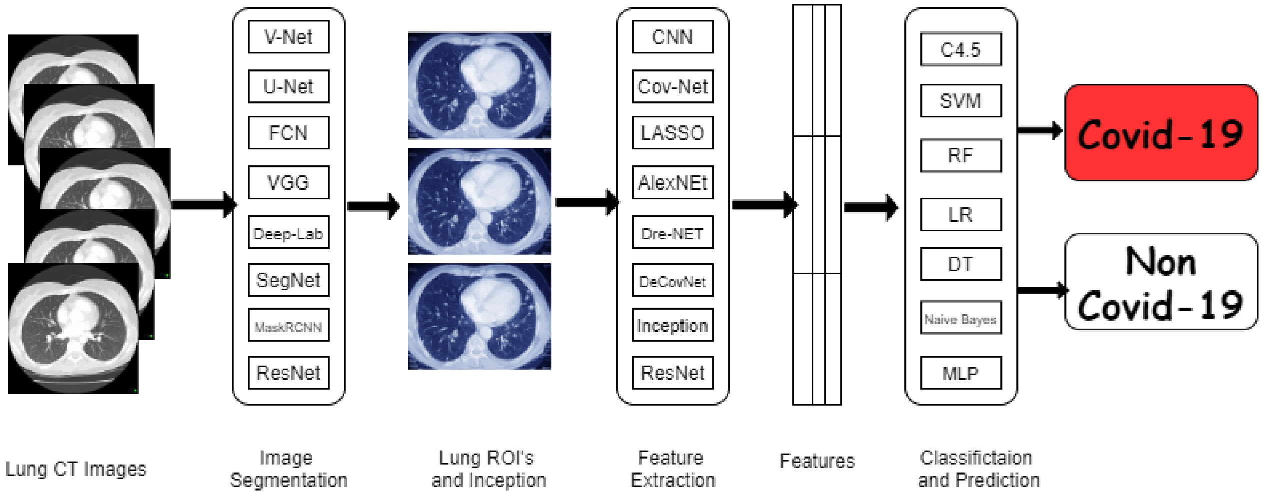


Fig. 2. Representative architectures of DL-based CT image classification and COVID-19 inspection [13].

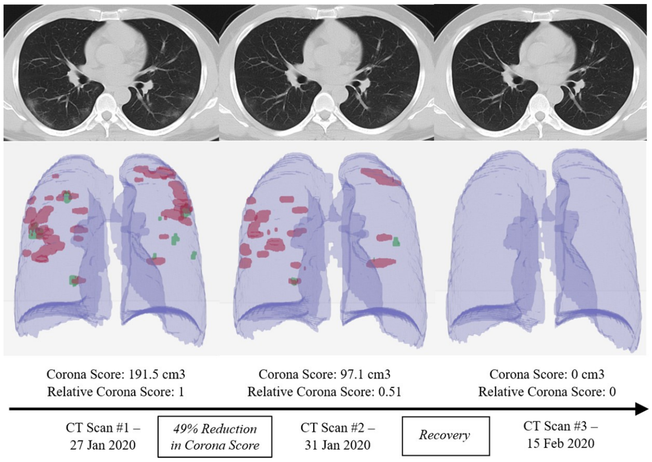


Fig. 3. Using three CT scans from a single COVID-19 patient, the RADLogics algorithm quantifies the amount of recovery with a Corona score [78].

on the basis of already known model Darknet-19 (form on the basis of a real-time object detection system named YOLO) named DarkCovidnet [62]. The obtained sensitivity, specificity, and F1-score values are 85.35%, 92.18%, and 87.37%, respectively using this model.

Many research works are done using different approaches to overcome COVID-19. In [49], Mangal et al. presented a COVID-19 AI-based Detector (CovidAID). CovidAID is a deep neural network based model to triage patients for proper testing on publicly accessible covid-chestxray-dataset dataset. They achieved 90 .5% accuracy with 100% sensitivity (recall) for the COVID-19 infection. In [17], a deep learning-based CNN model, called Truncated Inception Net, was proposed to display COVID-19 positive CXRs from other non-COVID and/or healthy cases. Six distinct forms of datasets have been carried out via way of means of taking the subsequent CXRs: COVID-19 positive, Pneumonia positive, Tuberculosis positive, and healthy cases into account. The proposed model achieved an accuracy of 99.96% (AUC of 100%) in classifying COVID-19 positive cases from combined Pneumonia and healthy cases. Similarly, it achieved an accuracy of 99.92% (AUC of 99%) in identifying COVID-19 positive cases from all combined Pneumonia, Tuberculosis, and healthy CXRs. According to [17], they proved the viability of using the proposed Truncated Inception Net as a screening tool and outperform all the existing tools. Minaee et al. [51] reported a study on COVID-19 prediction in CXR imaging utilizing transfer learning. They compared predictions of four popular pre-trained deep Convolutional Neural Networks (CNNs), which are ResNet18, ResNet50, SqueezeNet, and DenseNet-161. They instruct the models using COVID-19 and non-COVID datasets, including 14 subclasses containing normal images from the ChexPert dataset. The models demonstrated an average specificity rate of ∼90% with a sensitivity range of 97.5%. This strongly encourages the hope that COVID-19 can be recognized from other diseases and normal lung conditions by CXR imaging. A decision-tree classifier for COVID-19 diagnosis from Chest X-ray Imaging is implemented by [100]. It comprised three binary decision trees, each trained by a deep learning model with convolution neural network based on the PyTorch framework. The first decision tree classified the Chest X-Ray images as normal or abnormal. The second tree distinguished the abnormal CXR images that contain symptoms of tuberculosis, while the third classified equivalent second for COVID-19. The accuracy of the first decision trees is 98 and the second decision tree is 80%, whereas the average accuracy of the third decision tree is 95%. They stated that the proposed deep learning-based decision-tree classifier may be utilized in pre-screening cases to conduct triage and fast-track conclusion making before RT-PCR results are available. A study [46] presented GAN (Generative Adversarial Network) with deep transfer learning for Coronavirus detection in chest X-ray images having lack of chest x-ray images dataset. 307 images for four different types of classes i.e. COVID-19, normal, pneumonia bacterial, and pneumonia virus were collected. Three deep transfer models AlexNet, GoogLeNet, and ResNet18 were selected for inception. Three case scenarios are tested in this study, the first scenario contains four classes from the dataset, while the second scenario contains 3 classes and the third scenario contains only two classes.

Having COVID-19 class in all the scenarios was a must. In the first scenario, the GoogLeNet was picked to be the fundamental deep transfer model as it achieved 80.6% in testing accuracy. The second scenario achieved testing accuracy of 85.62% with the use of Alexnet. In third scenario (that contains two classes i.e. COVID-19 and normal), GoogLeNet was chosen as a fundamental deep transfer learning model that gave an ideal 100% in testing accuracy and 99.9% in the validation accuracy.

Particularly in low-resource settings (CXR) may play an significant part in triage for COVID-19. A deep learning-based AI system CAD4COVID-Xray was trained on 24,678 CXR images for the detection of COVID-19 [69]. A lung segmentation using U-net and a CNN were applied. From that 454 images tested on a set from an independent center (223 patients tested positive for COVID-19, the remaining 231 tested negative). The AI system CAD4COVID-XRay precisely classified Chest X-ray images as COVID-19 pneumonia with an AUC of 81%. According to the author [69] that the system may be useful as part of a process of looking at symptomatic topics, especially in low-resource settings where radiology technology is not available. A summary of highest performance AI-based ML and DL methods for COVID-19 diagnosis using radiology images is shown in Table 1.

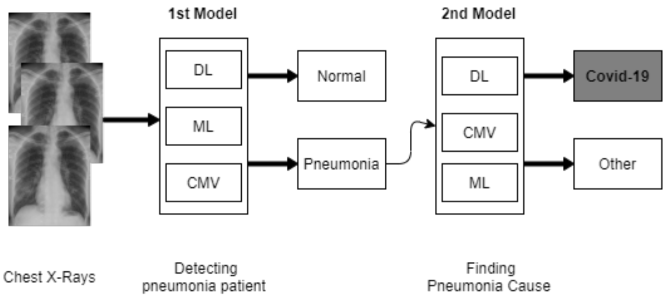


Fig. 4. Our representation of proposed computation intelligent models used at Cranfield University.

2.0.3 *COVID-19 Severity Detection Using Chest X-ray With Deep Learning*

Chest X-rays help us to understand more with the help of artificial intelligence, particularly by using ML and DL techniques. Chest X-rays (CXRs) provide a non-invasive tool to monitor the progression of the disease. In [16], a severity score predictor model of COVID-19 pneumonia for front-chest X-ray images is studied. Expansions of lung involvement and light intensity are also included in the CXR image database. A pre-trained neural network model (i.e. DenseNet) in large chest X-ray sets (non-COVID-19) is used to create features of COVID-19 images to predict this activity. 94 images of COVID-19 certified patients go to the study to predict the severity of COVID-19 using deep learning as shown in Figure 5. Table 2 provides examples of disease severity stages using a score system based on two types of scores: extent of lung involvement and degree of opacity presented in a single CXR image at a time.

