Chaos, Solitons and Fractals 139 (2020) 110059

Contents lists available at ScienceDirect

Chaos, Solitons and Fractals

Nonlinear Science, and Nonequilibrium and Complex Phenomena

journal homepage: www.elsevier.com/locate/chaos

Review

Applications of machine learning and artificial intelligence for Covid-19 (SARS-CoV-2) pandemic: A review

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ARTICLE INFO

Article history:
Received 10 June 2020
Accepted 23 June 2020
Available online 25 June 2020

Keywords:
Covid-19
Machine learning
Artificial intelligence
Pandemic

ABSTRACT

Background and objective: During the recent global urgency, scientists, clinicians, and healthcare experts around the globe keep on searching for a new technology to support in tackling the Covid-19 pandemic. The evidence of Machine Learning (ML) and Artificial Intelligence (AI) application on the previous epidemic encourage researchers by giving a new angle to fight against the novel Coronavirus outbreak. This paper aims to comprehensively review the role of AI and ML as one significant method in the arena of screening, predicting, forecasting, contact tracing, and drug development for SARS-CoV-2 and its related epidemic.

Method: A selective assessment of information on the research article was executed on the databases related to the application of ML and AI technology on Covid-19. Rapid and critical analysis of the three crucial parameters, i.e., abstract, methodology, and the conclusion was done to relate to the model's possibilities for tackling the SARS-CoV-2 epidemic.

Result: This paper addresses on recent studies that apply ML and AI technology towards augmenting the researchers on multiple angles. It also addresses a few errors and challenges while using such algorithms in real-world problems. The paper also discusses suggestions conveying researchers on model design, medical experts, and policymakers in the current situation while tackling the Covid-19 pandemic and ahead.

Conclusion: The ongoing development in AI and ML has significantly improved treatment, medication, screening, prediction, forecasting, contact tracing, and drug/vaccine development process for the Covid-19 pandemic and reduce the human intervention in medical practice. However, most of the models are not deployed enough to show their real-world operation, but they are still up to the mark to tackle the SARS-CoV-2 epidemic.

1. Introduction

There are several disease outbreaks that invaded humanity in World history. World Health Organization (WHO), its co-operating clinicians and various national authorities around the globe fight against these pandemics to date. Since the first Covid-19 (Coronavirus) disease case confirmed in China December 2019 Wuhan District, the outbreak continues to spread all across the world, and on 30th January 2020 WHO declared the pandemic as an international concern of public health emergency [1]. The novel Coronavirus (SARS-CoV-2) disease spread on more than 185 countries infecting more than 7,145,800 individuals and causing 407,067 deaths by June 09, 2020 [2,3]. To address this global novel pandemic, WHO, scientists and clinicians in medical industries are searching for new technology to screen infected patients in various stages, find best clinical trials, control the spread of this virus, develop a vaccine for curing infected patients, trace contact of the infected patient. Recent studies identified that Machine Learning and Artificial Intelligence are promising technology employed by various healthcare providers as they result in better scale-up, speed-up processing power, reliable and even outperform human in specific healthcare tasks [4]. Therefore, healthcare industries and clinicians worldwide employed various ML and AI technology to tackle the Covid-19 pandemic to address the challenges during the outbreak. In medical industries, AI is not applied to replace the human interactions, but to provide decision support for clinicians on what they are modeled for [5].

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https://doi.org/10.1016/j.chaos.2020.110059

This paper focuses on the novel Covid-19 epidemic and how the modern AI and ML technology were recently employed to solve the challenges during the outburst. We present comprehensive reviews of studies on the model and technology applied to tackle the novel Covid-19 pandemic. The studies further discuss types of AI and ML methods recently employed integration and types of the dataset, the final performance of each proposed model, and present on the pros and cons of modern techniques.

2. ML and AI recently employed to tackle health care SARS-CoV-2 outbreak

AI and ML technology are used to improve the accuracy of prediction for screening both infectious and non-infectious diseases [6]. The relation with health care begins with the evolution of the first expert system called MYCIN developed in 1976 [7]. MYCIN was designed to use 450 rules collected from a medical expert to treat bacterial infection by suggesting antibiotics to the patients. Such an expert system serves as clinical decision support for clinicians and medical experts [8]. Recent studies evident on the prospect of ML and AI technology for the various pandemic outbreak, it supports healthcare experts in various communicable diseases (SARS, EBOLA, HIV, COVID_19) [9-17] and non-communicable diseases (Cancer, Diabetic, Heart disease, and Stroke) [18-25] outbreak.

2.1. ML and AI technology in SARS-CoV-2 screening and treatment

Early detection of any disease, be it infectious and non-infectious, is critically an important task for early treatment to save more lives [26,27]. Fast diagnosis and screening process helps prevent the spread of pandemic diseases like SARS-CoV-2, cost-effective, and speed up the related diagnosis. The development of an expert system for health care assists in the new order of identification screening and management of SARS-CoV-2 carrier by more cost-effective compared to the traditional method. ML and AI are used to augment the diagnosis and screening process of the identified patient with radio imaging technology akin to Computed Tomography (CT), X-Ray, and Clinical blood sample data. In this regard, Table 1 shows selective information on diagnosis and screening proposed for the Coronavirus disease. The healthcare expert can use radiology images like X-ray and CT scans as routine tools to augment traditional diagnosis and screening. Unfortunately, the performance of such devices is moderate during the high outburst of the SARS-CoV-2 pandemic. In this regard, studies [28] show the potential of AI and ML tools by suggesting a new model that comes with rapid and valid method SARS-CoV-2 diagnosis using Deep Convolutional Network. The study shows that diagnosis utilizing an expert system employing AI and ML on 1020 CT images of 108 Covid-19 infected patients along with viral pneumonia of 86 patients, the remarkable performance suggests the use of the convolutional neural network (Resnet-101) as an adjuvant tool for radiologist resulting 86.27%, 83.33% of accuracy and specificity respectively.

Recent studies design an auxiliary tool to increase the accuracy of Covid-19 diagnosis with new model Automatic COVID-19 detection based on deep learning algorithm [29]. The developed model uses raw chest X-ray images of 127 infected patients with 500 no-findings and pneumonia cases of 500 records. With remarkable performance accuracy, binary class of 98.08%, and multi-class with 87.02%. Multi-classes proved the applicability of the expert system to assist radiology in validating in screening process rapidly and accurately.

Furthermore, researchers have found four important medical features combinations of clinical, laboratory features, and demographic information using GHS, CD3 percentage, total protein, and patient age employing Support Vector Machine as the primary feature classification model [30]. The new model is effective and robust in predicting patients in critical/severe conditions, and the empirical results show that a combination of the four-feature results an AUROC of 0.9996 and 0.9757 in training and testing datasets respectively. The survival and the cox-multivariant regression analysis revealed the model's significance towards and auxiliary tools for the healthcare expert.

Table 1
ML and AL technology in SARS-CoV-2 Screening.

Publication	ML/AI method	Types of data	No of patients	Validation method	Sample size	Accuracy
Ardakani, A. A *et al.*, [28]	Deep Convolutional Neural Network ResNet-101	Clinical, Mamographic	1020, 86	Holdout	1020 CT images of 108 volume of patients with laboratory confirmed Covid-19, 86 CT images of viral and atypical pneumonia patients,	Accuracy: 99.51% Specificity: 99.02%
Ozturk, T. *et al.*, [29]	Convolutional Neural Network DarkCovidNet Architecture	Clinical, Mamographic	127, 43 f, 82 m 500, 500	Cross-validation	127 X-ray images with 43 female and 82 male positive cases 500 no-findings and pneumonia cases of 500	Accuracy: 98.08% on Binary classes Accuracy: 87.02% on Multi-classes
Sun, L *et al.*, [30]	Support Vector Machine	Clinical, laboratory features, Demographics	336, 220	Holdout	336 infected patients with PCR kit, 26 severe/critical cases and 310 non-serious cases and with another related disease79 hypertension, 29diabetes, 17 coronary disease and 7 having history of tuberculosis	Accuracy: 77.5% Specificity: 78.4% AUROC reaches 0.99 training and 0.98 testing dataset
Wu, J. *et al.*, [31]	Random forest Algorithm	Clinical, Demographics	253, 169, 49,24	Cross-validataion	Total of 253 samples from 169 patients suspected with Covid-19 collected from multiple sources. Clinical blood test of 49 patients derived from commercial clinic center. 24 samples infected patient with Covid-19	Accuracy: 95.95% Specificity: 96.95%