The extent of lung involvement by ground glass opacity or consolidation and degree of opacity for each lung (right lung and left lung separately) was scored. The total extent and opacity score ranged from 0 to 8 and 0 to 6, respectively (right lung and left lung together). On the basis of the score the severity of a disease can be found that could be used for escalation or de-escalation of care as well as monitoring patient treatment efficacy, particularly in the ICU.

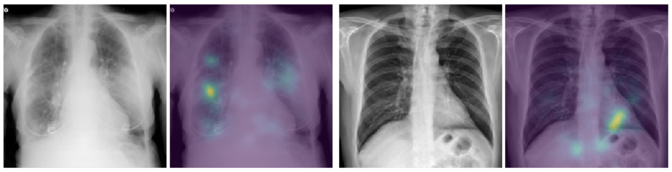
TABLE 2
Disease severity stages using a score system based on two types of parameters.

Parameters	**Severity Score**				
	0	**1**	**2**	**3**	**4**
Extent of Lung Involvement	No	<25%	25%-50%	50%-75%	>75%
Degree of Opacity	No	Ground glass opacity	Consolidation	White-out	-

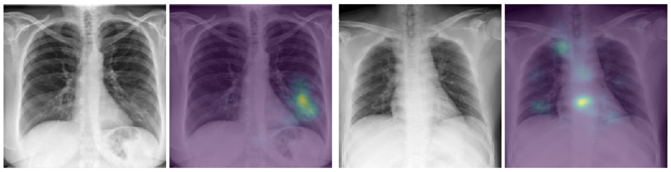
Mobile app development uses AI to predict COVID-19 severity are also in the game. In [20] [92], researchers from NYU College of Dentistry developed a mobile app using a dataset of 160 images of confirmed COVID-19 patients from China. The different bio-markers presented in blood are able to diagnose COVID-19 severity level using the mobile app from level 0 (mild) to 100 (extreme).

On the other hand, Ridley [74] trained a special type of deep-learning algorithm called a Convolutional Siamese Neural Network (CSNN) to provide a pulmonary X-ray severity (PXS) score of patients with COVID-19 and correlated well with assessments by radiologists and could also help to predict if a patient would need intubation or would die within three days of admission. The algorithm performed with two types of datasets internal and external. Internal testing was performed on a dataset of 154 COVID-19 admission chest X-rays, of those patients, 92 additionally had a follow-up chest X-ray and those had been used for longitudinal analysis. External testing was conducted on 113 consecutive admission chest X-rays from COVID-19 patients at a community hospital – Newton-Wellesley Hospital in Newton, MA in the United States. researchers determined that the median PXS score was higher on both the internal and external test sets in patients who were intubated or dead (PXS score = 7.9) compared with those who were not intubated (PXS score = 3.2). The difference was statistically significant ($p < 0.001$).

In [68], Qi et al. collected 71 CT scans from 52 patients with COVID-19 certified in 5 hospitals. They used pyradiomics technique to extract 1,218 traits from each CT image. CT radiomics models based on logistic regression (LR) and random forest (RF) developed on the extracts from pneumonia lesions in training and intermediate interactions. Predictability performance was also assessed in the experimental database at the lung lobe- and at the patient level. CT radiomics types are based on 6 second order which have been successful in discriminating short-term and long-term remain in patients with pneumonia related with SARS-CoV-2 infection, with AUC of 97% and 92% by LR and RF, respectively, in the test dataset. The LR model showed sensitivity and specificity of 100% and 89% and the RF model showed similar sensitivity and specificity of 75% and 100% in the test data. Short-term hospital stay ($\leq$10 days) and long-term hospital stay (>10 days).



(a) Geographic Extent Score: 5, Predicted: 5.3 (b) Geographic Extent Score: 0, Predicted: -0.8



(c) Geographic Extent Score: 2, Predicted: 0.62 (d) Geographic Extent Score: 0, Predicted: 1.05

Fig. 5. A presentation of a predicted severity scores for COVID-19 pneumonia for frontal chest X-ray images using DenseNet model [16].

2.0.4 Monitoring COVID-19 Through AI-based Cough Sound Analysis

Coughing is a symptom of more than 30 non-COVID-19 medical conditions. This makes the diagnosis of COVID-19 infection by coughing alone a major challenge for various problems. Sound signals produced by the human body (e.g., moaning, breathing, heartbeat, digestion, vibrating sounds) are frequently utilized by doctors as markers of diagnosis. Up to this point, such signals were typically gathered through manual auscultation at planned visits. Other research is being done using digital technology to collect body sounds (e.g., from digital stethoscopes) for cardiovascular and respiratory tests, which can be used for automatic COVID-19 analysis. Recent work has started exploring how respiratory sounds (e.g., coughs, breathing and voice) collected by devices from patients tested positive for COVID-19 in hospital differ from sounds from healthy people. In [36], a study of detection of coughs related to COVID-19 collected via phone app is presented using a cohort of 48 COVID-19, 102 bronchitis, 131 pertusses and 76 normal cough sounds to train and test this diagnosis system. Equation *1* is used in [36] to convert the cough data for all four classes into Mel scale m for further processing:

$$m = 2595 \times log_{10}\left(1 + \frac{f}{700}\right) \quad (1)$$

In [30], another mobile app called kAs has been developed using machine learning by Zensark Technologies (Hyderabad, Telangana, India to assess respiratory health of the patients and disease specific cough signatures. The app asks 15 questions to the subject and their cough sound into the mobile app which sends the cough sounds to the company's AI platform Swaasa, where it undergoes an audiometric analysis and produces a composite COVID-19 Risk Score, based on the answers to the questionnaire and the coughing sound. The app generates a rating on a scale of 1 to 10, with 10 being the highest risk level. The Risk Score of any individual can be tracked across multiple days or weeks.

Schuller et al. [77] discussed the possible use of Computer Audition (CA) and AI in the analysis of cough sounds in patients with COVID-19. They first assessed CA's ability to automatically detect speech and cough under various semantics, such as breathing, dry and wet cough or sneezing, flu-like speech, eating habits, drowsiness, or pain. Subsequently, they proposed the use of CA technology in the diagnosis and treatment of patients with COVID-19. However, because of an absence of accessible information and annotation details, there is no report on the use of this technology in COVID-19 testing. In [96], Wang et al. analyzed the respiratory tract of patients with COVID-19 and other respiratory tract patients with common cold and flu. In addition, they proposed a model of respiratory simulation (called BI-AT-GRU) for the diagnosis of COVID-19. The BI-AT-GRU model incorporates the GRU neural network with bidirectional bids and attention and can distinguish 6 types of clinical respiratory patterns, such as Eupnea, Tachypnea, Bradypnea, Biots, Cheyne-Stokes, and Central-Apnea. Sharma et al. [81] meant to enhance the COVID-19 laboratory diagnostic methods for sputum tests. The project, named is Coswara, utilized cough, breath, and speech sounds to evaluate biomarkers in acoustics. Nine different vocal sounds were collected for each namely, breathing (two kinds; shallow and deep), cough (two kinds; shallow and heavy), sustained vowel phonation (three kinds; /ey/ as in made, /i/ as in beet, /u:/ as in cool), and one to twenty digit counting (two kinds; normal and fast paced). They also collected some metadata information, namely, age, gender, location (country, state/province), current health status (healthy / exposed / cured / infected) and the presence of co-morbidity (pre-existing medical conditions). The nine voices take on different body-breathing patterns. Visual and temporary spectral features were extracted from audio files. The classification and data curation tasks are under process.

The University of Massachusetts Amherst developed a portable device named FluSense [21] [1]. Figure 6 shows the components of FluSense device powered by an AI-based neural network that can recognize cough and crowd size in real time, and analyze and collect data directly to flu-like illnesses such as COVID-19. The FluSense uses a microphone array and a thermal camera configuration and neural computing engine to make speech and cough signals passively and continuously as well as changes in the crowd density on the edge in a real-time way. These information sources can help decide the timing of flu vaccination campaigns, potential travel limitations, medication distribution, and more [97]. The creators of FluSense say the new edge-computing platform, which is thought to be used in hospitals, healthcare rooms and large public spaces, could expand the arsenal of health monitoring tools used to predict flu and other outbreaks of viruses, such as COVID-19 epidemics or SARS.

Studies [1] have shown that FluSense accurately predicted daily patient counts with a Pearson Correlation Coefficient of 95%. The FluSense platform did not consider all respiratory infections or additional health information. Cough data is important and relevant but not enough to be used for all respiratory infections. And some other research is working. They collect data from a variety of sources. In [72], Ravelo launched a cough against COVID-19, a web page dedicated to spreading cough sounds from individuals who have tested COVID-19. This project is supported by the

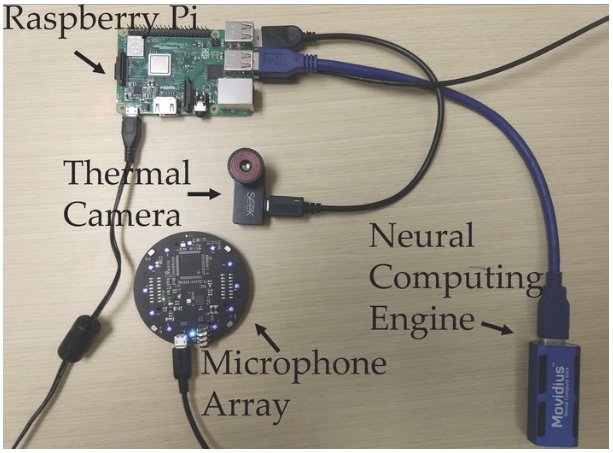


Fig. 6. The FluSense device houses these components [21] [1].