After evaluating 253 clinical blood samples from Wuhan, researchers found eleven (bilirubin total, creatine kinase isoenzyme, GLU, creatinine, kalium, lactate dehydrogenase, platelet distribution width, calcium, basophil, total protein, and magnesium) key relevant indices which can assist as a discrimination tool of Covid-19 for healthcare expert toward rapid diagnosis [31]. The studies show that 11 relevant indices are extracted after employing the Random Forest algorithm with an overall accuracy of 95.95% and 96.97% specificity respectively. Furthermore, the authors published that the tools were deployed and are available on web-server at http://lishuyan.lzu.edu.cn/COVID2019_2/ to assist healthcare experts.

The above studies give the evidence of an application of the expert system; designing rapid diagnosis was the main objective along with augmentation of accuracy. Prompt and early detection reduce the spread of the disease and reserve more time to the healthcare expert to correspond to the next diagnosis to save more lives, resulting in low-cost medical expenditure. However, majority of the studied paper employed a single classification algorithm on individual data or more. Therefore it is suggested to come up with a hybrid classification method applying more potential algorithm on multi-database or hybrid-database consisting of clinical, mammographic, and demographic data, as each type of data has a significant factor that could represent the true identity of the infected patients and deployment of the application in the real world.

2.2. ML and AI technology in SARS-Cov-2 contact tracing

If a person diagnoses and is confirmed with Covid-19, the next important step is contact tracing prevention of the wider spread of the disease. According to WHO, the infection spreads from person-to-person primarily through saliva, droplets, or discharges from the nose through contact transmission [32]. To take control on the spread of SARS-Cov-2, contact tracing is an essential public health tool used to break the chain of virus transmission [33]. The process of contact tracing is to identify and manage people who are recently exposed to an infected Covid-19 patient to avoid further spread. Generally, the process identifies the infected person with a follow-up for 14 days since the exposure. If employed thoroughly, this process can break the transmission chain of the current novel coronavirus and suppress the outbreak by giving a higher chance of adequate controls and helping reduce the magnitude of the recent pandemic. In this regard, various infected countries come up with a digital contact tracing process with the mobile application, utilizing different technologies like Bluetooth, Global Positioning System (GPS), Social graph, contact details, network-based API, mobile tracking data, card transaction data, and system physical address. The digital contact tracing process can perform virtually real-time and much faster compared to the non-digital system. All these digital apps are designed to collect individual personal data, which will be analyzed by ML and AI tools to trace a person who is vulnerable to the novel virus due to their recent contacted chain.

As shown in Table 2, articles [34,35] listed various countries competent with such ML and AL-based contact tracing applications. Studies show that over 36 Countries successfully employed digital contact tracing use following centralized, decentralized, or hybrid of both techniques were proposed to lessen the effort and augment the effectiveness of the traditional healthcare diagnosis processes.

Table 2
Contact tracing application used by Countries.