Bill and Melinda Gates Foundation. The process is simple. A person downloads a recording of his or her sputum and is asked to provide details such as symptoms, other illnesses, gender, and location - at least zip code - to determine if the person is from the region with high levels of COVID-19 infection or no. The process also asks individuals a picture of their COVID-19 test results. Once they have enough data, they can develop an ML or DL-based algorithm and check whether it can accurately determine the cough sounds associated with COVID-19 infection. Iqbal et al. [37] also discussed an anonymous framework that uses mobile app recognition function to capture and analyze suspicious sounds of people to determine whether a user is healthy or suffering from respiratory illness.

Researchers at the University of Cambridge [10] developed a cross-sectional system between vocal cords (coughing and breathing) to recognize healthy and unhealthy people. Voice sounds are used to discriminate between COVID-19, asthma, and healthy people. The three functions of binary separation are structured namely:

- Separate good COVID-19 users from healthy users.
- Separate COVID-19 users with cough from healthy cough users.
- Separate COVID-19 cough users from asthma users who have declared coughing.

More than 7,000 unique users (approximately 10K samples) participated in the crowdsourced data collection out of which more than 200 reported being COVID-19 positive. Typical audio amplification methods have been used to increase the sample size of a data set. Three classifications, namely, LR, Gradient Boosting Trees (GBT), and SVM were used for the classification task. The study used the combined curve area under the curve (AUC) to compare performance. More than 70 percent of AUCs are reported in all three binary split trades. The authors used respiratory samples to differentiate and found that the AUC was approximately 60%. However, when coughing and respiratory inputs are combined into phases, the AUC progresses to about 80% per activity due to the high number of features. A summary of AI-based ML and DL methods for speech and audio analysis related to COVID-19 health problems is shown in Table 3.

2.1 COVID-19 Diagnosis Based on Non-invasive Measurements

In [48], Maghdid et al. designed for the invisible diagnostic framework of COVID-19 based on smart phone sensors. In the proposed framework, smart phones can be utilized to collect potential patient's disease characteristics. For example, sensors can detect a patient's voice through a recording function and can detect a patient's body temperature through a finger recognition function. Thereafter, the collected data is uploaded to a cloud server supported by AI for diagnostic and analysis of diseases. Indeed, comparing various CT images takes quite a while and its understanding, by radiologists, can't be finished physically. In this manner, the proposed framework helps radiologists and empowers individuals to make effective and reliable decisions in suspected cases.

3 ML AND DL FOR DRUG AND VACCINE DEVELOPMENT

The ability of automatic abstract component learning, joined with a large amount of data, has had a significant impact on the effective use of ML. Two areas of high impact were affected by drug discovery and vaccination, where ML provided integrated property predictions, activity prediction, response prediction, and ligand-protein interactions. Based on proteomics and genomics research, various drug development programs and vaccines for SARS-CoV-2 and COVID-19 have been proposed. The use of ML and DL in the development of new drugs and vaccines is one of the major contributions to intelligent medicine and plays a significant role in the fight against COVID-19.

3.1 ML and DL For Vaccine Development

ML and DL play two significant supporting roles in this application: propagation of vaccine components by understanding the structure of viral proteins, and helping medical researchers examine a huge number of significant research papers at an exceptional rate. There are three main types of vaccines: vaccines for every pathogen, such as the flu or MMR, use deadly or weakened infections to get the immune response; subunit vaccines, (e.g., pertussis, shingles) use only part of the virus, such as protein; and nucleic acid vaccines insert viral genes into human cells to promote the body's response. The latest is a COVID-19 vaccine that started trials this week in the United States. AI helps to accelerate the development of subunits and nucleic acids [19].

Understanding protein composition is important in understanding how it works. Once the condition is understood, researchers can create drugs that work with different protein shapes. But it can take a long time to test every protein structure before discovering its unique 3D structure. AI systems based on DL can simplify the process of determining protein composition and its genetic sequence.

In January, Google DeepMind [79] [31] introduced AlphaFold, a sophisticated system that predicts 3D protein formation based on its genetic sequence. In early March, the system was tested in COVID-19. DeepMind has released a protein prediction for many untreated proteins related

TABLE 3
A summary of AI-based ML and DL methods for speech and audio analysis related to COVID-19 health problems.

Author	Application	ML/DL Method	Dataset	Performance
Miranda et al. [52]	TB Diagnosis	MFB, MFCC, STFT with CNN	Google audio set from 1.8 million Youtube Freesound videos and audio database	94.6% AUC
Yadav et al. [99]	Asthmatic Discovery	INTERSPEECH 2013 (The basis of the Computational Paralinguistics challenge acoustic features)	Speech from 47 asthmatic and 48 healthy controls	48% Accuracy
Larson et al. [44]	Avoid recording of speech while hearing cough	PCA on audio spectrograms, FFT coefficients and random separation	Acted cough from 17 patients having 8 people cough due to cold weather, 3 patients because of Asthama, 1 patient because of allergies and 5 patients who cough due to chronic cough condition	True positive rate is 92% and false positive rate is 50%
Simply et al. [84]	Obstructive sleep apnea (OSA) acquisition from sounds breathing in speech	MFCCs have a single layer neural network for respiration and MFCCs, strength, tone, kurtosis and ZCR with OV SVM separation	90 Male subjects' speech and sleep quality measures using WatchPAT[98Ref]	Cohen's kappa coefficient of 0.5 for breathing detection and 0.54 for OSA detection
Routray [75]	Automatic speech breathing average rating	Cepstrogram and support Vector machine with radial base work	16 recording of speeches 21-year-old group participants age means	89% F1-measure
Nallanthighal and Strik [55]	Receiving a breathing signal in conversational speech	Pectrogram with CNN and RNN	20 healthy speeches recordings using a microphone and a breathing signal using two respirator transducers belts	91.2% respiratory sensitivity
Partila et al. [65]	Pressure detection in speech in cases such as a car accident, domestic violence, and conditions near death	LLD and functional characteristics are extracted using openSMILE with k-NN, SVM, and CNN separators	312 emergency call recording of 112 Emergency Cable Emergency Plan from the Czech Republic	87.9% accuracy with SVM and 87.5% Accuracy with CNN (In separating stress from neutral speech)

to SARS-CoV-2, the virus that causes COVID-19, to help the research community better virus understanding. At the same time, [57] researchers from The University of Texas at Austin and the National Institutes of Health have used a popular biological process to develop the first 3D atomic map on the scale of a part of a virus that attaches to human cells — a spike protein. The team responsible for this critical breakthrough has spent years working with other Coronaviruses, including SARS-CoV and MERS-CoV. One of the predictions released by AlphaFold provided accurate predictions for this spike structure. Another effort [22] at the University of Washington's Institute for Protein Design also used computer models to develop 3D atom models on the SARS-CoV-2 spike protein scale closely related to those found on the UT Austin board. They are now building on this work by building new proteins to reduce Coronavirus. In theory, these proteins will adhere to a spike protein that prevents viral particles from infecting healthy cells.

The potential vaccine for COVID-19 [73] was created by researchers utilizing AI and cloud computing to prevent the Spike protein from binding to the ACE2 receptor in human cells. researchers at Flinders University analyzed the COVID-19 virus and then used this information to design a vaccine called Covax-19 as shown in Figure 7.

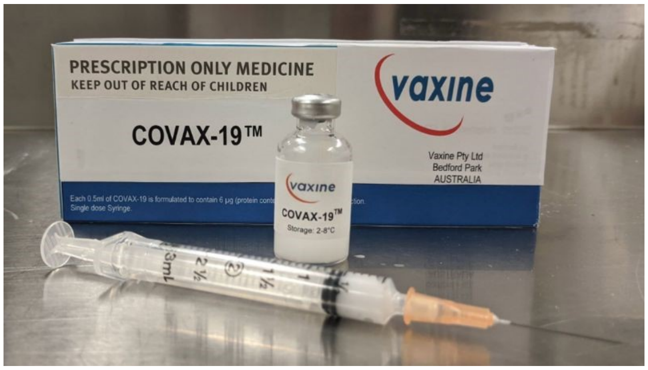


Fig. 7. Covax-19™ is an Australian-developed COVID-19 vaccine developed with the help of computational and artificial intelligence (AI)-based technologies [86].

The researchers used computer models of the S protein and its human receptor, the enzyme-converting angiotensin 2 (ACE2), to determine how the virus was affecting human cells. They were then able to design a vaccine that can block this process. The team used the most advanced technologies in AI and advanced manufacturing in cloud computing to speed up the development of vaccines [73] [91] [32].

In [28], Herst et al. detected the SARS-CoV-2 protein sequence from GenBank and used the MSA algorithm to determine nucleocapsid phosphoprotein sequence in possible peptide sequencing. It also suggests that a peptide vaccine based on CD8 + T-cell immunity in EBOV (West African epidemic 2013-2016) survivors is reasonable and possible. In [60], Ong et al. used ML and Reverse Vaccinology (RV) methods to anticipate and test potential COVID-19 vaccines. They utilized RV to examine bioinformatics pathogen genomes to identify promising baptismal candidates. They found the SARS-CoV-2 sequence and all proteins of the six known types of human Coronavirus from NCBI including SARS-CoV, MERS-CoV, HCoV-229E, HCoVOC43, HCoV-NL63, and HCoV-HKU1 is extracted from Uniprot proteomes. Subsequently, they utilized Vaxign and Vaxign-ML to examine the complete proteome of Coronaviruses and predict the functioning of biological signals. Next, they developed the Vaxign-ML model in terms of ML and RV using structural, vector support, proximity neighbor, random forest, and overgrowth (XGB) strategies and predicted the protein level of all SARS-CoV-2 protein. The most efficient XGB model was selected to predict the protegenicity rate of all WSH-CoV-2 proteins that separate Wuhan-Hu-1, downloaded from NCBI. Protein with a protegenicity point greater than 90% is considered a strong immunodeficiency vaccine (weight of F1-points $> 94\%$ in five-fold combined validation). NSP3 protein was selected for phylogenetic analysis, and the immunogenicity of NSP3 was assessed by predicting T cells MHC-I and MHC-II and Linear B cell epitopes.

A team of researchers [18] from MIT's Computer Science and AI Laboratory (CSAIL) have now taken a new approach in which they have used an integrated ML-based system that selects peptides (short amino acid fibers) that are predicted to give high numbers of vaccines. The design program called "OptiVax" introduces ways to develop new peptide drugs, test existing vaccines, and increase the composition of existing vaccines. In this program, peptides receive mechanical learning points for their ability to be expressed in response to antibodies and are selected to increase coverage of who can benefit from this vaccine.

In [70], Rahman et al. used immuno-informatics methods and comparative methods for the development of a SARS-CoV-2 anti-peptide vaccine, consisting of S (spike), E (envelop), and M (Membrane epitopes)) protein. They used the Ellipro antibody epitope predictive tool to predict B-specific epitopes in S-proteins. Ellipro uses many ML methods to predict and visualize a given protein sequence or B-cell epitope in a structure. In addition, Sarkar et al. [76] studied the epitope-based vaccine design of COVID-19 and used the SVM method to predict the toxicity of selected epitopes. In [67], Prachar et al. used 19 integrated epitope-HLA tools including the IEDB, ANN, and PSSM algorithm to predict and validate 174 SARS-CoV-2 epitopes.

3.2 Drug Development

AI systems based on ML and DL are used in field design with the production of a predictive learning model and perform a fast-paced test to precisely reflect the output. With a drug rehabilitation method, the AI systems can rapidly identify drugs that can battle emerging diseases such as COVID-19. This innovation can possibly improve drug accessibility, planning, treatment, and reported patient outcomes of COVID-19, which is a medical evidence-based tool. Drug discovery is a very risky, long and expensive process. According to a report by the Eastern Research Group (ERG), while it takes 10-15 years to make a new molecular company, the success rate is only 2.01 percent [98]. The concept of drug repurposing reuses old drugs for the treatment of a never-considered therapeutic indication. It is an experimental approach of identifying the pre-approved, discontinued, shelved and investigational drugs for authorized restatement for the treatment of other diseases. Conventional drug development usually includes five stages [53]:

- Discovery and development.
- Pre-clinical research.
- Clinical research.
- FDA review.
- FDA post-market safety monitoring and development.

However, there are only four steps in drug repurposing [53]:

- Compound identification.
- Compound acquisition.
- Clinical research.
- FDA post-market safety monitoring and development.

The discovery and development of new molecular entities being lengthy, time-killing and high-priced. So the best approach is to rebuild the approved drugs for the treatment of SARS-COV-2. In this context, Chloroquine (CQ) and it's Hydroxyl analogue Hydroxychloroquine (HCQ) have been reported in the treatment of viral infection. These drugs have antimalarial activity and also showed in vitro treatment against COVID-19 [42].

One group of AI-based drug development centers around the discovery of new drug-like compounds at the molecular level. In [9], Beck et al. proposed a DL-based drug-target interaction model named as Molecule Transformer-Drug Target Interaction (MT-DTI) to predict potential drug candidates for COVID-19. The MT-DTI model used SMILES strings and amino-acid sequences to predict target proteins with 3D crystal structures. The result showed that atazanavir, an antiretroviral medication used to treat and prevent the Human Immunodeficiency Virus (HIV), is the best chemical compound, showing an inhibitory potency with Kd of 94.94 nM against the SARS-CoV-2 3C-like proteinase, followed by remdesivir (113.13 nM), efavirenz (199.17 nM), ritonavir (204.05 nM), and dolutegravir (336.91 nM). The authors collected the amino-acid sequences of 3C-like proteases and related antiviral drugs and drug targets from the databases of NCBI, Drug Target Common (DTC), and BindingDB. In addition, they used a molecular docking and virtual screening tool (AutoDock Vina) to predict the binding affinity between 3,410 drugs and SARS-CoV-2 3CLpro. The experimental outcomes provided 6 potential drugs, such as Remdesivir, Atazanavir, Efavirenz, Ritonavir, Dolutegravir, Kaletra (lopinavir/ritonavir). Note that Remdesivir shows promising in clinical trial.

Two similarity-based methods, KronRLS [63] and SimBoost [26] have been proposed using efficient machine learn-

TABLE 4
A summary of drug development of COVID-19 based on AI-based ML and DL methods [13].

Author	Method	Role of ML/DL Method	COVID-19 Target	Potent In Drugs
Moskal et al. [54]	VAE, CNN, LSTM, and MLP	Help in generating SMILES strings and molecules	N/A	110 Drugs
Beck et al. [9]	MT-DTI	Predict binding affinity between drugs and protein targets	3CLpro, RdRp, Helicase	6 Drugs
Hu et al. [33]	DL	Predict binding between drugs and protein targets	3CLpro, RdRp	10 drugs
Kadioglu et al. [41]	NN and Naive Bayes	Construct drug likelihood prediction model	spike protein and more	3 drugs
Hofmarcher et al. [29]	ChemAI	Predict inhibitory effects of molecules on COVID-19 proteases	3CLpro, PLpro	30,000 molecules
Bung et al. [11]	RNN and RL	Classify protease inhibitor molecules	3CLpro	31 compounds
Zhavoronkov et al. [103]	28 ML	generate new molecular structures for 3CL-pro	3CLpro	100 molecules
Tang et al. [87]	RL and DQN	Predict molecules and lead compounds for each target fragment	3CLpro	47 compounds

ing methods. But this matrix has two downsides. Firstly, feature representation is limited which would make the prediction inaccurate. Secondly, it necessitates the calculation of the similarity matrix which can limit the maximum number of molecules in the training process. To overcome these limitations, a deep learning-based DTI model, DeepDTA [61], was proposed. It is an end-to-end CNN-based model that dispenses with the requirement for feature engineering. The model automatically finds valuable features from a raw molecule and protein sequence. Its success has been demonstrated on two publicly available DTI benchmarks i.e. KronRLS and Sim-Boost. They employed CNN blocks to learn representations from the raw protein sequences and SMILES strings and combine these representations to feed into a fully-connected layer block and called it DeepDTA. similarity matrices for proteins and compounds as input were used. The Smith-Waterman (S-W) and Pubchem Sim algorithms were used to process the pairwise similarities for the proteins and ligands, respectively. three alternative combinations in learning the hidden patterns of the data and used this information as input to the proposed ad enhanced DeepDTA model. The three alternative combinations for learning this model are as follows:

- Learning only compound representation with a CNN block and using S-W similarity as protein representation.
- Learning only protein sequence representation with a CNN block and using Pubchem Sim to describe compounds.
- Learning both protein representation and compound representations with a CNN block.

The last combination used with DeepDTA is the combined model. And that model is used in many researches [3], [9], [34] for COVID-19 drug repurposing.

In this study [101], they developed a network-based deep-learning approach, termed deepDR, for in silico drug repurposing by integrating 10 networks: one drug–disease, one drug-side-effect, one drug–target and seven drug–drug networks. Specifically, the deepDR learns high-stage functions of medication from the heterogeneous networks with the aid of using a multi-modal deep Autoencoder. Then, the learned low-dimensional representation of drugs together with clinically reported drug–disease pairs are encoded and decoded together thru a Variational Autoencoder to deduce applicants for approved drugs for which they had been now no longer firstly authorized. It results that deepDR revealed a high performance of 90.8% AUC, outperforming other CNN based and ML based approaches. Some of other deep learning-based approaches for Drug testing, repurposing and discovery for COVID-19 are DeepPurpose [34], kGCN [43], DeepChem [71], and D3Targets-2019-nCoV [83].