Sl. No	Country	Contact tracing App	Location tracking	Launch on
1	Australia	COVIDSafe	BlueTrace protocol: Bluetooth	April 14, 2020
2	Austria	Stopp Corona	Bluetooth, Google/Apple	March, 2020
3	Bahrain	BeAware Bahrain	Bluetooth & GSM	March 31, 2020
4	Bulgaria	ViruSafe	GSM	May, 2020
5	China	conjunction with Alipay	GPS, GSM, credit-card-transaction-history	Very little Info
6	Cyprus	CovTracer	GPS, GSM	May, 2020
7	Colombia	CoronApp	GPS	April 12, 2020
8	Czech Republic	eRouška (eFacemask)	BlueTrace protocol: Bluetooth	April 15, 2020
9	Estonia	Estonia's App	Google/Apple, DP-3T, Bluetooth	April, 2020
10	Finland	Ketju	DP-3T, Bluetooth	May, 2020
11	France	StopCovid	Bluetooth	May, 2020
12	Germany	CoronaApp	Bluetooth, Google/Apple	May, 2020
13	Ghana	GH Covid-19 Tracker App	GPS	April 12, 2020
14	Hungary	VírusRadar	Bluetooth	May 13, 2020
15	Iceland	Rakning C-19	GPS	April 2020
16	India	Aarogya Setu	Bluetooth & location-generated social graph	April 2, 2020
17	Iran	Mask.ir	GSM	May, 2020
18	Ireland	HSE Covid-19 App	Bluetooth, Google/Apple	May, 2020
19	Israel	HaMagen	Standard location APIs	March, 2020
20	Italy	Immuni	Bluetooth, Google/Apple	May, 2020
21	Jordan	AMAN App - Jordan	GPS	May, 2020
22	Latvia	Apturi Covid	Bluetooth	May, 29, 2020
23	Malaysia	MyTrace	Bluetooth, Google/Apple	May 3, 2020
24	Mexico	CovidRadar	Bluetooth	May, 2020
25	New Zealand	NZ COVID Tracer	Contact details and physical address	May 20, 2020
26	North Macedonia	StopKorona	Bluetooth	April 13, 2020
27	Norway	Smittestopp	Bluetooth and GSM	April 16, 2020
28	Poland	ProteGO	Bluetooth	May, 2020
29	Qatar	Ehteraz	Bluetooth and GSM	May, 2020
30	Saudi Arabia	Corona Map	Bluetooth	April 3, 2020
31	Singapore	TraceTogether	BlueTrace protocol, Bluetooth	March 20, 2020
32	South Korea	Non-app-based	Mobile device tracking data and card transaction data	May, 2020
33	Switzerland	SwissCovid	DP-3T protocol, Bluetooth, Google/Apple	May 20, 2020
34	Turkey	Hayat Eve Sigar	Bluetooth, GSM	April, 2020
35	UAE	TraceCovid	Bluetooth	May, 2020
36	UK	NHS Covid-19 App	Bluetooth	May, 2020

Concerning contact tracing, studies have proven the use of ML and AI in augmentation of contact tracing process against infectious Chronic Wasting disease [36]. After applying Graph theory on infectious animal disease epidemics data, mainly shipment data between each farm, the resultant graph properties generated by the proposed model can be used to exploit to augment contact tracing more efficiently. Moreover, the generated graphs have a potential prediction impact on the number of infections that can take place. However, there are still limitations in addressing the scenario, privacy, control over the data, and even data security breach. Countries are working to overcome the challenges; some countries like Israel "passed an emergency law to use mobile phone data" to tackle the current pandemic [37]. Among the world contact tracing apps, some countries app violated privacy law and reported unsafe [35] so far they do the job acceptably by supplement the manual tracing process. However, virtually every country has their contact tracing application individually, as the outbreak continues to spread across the world, it becomes a global health emergency. To fight against the Covid-19 as one, one should provide a standard de-facto centralized contact tracing application to trace every human being all around the world. Also, it is reported that some specific query needs to address: "Is it mandatory or voluntary?" "Is the attempt clear or translucent?" "Is information gathering lessened?" "Will collected information be demolished as declared?", "Is the data safe with the host" and "Are there any restrictions or control on utilizing the information?".