In [11], Bung et al. committed to the development of new SARS-CoV-2 3CLpro chemical frameworks based on deep learning technology. They developed an RL-based RNN model for protease inhibitor molecule molecules and found a small set that prefers chemical space. Subsequently, they collected 2515 protease inhibitor molecules in SMILES format from the ChEMBL database as a training data, in which each SMILES series was considered a time series, and each position or symbol was considered a point of time. The release of small molecules was embedded in the 3CLpro structure with minimal force and was calculated based on a visual test note obtained by selecting anti-SARS-CoV-2 participants. In [87], Tang et al. analyzed 3CLpro with a 3D structure similar to SARS-CoV and evaluated it as an attractive target for the development of anti-COVID-19 drugs. They have developed a comprehensive Q-learning network (called ADQN-FBDD) to produce leading SARS-CoV-2 3CL-pro compounds. They collected 284 reported molecules as SARS-CoV-2 3CLpro inhibitors. These molecules are classified using an improved BRICS algorithm to obtain a SARS-CoV-2 3CLpro targeted library. Thereafter, the proposed ADQN-FBDD model trains each piece of the target and predicts the corresponding molecules with the leading elements. Through the Structure-Based Optimization Policy (SBOP), they have finally identified the 47 alternatives to the inhibitory effects on SARS-CoV-2 3CLpro in these lead compounds, which are considered to be anti-SARS-CoV-2 drugs. A summary of drug development of COVID-19 based on AI-based ML and DL methods is shown in Table 4.

4 CHALLENGES AND FUTURE DIRECTIONS

In this section, we provide details on the challenges using ML and DL to tackle the problem of COVID-19. Also, we show future research directions that ML and DL can contribute to the battle of COVID-19.

4.1 Challenges

At present, the applications of AI-based ML and DL in COVID-19 research face many challenges such as regulations, the lack of available large-scale training data, massive noisy data and rumors, the limited knowledge on the intersection of computer science and medicine, data privacy and human rights protection, inaccurate text data availability and more.

- **Regulation.** As the outbreak grows and the daily number of confirmed cases (infected and dead) increased dramatically, various measures have been taken to control this outbreak, e.g. Lockdown, social distancing, screen and large-scale testing. In this way, regulatory authorities play a key role in defining policies that can encourage the involvement of residents, scientists and investigators, industry, giant techs and large firms, as well as harmonize mechanisms by various organizations to avoid any barriers to the prevention of COVID-19.
- **Lack of available large-scale training data.** Many AI methods rely on large-scale training data defined, including medical imaging and various environmental details. However, due to the rapid explosion of COVID-19, there are insufficient datasets available for AI. In addition, interpreting training samples is time consuming and requires professional medical staff.
- **Massive noisy data and rumors.** The challenges arise from relying on portable internet and social media; Massive audio details and false stories about COVID-19 have been published in various online sources without any major updates. However, AI-based ML and DL algorithms appear to be weak at judging and filtering audio and error data. This problem reduces the use and functionality of AI, especially in epidemic predictions and transmission analysis.
- **Limited knowledge in the intersection of computer science and medicine.** Many AI scientists are from computer science, but the use of AI in the COVID-19 war requires a deep collaboration in computer science, medical imaging, bioinformatics, virology, and many other related fields. Therefore, it is important to coordinate the collaborative work of researchers from different fields and to integrate the knowledge of multiple studies to deal with COVID-19.
- **Data privacy and human rights protection.** In the age of big data and AI, the cost of obtaining personal privacy data is very low. Faced with public health problems such as COVID-19, many governments seek to obtain a variety of personal information, including cell phone data, personal mobility data, and patient disease data. How to effectively protect your privacy and human rights during AI-based discovery and processing is an issue worth discussing.
- **Incorrect structured and unstructured data (e.g. image, text, and numerical data) for the COVID-19 virus such as scholarly articles in the COVID-19 database.** Dealing with inaccurate and confusing information in text details. Large volume of data from various sources. Excess data makes it difficult to extract important pieces of information.
- **COVID-19 early diagnosis using medical imaging e.g. Chest X-ray and CT scan.** Dealing with imbalanced datasets due to insufficient COVID-19 data for medical imaging and long training time and unable to explain the results challenges.
- **Screen and triage patients, identify effective therapies and treatments, risk assessments, survival predictions, health care and medical resource planning.** The challenge is to gather physical features and treatment outcomes for patients. Another challenge is dealing with low quality data that can lead to biased and inaccurate predictions.

4.2 Future Research Direction

AI-based ML and DL systems can also contribute to the battle against COVID-19 from the following potential directions.

- **Detection of non-contact disease.** In CXR and CT imaging, the use of automatic image assessment can effectively prevent the risk of infection between radiologists and patients during the COVID-19 epidemic. AI can be used for patient posture, standard phase detection of CXR and CT images, and camera equipment.
- **Remote video diagnosis and consultations.** Combining AI and Natural Language Processing (NLP) technologies can be used to develop remote video diagnostic programs and chat robot systems and to provide consultations for COVID-19 patients as well as first community diagnoses.
- **Biological research.** In the field of biological research, AI-based ML and DL systems can be used to detect protein formation and viral factors through accurate analysis of biomedical information, such as major protein structures, genetic sequences, and viral trajectories.
- **Drug development and vaccination.** AI-based ML and DL systems can't only be used to detect potential drugs and vaccines but also can be used to mimic the interactions between drugs and proteins and between vaccines and receptors, thus predicting possible responses to drugs and vaccines for patients with different COVID-19 patients.
- **Identification and screening of false information.** AI-based ML and DL systems can be used to reduce and delete false news and audio data on online forums to provide reliable, accurate, and scientific information about the COVID-19 epidemic.
- **Impact assessment and evaluation.** Different types of simulations can use AI-based ML and DL systems to analyze the impact of different social control modes on disease transmission. Thereafter, they can be used to

test effective and scientific methods of disease prevention and community control.

- **Patient contact tracking.** By building social networks and information graphs, AI-based ML and DL systems can detect and track the traits of people closest to patients with COVID-19, thus accurately predicting and controlling the possible spread of the disease.
- **Smart robots.** Smart robots are expected to be used in projects such as disinfection and cleaning in public places, distribution of products, and patient care without the needs of human services. This will stop the transmission of the COVID-19 disease.
- **Future work with descriptive AI-based ML and DL techniques.** To explain the effectiveness of deep learning models and graphical features that contribute to the distinction between COVID-19 and other types of pneumonia is needed. This will help radiologists and clinicians to gain an understanding of the virus and to evaluate future Coronavirus CT and X-ray images effectively.
- **COVID-19 diagnosis and treatment, which one is important?** Both are important, but definitely finding a cure for COVID-19 is more important. From the literature review in this survey, we find that most of the current AI-based ML and DL approaches are more focused on detecting COVID-19. More future research work based on ML and DL are needed for finding COVID-19 treatment.

5 CONCLUSION

The COVID-19 epidemic has had a profound effect on people's lives around the world and the number of deaths related to the disease continues to rise worldwide. While AI, particularly in ML and DL, technologies has infiltrated our daily lives with great success, it has also contributed to helping people in the difficult battle against COVID-19. In this survey, we investigated the AI-based ML and DL towards COVID-19 diagnosis and treatment. In addition, we summarized the AI-based ML and DL methods and the available datasets, resources, and results in the fight against COVID-19. This survey provides the ML and DL researchers and the wider health community a comprehensive overview of the current state-of-the-art methodologies and applications with details of how ML and DL and data can improve the status of COVID-19, and further studies to stop the COVID-19 outbreak. Challenges and future directions using ML and DL were also provided.

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REFERENCES

[1] Forsad Al Hossain, Andrew A Lover, George A Corey, Nicholas G Reich, and Tauhidur Rahman. Flusense: a contactless syndromic surveillance platform for influenza-like illness in hospital waiting areas. *Proceedings of the ACM on Interactive, Mobile, Wearable and Ubiquitous Technologies*, 4(1):1–28, 2020.

[2] Health IT Analytics. Deep Learning Models Can Detect COVID-19 in Chest CT Scans. https://healthitanalytics.com/news/deep-learning-models-can-detect-covid-19-in-chest-ct-scans., 2020. [Online; accessed 3-September-2020].

[3] Muhammad Umer Anwar, Farjad Adnan, Asma Abro, Muhammad Rayyan Khan, Asad Ur Rehman, Muhammad Osama, Saad Javed, Ahmadullah Baig, Muhammad Raffey Shabbir, Muhammad Zaman Assir, et al. Combined deep learning and molecular docking simulations approach identifies potentially effective fda approved drugs for repurposing against sars-cov-2, 2020.

[4] Ioannis D Apostolopoulos, Sokratis I Aznaouridis, and Mpesiana A Tzani. Extracting possibly representative covid-19 biomarkers from x-ray images with deep learning approach and image data related to pulmonary diseases. *Journal of Medical and Biological Engineering*, page 1, 2020.

[5] Ioannis D Apostolopoulos and Tzani A Mpesiana. Covid-19: automatic detection from x-ray images utilizing transfer learning with convolutional neural networks. *Physical and Engineering Sciences in Medicine*, page 1, 2020.

[6] Xiang Bai, Cong Fang, Yu Zhou, Song Bai, Zaiyi Liu, Liming Xia, Qianlan Chen, Yongchao Xu, Tian Xia, Shi Gong, et al. Predicting covid-19 malignant progression with ai techniques. 2020.

[7] Sanhita Basu and Sushmita Mitra. Deep learning for screening covid-19 using chest x-ray images. *arXiv preprint arXiv:2004.10507*, 2020.

[8] BBVA. Artificial intelligence to detect COVID-19 in less than a second using x-rays. https://www.bbva.com/en/artificial-intelligence-to-detect-covid-19-in-less-than-a-second-using-x-rays/, 2019. [Online; accessed 6-September-2020].

[9] Bo Ram Beck, Bonggun Shin, Yoonjung Choi, Sungsoo Park, and Keunsoo Kang. Predicting commercially available antiviral drugs that may act on the novel coronavirus (sars-cov-2) through a drug-target interaction deep learning model. *Computational and structural biotechnology journal*, 2020.

[10] Chloë Brown, Jagmohan Chauhan, Andreas Grammenos, Jing Han, Apinan Hasthanasombat, Dimitris Spathis, Tong Xia, Pietro Cicuta, and Cecilia Mascolo. Exploring automatic diagnosis of covid-19 from crowdsourced respiratory sound data. *arXiv preprint arXiv:2006.05919*, 2020.

[11] Navneet Bung, Sowmya Ramaswamy Krishnan, Gopalakrishnan Bulusu, and Arijit Roy. De novo design of new chemical entities (nces) for sars-cov-2 using artificial intelligence. *ChemRxiv*, 2020.

[12] Charmaine Butt, Jagpal Gill, David Chun, and Benson A Babu. Deep learning system to screen coronavirus disease 2019 pneumonia. *Applied Intelligence*, page 1, 2020.

[13] Jianguo Chen, Kenli Li, Zhaolei Zhang, Keqin Li, and Philip S Yu. A survey on applications of artificial intelligence in fighting against covid-19. *arXiv preprint arXiv:2007.02202*, 2020.

[14] Jun Chen, Lianlian Wu, Jun Zhang, Liang Zhang, Dexin Gong, Yilin Zhao, Shan Hu, Yonggui Wang, Xiao Hu, Biqing Zheng, et al. Deep learning-based model for detecting 2019 novel coronavirus pneumonia on high-resolution computed tomography: a prospective study. *MedRxiv*, 2020.

[15] Muhammad EH Chowdhury, Tawsifur Rahman, Amith Khandakar, Rashid Mazhar, Muhammad Abdul Kadir, Zaid Bin Mahbub, Khandaker Reajul Islam, Muhammad Salman Khan, Atif Iqbal, Nasser Al-Emadi, et al. Can ai help in screening viral and covid-19 pneumonia? *arXiv preprint arXiv:2003.13145*, 2020.

[16] Joseph Paul Cohen, Lan Dao, Paul Morrison, Karsten Roth, Yoshua Bengio, Beiyi Shen, Almas Abbasi, Mahsa Hoshmand-Kochi, Marzyeh Ghassemi, Haifang Li, et al. Predicting covid-19 pneumonia severity on chest x-ray with deep learning. *arXiv preprint arXiv:2005.11856*, 2020.

[17] Dipayan Das, KC Santosh, and Umapada Pal. Truncated inception net: Covid-19 outbreak screening using chest x-rays. *Physical and engineering sciences in medicine*, pages 1–11, 2020.

[18] Srishti Deoras. How ML Is Assisting In Development Of Covid-19 Vaccines. https://analyticsindiamag.com/how-ml-is-assisting-in-development-of-covid-19-vaccines/, 2020. [Online; accessed 19-September-2020].

[19] Oren Etzioni and Nicole Decario. AI Can Help Scientists Find a Covid-19 Vaccine. https://www.wired.com/story/opinion-ai-can-help-find-scientists-find-a-covid-19-vaccine/, 2020. [Online; accessed 16-September-2020].

[20] HEALTH EUROPA. Using Artificial Intelligence to determine COVID-19 severity. https://www.healtheuropa.eu/using-artificial-intelligence-to-determine-covid-19-severity/100501/, 2020. [Online; accessed 12-September-2020].

[21] FluSense. AI-Powered COVID-19 Cough Analyzer App Assesses Respiratory Health and Associated Risks. https://www.umass.edu/gateway/feature/flusense, 2020. [Online; accessed 16-September-2020].

[22] Institute for Protein Design. Rosetta's role in fighting coronavirus. https://www.ipd.uw.edu/2020/02/rosettas-role-in-fighting-coronavirus/, 2020. [Online; accessed 10-September-2020].

[23] Biraja Ghoshal and Allan Tucker. Estimating uncertainty and interpretability in deep learning for coronavirus (covid-19) detection. *arXiv preprint arXiv:2003.10769*, 2020.

[24] Ophir Gozes, Maayan Frid-Adar, Hayit Greenspan, Patrick D Browning, Huangqi Zhang, Wenbin Ji, Adam Bernheim, and Eliot Siegel. Rapid ai development cycle for the coronavirus (covid-19) pandemic: Initial results for automated detection & patient monitoring using deep learning ct image analysis. *arXiv preprint arXiv:2003.05037*, 2020.

[25] Lawrence O Hall, Rahul Paul, Dmitry B Goldgof, and Gregory M Goldgof. Finding covid-19 from chest x-rays using deep learning on a small dataset. *arXiv preprint arXiv:2004.02060*, 2020.

[26] Tong He, Marten Heidemeyer, Fuqiang Ban, Artem Cherkasov, and Martin Ester. Simboost: a read-across approach for predicting drug–target binding affinities using gradient boosting machines. *Journal of cheminformatics*, 9(1):1–14, 2017.

[27] Ezz El-Din Hemdan, Marwa A Shouman, and Mohamed Esmail Karar. Covidx-net: A framework of deep learning classifiers to diagnose covid-19 in x-ray images. *arXiv preprint arXiv:2003.11055*, 2020.

[28] Charles V Herst, Scott Burkholz, John Sidney, Alessandro Sette, Paul E Harris, Shane Massey, Trevor Brasel, Edecio Cunha-Neto, Daniela S Rosa, William Chong Hang Chao, et al. An effective ctl peptide vaccine for ebola zaire based on survivors' cd8+ targeting of a particular nucleocapsid protein epitope with potential implications for covid-19 vaccine design. *Vaccine*, 2020.

[29] Markus Hofmarcher, Andreas Mayr, Elisabeth Rumetshofer, Peter Ruch, Philipp Renz, Johannes Schimunek, Philipp Seidl, Andreu Vall, Michael Widrich, Sepp Hochreiter, et al. Large-scale ligand-based virtual screening for sars-cov-2 inhibitors using deep neural networks. *Available at SSRN 3561442*, 2020.

[30] HospiMedica. AI-Powered COVID-19 Cough Analyzer App Assesses Respiratory Health and Associated Risks. https://www.hospimedica.com/covid-19/articles/294784217/ai-powered-covid-19-cough-analyzer-app-assesses-respiratory-health-and-associated-risks.html, 2020. [Online; accessed 14-September-2020].

[31] HospiMedica. Scientists Use Cloud-Based Supercomputing and AI to Develop COVID-19 Treatments and Vaccine Models. https://www.hospimedica.com/covid-19/articles/294784537/scientists-use-cloud-based-supercomputing-and-ai-to-develop-covid-19-treatments-and-vaccine-models.html, 2020. [Online; accessed 15-September-2020].

[32] HospiMedica. Scientists Use Cloud-Based Supercomputing and AI to Develop COVID-19 Treatments and Vaccine Models. https://www.hospimedica.com/covid-19/articles/294784537/scientists-use-cloud-based-supercomputing-and-ai-to-develop-covid-19-treatments-and-vaccine-models.html, 2020. [Online; accessed 18-September-2020].

[33] Fan Hu, Jiaxin Jiang, and Peng Yin. Prediction of potential commercially inhibitors against sars-cov-2 by multi-task deep model. *arXiv preprint arXiv:2003.00728*, 2020.

[34] Kexin Huang, Tianfan Fu, Lucas Glass, Marinka Zitnik, Cao Xiao, and Jimeng Sun. Deeppurpose: a deep learning library for drug-target interaction prediction and applications to repurposing and screening, 2020.

[35] Lu Huang, Rui Han, Tao Ai, Pengxin Yu, Han Kang, Qian Tao, and Liming Xia. Serial quantitative chest ct assessment of covid-19: Deep-learning approach. *Radiology: Cardiothoracic Imaging*, 2(2):e200075, 2020.

[36] Ali Imran, Iryna Posokhova, Haneya N Qureshi, Usama Masood, Sajid Riaz, Kamran Ali, Charles N John, and Muhammad Nabeel. Ai4covid-19: Ai enabled preliminary diagnosis for covid-19 from cough samples via an app. *arXiv preprint arXiv:2004.01275*, 2020.

[37] Mohammad Zafar Iqbal and Md Faiz Iqbal Faiz. Active surveillance for covid-19 through artificial in-telligence using concept of real-time speech-recognition mobile application to analyse cough sound. 2020.

[38] itn. CT Provides Best Diagnosis for Novel Coronavirus (COVID-19). https://www.itnonline.com/content/ct-provides-best-diagnosis-novel-coronavirus-covid-19, 2020. [Online; accessed 20-September-2020].