2.3. ML and AI technology in SARS-CoV-2 prediction and forecasting

Selective information shown in Table 3 indicates the applications of ML and AI in forecasting and predicting the novel pandemic. A new novel model, that forecast and predicting 1-3 to 6 days ahead of total Covid-19 patient of 10 Brazilian states, using stacking-ensemble with support vector regression algorithm on the cumulative positive Covid-19 cases of Brazilian data was proposed, thus augmenting the short-term forecasting process to alert the healthcare expert and the government to tackle the pandemic [38]. Recent studies suggested a novel model using a supervised multi-layered recursive classifier called XGBoost on clinical and mammographic factor datasets. After applying the model, researchers found out those three significant key features (high-sensitivity C-reactive protein, lymphocyte and lactic dehydrogenase (LDH)) of the 75 features clinical and blood test samples result to be the highest rank of 90% accuracy in predicting and assessing Covid-19 patient into general, severe and mortality rate [39]. Furthermore, comparatively higher value in single lactic dehydrogenase appears to be a significant factor in classifying most patients in need of intensive medical care, as LDH degree related to various respiratory disorder diseases, namely asthma and bronchitis, and pneumonia. The forecast model employed decision rule to forecast rapidly and predict infected individuals at the highest risk, authorized patients to be manageable for intensive care, and possibly lessen the transience rate. A Canadian based forecasting model using time-series was developed employing Deep learning algorithm for the long-short-term-memory network, the studies found out a key factor intended for predicting the course with an ending point estimation of the current SARS-CoV-2 epidemic in Canada and all over the globe [40]. The suggested model forecast ending point of this SARS-CoV-2 outbreak in Canada will be around June 2020. Based on the data collected from John Hopkins University [3], the prediction was likely to be accurate as newly infected cases have dropped rapidly and proven the applicability of the expert system in predicting and forecasting for the current pandemic outbreak by revealing key significant features. The real-time forecasting model was proposed combining the goodness of the wavelet-based forecasting model and autoregressive integrated moving average based time-series model [41]. The model solves the problem by generating short-term forecasts of the SARS-CoV-2 for various countries (India, United Kingdom, Canada, South Korea, and France) to assist healthcare experts and policymakers as a preliminary cautioning module for each target country.

2.4. ML and AI technology in SARS-CoV-2 drugs and vaccination

Since the coronavirus epidemic fury, researchers and healthcare experts around the globe ubiquitously urged to develop a possible choice to tackle the development of drug and vaccine for the SARS-CoV-2 pandemic, and ML/AI technology constitutes to be an enthralling road. Concerning the possibility of drug choice for infected patient's treatment, instant testing on the existing old marketable medicines for novel SARS-CoV-2 carrier in a human being is essential.

Researchers from Taiwan are building a new model to augment the development of a novel drug [42]. After applying the ML and AI technology-based model on two datasets (one using the 3C-like protease constraint and other data-holding records of infected SARS-CoV, SARS-Cov-2, influenza, and human immunodeficiency virus (HIV)) using Deep Neural Network on the eighty old drugs with potential for Covid-19 treatment, the study suggested eight drugs, i.e., vismodegib, gemcitabine, clofazimine, celecoxib, brequinar, conivaptan, bedaquiline and tolcapone are found virtually effective against feline infectious peritonitis coronavirus. Furthermore, other five drugs like homoharringtonine, salinomycin,

Table 3
ML and AI applications: prediction and forecasting SARS-CoV-2.

Publication	ML/AI method	Types of data	No of patients	Validation method	Results
Ribeiro, M. H. D. M., *et al.*, [37]	Support Vector Regression and stacking-ensemble	Clinical	40.581	Holdout	Accuracy: Error in range of 0.87%-3.51% one, 1 .02%–5.63% three and 0.95% -6.90% six day ahead
Yan, L. *et al.*, [38]	XGBoost classifier	Clinical, Blood samples of 75 features	485	Cross-validation	Accuracy: 90%
Chimmula, V.K.R., *et al.*, [39]	Deep Learning using LSTM network	Demographic	John Hopkins University & Canadian Health authority, data containing infected cases upto March 31, 2020	Cross-validation	Ending point of the pandemic outbreak in Canada was predicted on June 2020
Chakraborty, T. and Ghosh, I. [40]	Hybrid Wavelet- autoregressive integrated moving average model and regression tree	Demographic	India: 64 UK: 65 Canada:70 France: 71 South Korea: 76	Cross-validation	Real-time forecast and 10 days ahead, Observed seven key features associated with dead rate.

boceprevir, tilorone and chloroquine are also found operational during AI experimental environment.