[39] Cheng Jin, Weixiang Chen, Yukun Cao, Zhanwei Xu, Xin Zhang, Lei Deng, Chuansheng Zheng, Jie Zhou, Heshui Shi, and Jianjiang Feng. Development and evaluation of an ai system for covid-19 diagnosis. *medRxiv*, 2020.

[40] Shuo Jin, Bo Wang, Haibo Xu, Chuan Luo, Lai Wei, Wei Zhao, Xuexue Hou, Wenshuo Ma, Zhengqing Xu, Zhuozhao Zheng, et al. Ai-assisted ct imaging analysis for covid-19 screening: Building and deploying a medical ai system in four weeks. *medRxiv*, 2020.

[41] Onat Kadioglu, Mohamed Saeed, H Johannes Greten, and Thomas Efferth. Identification of novel compounds against three targets of sars cov-2 coronavirus by combined virtual screening and supervised machine learning. *Bull. World Health Organ*, 2020.

[42] Mohammad Sultan Khuroo, Ahmad A Sofi, and Mohammad Khuroo. Chloroquine and hydroxychloroquine in coronavirus disease 2019 (covid-19). facts, fiction & the hype. a critical appraisal. *International journal of antimicrobial agents*, page 106101, 2020.

[43] Ryosuke Kojima, Shoichi Ishida, Masateru Ohta, Hiroaki Iwata, Teruki Honma, and Yasushi Okuno. kgcn: a graph-based deep learning framework for chemical structures. *Journal of Cheminformatics*, 12:1–10, 2020.

[44] Eric C Larson, TienJui Lee, Sean Liu, Margaret Rosenfeld, and Shwetak N Patel. Accurate and privacy preserving cough sensing using a low-cost microphone. In *Proceedings of the 13th international conference on Ubiquitous computing*, pages 375–384, 2011.

[45] Lin Li, Lixin Qin, Zeguo Xu, Youbing Yin, Xin Wang, Bin Kong, Junjie Bai, Yi Lu, Zhenghan Fang, Qi Song, et al. Artificial intelligence distinguishes covid-19 from community acquired pneumonia on chest ct. *Radiology*, 2020.

[46] Mohamed Loey, Florentin Smarandache, and Nour Eldeen M Khalifa. Within the lack of chest covid-19 x-ray dataset: A novel detection model based on gan and deep transfer learning. *Symmetry*, 12(4):651, 2020.

[47] Halgurd S Maghdid, Aras T Asaad, Kayhan Zrar Ghafoor, Ali Safaa Sadiq, and Muhammad Khurram Khan. Diagnosing covid-19 pneumonia from x-ray and ct images using deep learning and transfer learning algorithms. *arXiv preprint arXiv:2004.00038*, 2020.

[48] Halgurd S Maghdid, Kayhan Zrar Ghafoor, Ali Safaa Sadiq, Kevin Curran, and Khaled Rabie. A novel ai-enabled framework to diagnose coronavirus covid 19 using smartphone embedded sensors: Design study. *arXiv preprint arXiv:2003.07434*, 2020.

[49] Arpan Mangal, Surya Kalia, Harish Rajgopal, Krithika Rangarajan, Vinay Namboodiri, Subhashis Banerjee, and Chetan Arora. Covidaid: Covid-19 detection using chest x-ray. *arXiv preprint arXiv:2004.09803*, 2020.

[50] Xueyan Mei, Hao-Chih Lee, Kai-yue Diao, Mingqian Huang, Bin Lin, Chenyu Liu, Zongyu Xie, Yixuan Ma, Philip M Robson, Michael Chung, et al. Artificial intelligence–enabled rapid diagnosis of patients with covid-19. *Nature Medicine*, pages 1–5, 2020.

[51] Shervin Minaee, Rahele Kafieh, Milan Sonka, Shakib Yazdani, and Ghazaleh Jamalipour Soufi. Deep-covid: Predicting covid-19 from chest x-ray images using deep transfer learning. *arXiv preprint arXiv:2004.09363*, 2020.

[52] Igor DS Miranda, Andreas H Diacon, and Thomas R Niesler. A comparative study of features for acoustic cough detection using deep architectures. In *2019 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, pages 2601–2605. IEEE, 2019.

[53] Sweta Mohanty, Md Harun Ai Rashid, Mayank Mridul, Chandana Mohanty, and Swati Swayamsiddha. Application of artificial intelligence in covid-19 drug repurposing. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 2020.

[54] Martyna Moskal, Wiktor Beker, Rafał Roszak, Ewa P Gajewska, Agnieszka Wołos, Karol Molga, Sara Szymkuć, and Bartosz A Grzybowski. Suggestions for second-pass anti-covid-19 drugs based on the artificial intelligence measures of molecular similarity, shape and pharmacophore distribution. 2020.

[55] Venkata Srikanth Nallanthighal and H Strik. Deep sensing of breathing signal during conversational speech. 2019.

[56] Ali Narin, Ceren Kaya, and Ziynet Pamuk. Automatic detection of coronavirus disease (covid-19) using x-ray images and deep convolutional neural networks. *arXiv preprint arXiv:2003.10849*, 2020.

[57] UT NEWS. Breakthrough in Coronavirus Research Results in New Map to Support Vaccine Design. https://news.utexas.edu/2020/02/19/breakthrough-in-coronavirus-research-results-in-new-map-to-support-vaccine-design/, 2020. [Online; accessed 8-September-2020].

[58] Qianqian Ni, Zhi Yuan Sun, Li Qi, Wen Chen, Yi Yang, Li Wang, Xinyuan Zhang, Liu Yang, Yi Fang, Zijian Xing, et al. A deep learning approach to characterize 2019 coronavirus disease (covid-19) pneumonia in chest ct images. *European radiology*, pages 1–11, 2020.

[59] European Society of Medical Imaging Informatics. Automated diagnosis and quantitative analysis of COVID-19 on imaging. https://imagingcovid19ai.eu/, 2020. [Online; accessed 1-September-2020].

[60] Edison Ong, Mei U Wong, Anthony Huffman, and Yongqun He. Covid-19 coronavirus vaccine design using reverse vaccinology and machine learning. *BioRxiv*, 2020.

[61] Hakime Öztürk, Arzucan Özgür, and Elif Ozkirimli. Deepdta: deep drug–target binding affinity prediction. *Bioinformatics*, 34(17):i821–i829, 2018.

[62] Tulin Ozturk, Muhammed Talo, Eylul Azra Yildirim, Ulas Baran Baloglu, Ozal Yildirim, and U Rajendra Acharya. Automated detection of covid-19 cases using deep neural networks with x-ray images. *Computers in Biology and Medicine*, page 103792, 2020.

[63] Tapio Pahikkala, Antti Airola, Sami Pietilä, Sushil Shakyawar, Agnieszka Szwajda, Jing Tang, and Tero Aittokallio. Toward more realistic drug–target interaction predictions. *Briefings in bioinformatics*, 16(2):325–337, 2015.

[64] Mohammad Khalid Pandit and Shoaib Amin Banday. Sars n-cov2-19 detection from chest x-ray images using deep neural networks. *International Journal of Pervasive Computing and Communications*, 2020.

[65] Pavol Partila, Jaromir Tovarek, Jan Rozhon, and Jakub Jalowiczor. Human stress detection from the speech in danger situation. In *Mobile Multimedia/Image Processing, Security, and Applications 2019*, volume 10993, page 109930U. International Society for Optics and Photonics, 2019.

[66] PhysicsWorld. AI checks CT scans for COVID-19. https://physicsworld.com/a/ai-checks-ct-scans-for-covid-19/, 2020. [Online; accessed 1-September-2020].

[67] Marek Prachar, Sune Justesen, Daniel B Steen-Jensen, Stephan P Thorgrimsen, Erik Jurgons, Ole Winther, and Frederik Otzen Bagger. Covid-19 vaccine candidates: Prediction and validation of 174 sars-cov-2 epitopes. *bioRxiv*, 2020.

[68] Xiaolong Qi, Zicheng Jiang, Qian Yu, Chuxiao Shao, Hongguang Zhang, Hongmei Yue, Baoyi Ma, Yuancheng Wang, Chuan Liu, Xiangpan Meng, et al. Machine learning-based ct radiomics model for predicting hospital stay in patients with pneumonia associated with sars-cov-2 infection: A multicenter study. *medRxiv*, 2020.

[69] RadBoudumc. Evaluation of an AI system for detection of COVID-19 on Chest X-Ray images. https://www.radboudumc.nl/en/news/2020/evaluation-of-an-ai-system-for-detection-of-covid-19-on-chest-x-ray-images, 2020. [Online; accessed 13-September-2020].

[70] M Shaminur Rahman, M Nazmul Hoque, M Rafiul Islam, Salma Akter, ASM Rubayet-Ul-Alam, Mohammad Anwar Siddique, Otun Saha, Md Mizanur Rahaman, Munawar Sultana, Keith A Crandall, et al. Epitope-based chimeric peptide vaccine design against s, m and e proteins of sars-cov-2 etiologic agent of global pandemic covid-19: an in silico approach. *PeerJ*, 8:e9572, 2020.

[71] Bharath Ramsundar, Peter Eastman, Patrick Walters, and Vijay Pande. *Deep learning for the life sciences: applying deep learning to genomics, microscopy, drug discovery, and more.* " O'Reilly Media, Inc.", 2019.

[72] Jenny Ravelo. This nonprofit needs your cough sounds to detect COVID-1. https://www.devex.com/news/this-nonprofit-needs-your-cough-sounds-to-detect-covid-19-97141, 2020. [Online; accessed 12-September-2020].

[73] Victoria Rees. AI and Cloud Computing Used to Develop COVID-19 Vaccine. https://www.drugtargetreview.com/news/59650/ai-and-cloud-computing-used-to-develop-covid-19-vaccine/, 2020. [Online; accessed 17-September-2020].

[74] Erik Ridley. AI can assess COVID-19 severity on chest x-rays. https://www.auntminnie.com/index.aspx?sec=ser&sub=def&pag=dis&ItemID=129674, 2020. [Online; accessed 12-September-2020].

[75] Aurobinda Routray et al. Automatic measurement of speech breathing rate. In *2019 27th European Signal Processing Conference (EUSIPCO)*, pages 1–5. IEEE, 2019.

[76] Bishajit Sarkar, Md Asad Ullah, Fatema Tuz Johora, Masuma Afrin Taniya, and Yusha Araf. The essential facts of wuhan novel coronavirus outbreak in china and epitope-based vaccine designing against 2019-ncov. *BioRxiv*, 2020.

[77] Björn W Schuller, Dagmar M Schuller, Kun Qian, Juan Liu, Huaiyuan Zheng, and Xiao Li. Covid-19 and computer audition: An overview on what speech & sound analysis could contribute in the sars-cov-2 corona crisis. *arXiv preprint arXiv:2003.11117*, 2020.

[78] Megan Scudellari. Hospitals Deploy AI Tools to Detect COVID-19 on Chest Scans. https://spectrum.ieee.org/the-human-os/biomedical/imaging/hospitals-deploy-ai-tools-detect-covid19-chest-scans, 2020. [Online; accessed 10-September-2020].

[79] Anderw Senior, John Jumper, Demis Hassabis, and Pushmeet Kohli. Alphafold: Using ai for scientific discovery. *DeepMind. Recuperado de: https://deepmind. com/blog/alphafold*, 2018.

[80] Prabira Kumar Sethy and Santi Kumari Behera. Detection of coronavirus disease (covid-19) based on deep features. *Preprints*, 2020030300:2020, 2020.

[81] Neeraj Sharma, Prashant Krishnan, Rohit Kumar, Shreyas Ramoji, Srikanth Raj Chetupalli, Prasanta Kumar Ghosh, Sriram Ganapathy, et al. Coswara–a database of breathing, cough, and voice sounds for covid-19 diagnosis. *arXiv preprint arXiv:2005.10548*, 2020.

[82] Feng Shi, Liming Xia, Fei Shan, Dijia Wu, Ying Wei, Huan Yuan, Huiting Jiang, Yaozong Gao, He Sui, and Dinggang Shen. Large-scale screening of covid-19 from community acquired pneumonia using infection size-aware classification. *arXiv preprint arXiv:2003.09860*, 2020.

[83] Yulong Shi, Xinben Zhang, Kaijie Mu, Cheng Peng, Zhengdan Zhu, Xiaoyu Wang, Yanqing Yang, Zhijian Xu, and Weiliang Zhu. D3targets-2019-ncov: a webserver for predicting drug targets and for multi-target and multi-site based virtual screening against covid-19. *Acta Pharmaceutica Sinica B*, 2020.

[84] Ruby M Simply, Eliran Dafna, and Yaniv Zigel. Obstructive sleep apnea (osa) classification using analysis of breathing sounds during speech. In *2018 26th European Signal Processing Conference (EUSIPCO)*, pages 1132–1136. IEEE, 2018.

[85] Mohammed A Soghaier, Khwaja MI Saeed, and Khushhal K Zaman. Public health emergency of international concern (pheic) has declared twice in 2014; polio and ebola at the top. *AIMS public health*, 2(2):218, 2015.

[86] TABIP. Coronavirus Vaccine Candidate Developed In Adelaide Lab To Start Human Trials. https://covid19.tabipacademy.com/2020/07/03/coronavirus-vaccine-candidate-developed-in-adelaide-lab-to-start-human-trials/, 2020. [Online; accessed 20-September-2020].

[87] Bowen Tang, Fengming He, Dongpeng Liu, Meijuan Fang, Zhen Wu, and Dong Xu. Ai-aided design of novel targeted covalent inhibitors against sars-cov-2. *bioRxiv*, 2020.

[88] Cranfield University. Artificial intelligence spots COVID-19 in chest X-rays. https://pharmaphorum.com/news/artificialintelligence-spots-covid-19-from-chest-x-rays/, 2020. [Online; accessed 12-September-2020].

[89] Cranfield University. Using artificial intelligence to detect COVID-19 in X-rays. https://medicalxpress.com/news/2020-05-artificial-intelligence-covid-x-rays.html, 2020. [Online; accessed 11-September-2020].

[90] Cranfield University. Using machine learning to detect COVID-19 in X-rays. https://tectales.com/ai/using-ai-to-detect-covid-19-in-x-rays.html, 2020. [Online; accessed 11-September-2020].

[91] Flinders University. Microsoft's AI for Health Supports COVID-19 Vaccine. https://medicalxpress.com/news/2020-08-microsoft-ai-health-covid-vaccine.html, 2020. [Online; accessed 18-September-2020].

[92] New York University. App determines COVID-19 disease severity using artificial intelligence, biomarkers. https://www.sciencedaily.com/releases/2020/06/200603132529.htm, 2020. [Online; accessed 14-September-2020].

[93] VIDA. LungPrint Clinical Solutions. https://vidalung.ai/clinical_solutions/, 2020. [Online; accessed 2-September-2020].

[94] Linda Wang and Alexander Wong. Covid-net: A tailored deep convolutional neural network design for detection of covid-19 cases from chest x-ray images. *arXiv preprint arXiv:2003.09871*, 2020.

[95] Shuai Wang, Bo Kang, Jinlu Ma, Xianjun Zeng, Mingming Xiao, Jia Guo, Mengjiao Cai, Jingyi Yang, Yaodong Li, Xiangfei Meng, et al. A deep learning algorithm using ct images to screen for corona virus disease (covid-19). *MedRxiv*, 2020.

[96] Yunlu Wang, Menghan Hu, Qingli Li, Xiao-Ping Zhang, Guangtao Zhai, and Nan Yao. Abnormal respiratory patterns classifier may contribute to large-scale screening of people infected with covid-19 in an accurate and unobtrusive manner. *arXiv preprint arXiv:2002.05534*, 2020.

[97] ET Health World. Scientists develop portable AI device that can use coughing sounds to monitor COVID-19 trends. https://health.economictimes.indiatimes.com/news/diagnostics/scientists-develop-portable-ai-device-that-can-use-coughing-sounds-to-monitor-covid-19-trends/74730537, 2020. [Online; accessed 11-September-2020].

[98] Hanqing Xue, Jie Li, Haozhe Xie, and Yadong Wang. Review of drug repositioning approaches and resources. *International journal of biological sciences*, 14(10):1232, 2018.

[99] Shivani Yadav, Merugu Keerthana, Dipanjan Gope, Prasanta Kumar Ghosh, et al. Analysis of acoustic features for speech sound based classification of asthmatic and healthy subjects. In *ICASSP 2020-2020 IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP)*, pages 6789–6793. IEEE, 2020.

[100] Seung Hoon Yoo, Hui Geng, Tin Lok Chiu, Siu Ki Yu, Dae Chul Cho, Jin Heo, Min Sung Choi, Il Hyun Choi, Cong Cung Van, Nguen Viet Nhung, et al. Deep learning-based decision-tree classifier for covid-19 diagnosis from chest x-ray imaging. *Frontiers in medicine*, 7:427, 2020.

[101] Xiangxiang Zeng, Siyi Zhu, Xiangrong Liu, Yadi Zhou, Ruth Nussinov, and Feixiong Cheng. deepdr: a network-based deep learning approach to in silico drug repositioning. *Bioinformatics*, 35(24):5191–5198, 2019.

[102] Kang Zhang, Xiaohong Liu, Jun Shen, Zhihuan Li, Ye Sang, Xingwang Wu, Yunfei Zha, Wenhua Liang, Chengdi Wang, Ke Wang, et al. Clinically applicable ai system for accurate diagnosis, quantitative measurements, and prognosis of covid-19 pneumonia using computed tomography. *Cell*, 2020.

[103] Alex Zhavoronkov, Vladimir Aladinskiy, Alexander Zhebrak, Bogdan Zagribelnyy, Victor Terentiev, Dmitry S Bezrukov, Daniil Polykovskiy, Rim Shayakhmetov, Andrey Filimonov, Philipp Orekhov, et al. Potential covid-2019 3c-like protease inhibitors designed using generative deep learning approaches. *Insilico Medicine Hong Kong Ltd A*, 307:E1, 2020.

[104] Chuansheng Zheng, Xianbo Deng, Qing Fu, Qiang Zhou, Jiapei Feng, Hui Ma, Wenyu Liu, and Xinggang Wang. Deep learning-based detection for covid-19 from chest ct using weak label. *medRxiv*, 2020.