A novel molecule transformer-drug target interaction model was proposed jointly by researchers from the US and Korea to tackle the need for an antiviral drug that can treat the Covid-19 virus [43]. The study compares the accessible virtual screening and molecular docking application called AutoDock Vina with the proposed model employing a deep learning algorithm on 3C-like proteinase of Covid-19 and FDA approved 3,410 existing drugs available in the market. The result revealed that a popular antiretroviral drug used to treat HIV called Antazanavir (Kd of 94.94 nM) is the best drug for Covid-19 medication, followed by Remdisivir (Kd of 113.13 nM). Furthermore, results revealed that some medications like darunavir, ritonavir, and lopinavir were outlined to tackle viral proteinases. It was also found that various antiviral compounds like Kaletra might be utilized for the medicine of Covid-19 human patients.

A group of researchers from the USA discovered an antiviral drug for treating the Ebola virus. The discovery was first active in the year 2014 [44], starting with ML and AI-based pharmacophore computational analyzing on a limited size of in vitro infected carriers of the Ebola virus. The study proposed an amodiaquine and chloroquine compound popularly used to treat the malaria virus. Furthermore, after uncovering a decade of drug development based on ML and AI technology, a fusion of computational screening method with docking application and machine learning for choosing supplementary medication to investigate on SARS-CoV-2 was proposed [45]. Researchers refer to the successful discovery of Ebola [44], and the Zika virus [46] experience gain belief that the same model could be repeatedly utilized for drug discovery on Covid-19 and future virus pandemic ahead.

The selected review paper adopted various methodologies and technologies addressing the classical method of classification based on statistics to an advanced modern AI and ML algorithm. The use of computational tools, combined with docking application, was found to be more active in predicting the reusability of an existing old drug on Covid-19 medication and dramatically minimize the level of a risk factor in the development of medicine more cost-effective process. During this urgency, the use of ML and AI can augment the drug development process by lessening the time slot on discovering a supplementary treatment and medication for the carrier by drawing a vast probability over security, manageability, and clinical information on the existing drug compound. Issues and challenges found in this area were the limited resource of comprehensive hybrid data and real-life deployment of the application.

3. Conclusion and discussion

Since the outbreak of the novel SARS-CoV-2, scientists and medical industries around the globe ubiquitously urged to fight against the pandemic, searching alternative method of rapid screening and prediction process, contact tracing, forecasting, and development of vaccine or drugs with the more accurate and reliable operation. Machine Learning and Artificial Intelligence are such promising methods employed by various healthcare providers. This paper addresses on recent studies that apply such advance technology in augmenting the researchers in multiple angles, addressing the troubles and challenges while using such algorithm in assisting medical expert in real-world problems. This paper also discusses suggestions conveying researchers on AI/ML-based model design, medical experts, and policymakers on few errors encountered in the current situation while tackling the current pandemic. This review shows that the use of modern technology with AI and ML dramatically improves the screening, prediction, contact tracing, forecasting, and drug/vaccine development with extreme reliability. Majority of the paper employed deep learning algorithms and is found to have more potential, robust, and advance among the other learning algorithms. However, the current urgency requires an improved model with high-end performance accuracy in screening and predicting the SARS-CoV-2 with a different kind of related disease by analyzing the clinical, mammographic, and demographic information of the suspects and infected patients. Finally, it is evident that AI and ML can significantly improve treatment, medication, screening & prediction, forecasting, contact tracing, and drug/vaccine development for the Covid-19 pandemic and reduce the human intervention in medical practice. However, most of the models are not deployed enough to show their real-world operation, but they are still up to the mark to tackle the pandemic.

Declaration of Competing Interest

None.

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