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The Role of Artificial Intelligence and Machine Learning Techniques: Race for COVID-19 Vaccine

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Abstract

Context: In the healthcare system, Artificial Intelligence (AI) is emerging as a productive tool. There are instances where AI has done marvels in the diagnosis of various health conditions and the interpretation of complex medical disorders. Although AI is far from human intelligence, it can be used as an effective tool to study the SARS-CoV-2 and its capabilities, virulence, and genome. The progress of the pandemic can be tracked, and the patients can be monitored, thereby speeding up the research for the treatment of COVID-19. In this review article, we highlighted the importance of AI and Machine learning (ML) techniques that can speed up the path to the discovery of a possible cure for COVID-19. We also deal with the interactions between viromics and AI, which can hopefully find a solution to this pandemic.

Evidence Acquisition: A review of different articles was conducted using the following databases: MEDLINE/PubMed, SCOPUS, Web of Science, ScienceDirect, and Google Scholar for recent studies regarding the use of AI, seeking the spread of different infectious diseases using relevant MeSH subheadings.

Results: After a thorough screening of different articles, 30 articles were considered, and key information was obtained from them. Finally, the scope was broadened to obtain more information. Our findings indicated that AI/ML is a promising approach to drug development.

Conclusions: The field of AI has enormous potential to predict the changes that may take place in the environment. If this technology is applied to situations of a pandemic such as COVID-19, breakthroughs could potentially pave the way for new vaccines and antiviral drugs.

Keywords: Artificial Intelligence, Neural Networks, Machine Learning, Algorithms, Spike Glycoprotein, Deep Learning

1. Context

Among recent revolutions in technology, Artificial Intelligence (AI) is one emerging boom that is happening all over the world. Considering supercomputers, facial recognition, robots in surgery, or automated manufacturing, AI has taken over the world. This is the reason why AI futurists and economists tend to call AI the "fourth industrial revolution" (1). Although the mortality rate of the SARS-CoV-2 virus is low, this novel coronavirus (COVID-19) is one of the most infectious diseases affecting our planet in the past decades. This virus was first spotted in Wuhan, China, and has now globally spread to over 190 countries, infecting more than 400,000 people and more than 15,000 deaths (2, 3). Governments and health organizations of the world are constantly working day and night to combat the disease, but it has so far proved to be a major hurdle. Many scientists are seeking the help of AI. Artificial intelligence can aid as an effective tool to study the virus and its capabilities, virulence, and genome. Furthermore, it can help predict the protein structure of the virus and its interaction with other chemical compounds. This can help accelerate the preparation of new antiviral drugs and vaccines (4). Artificial Intelligence and Machine Learning (ML) are two giant effective weapons that we have against this notoriously fast progressive virus. The main aim of our review was to deal with the interaction between viromics and AI/Deep Learning, which might remarkably help find a solution to this pandemic. We also offered our processed data and code after analyzing different articles, which might be used for diagnostic purposes by doctors, researchers, scientists, and virologists who are involved in finding a solution for the SARS-CoV-2 pandemic. This technology is a promising approach in healthcare and can

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meet the needs of researchers and scientists in antiviral drugs and vaccine development (5, 6). The main objective of this article was to emphasize the importance of AI/Deep learning technologies in the field of healthcare and curbing infectious diseases like COVID-19. Using these tools, researchers can speed up the way of finding a possible cure to COVID-19.

2. Evidence Acquisition

2.1. Data Sources and Research Strategies

A systematic review was conducted on the following databases: MEDLINE/PubMed, SCOPUS, Web of Science, ScienceDirect, and Google Scholar for different studies regarding AI and ML technologies. We used the following combined Medical Subject Headings (MeSH) terms in Google Scholar, such as "Deep Learning", "Spike Glycoproteins", "Artificial Intelligence", "Algorithms", etc. Finally, the articles were deeply studied, of which key, in-depth information was obtained. The same search process was adopted for other databases.

2.2. Eligibility Criteria

Articles were included on the following basis: (a) majorly published in the English language between 2013 and 2020; (b) accounts of successful trials and experimentations with various AI/Deep Learning technologies such as Tensorflow, Keras, and Python tools; (c) recent WHO and CDC reports of COVID-19; (d) Viral genomic studies; and (e) original and peer-reviewed articles.

The articles were excluded on the following basis: (a) insufficient or no data and (b) articles that did not have a proper study or design approach.

2.3. Tools Employed

NCBI Genome WorkBench was used for processing the sequences, and ClustalX (version 2.1) was used for the alignment of the sequences. NCBI Tree Viewer was used for visualization of the phylogenetic tree. Additionally, python tools were employed in Jupyter Notebook (version to explore the spike glycoprotein structures of betacoronaviruses obtained from different hosts such as bats (*Chiroptera*), human (*Homo sapiens*) around the world, rabbits (*Oryctolagus cuniculus*), brown rats (*Rattus norvegicus*), and many other possible potential hosts for SARS-Cov-2 updated in NCBI till date. BioPython (version 1.76) was used for importing modules. We used PyMol software for the molecular visualization of the SARS-CoV-2 spike glycoprotein structure.

3. Results

3.1. Artificial Intelligence to Spot Patterns and Changes

The primary way to monitor the spread of infectious diseases is to look for "signs" or "signals". Artificial intelligence can see these signals in data earlier than humans. In late December of 2019, Li Wenliang warned his fellow colleagues and officials in Wuhan, China, about an upcoming possible SARS-like epidemic that shook the nation in the early 2000s before tragically succumbing to the disease (7). Simultaneously, a computer as AI server named BlueDot also alerted systems regarding an emerging risk of COVID-19 in Hubei province, China. This is not the first kind of disease that this software has alerted about. It has previously detected the outbreaks of 150 different pathogens, including SARS, Zika, Hepatitis A, Measles, etc. (8, 9). Many biotech companies are relying on AI to speed up the way to cure COVID-19. The hope is that it can spot patterns and changes and provide a promising approach for vaccine development. As coronaviruses such as SARS-CoV-2 have tendencies to mutate or even become drug-resistant, the drug developed should be effective for all forms (Broad Spectrum). Many drug companies such as Insilico Medicine Inc., Iktos, Vir Biotechnology Inc., Moderna Therapeutics, and Atomwise are utilizing AI technologies to develop a cure for this disease. Studies estimate that it will probably still take a year or more for the drug to be completely, successfully developed, and introduced to the market. However, in the case of AI, if the tendency of the potential virus is identified easily, the drug development can be achieved at a faster rate (10). Using informative techniques such as AI Neural Networks, Convolutional Neural Networks, Deep Generative Neural Networks, etc., initial potential molecular compounds and viral strains from different places around the world can be analyzed. Although its impact may seem relatively limited at first, this technology has great potential in the field of drug discovery and development (11).

3.2. Viral Host Prediction with Deep Learning

Zoonotic diseases, which involve animal to human transmission of infectious diseases, are current global problems. It could be understood from the recent problem of COVID-19 that wreaked havoc on the world. The first outbreak of SARS-CoV-2 in China can be traced back to Huanan Seafood Market in Wuhan. It is a wet market meaning that meat is sold alongside wild, exotic animals such as civets, bats, pangolins, etc. There could be numerous cases of possible transmission between these animals, either dead/ alive/vectors to humans. In such cases, it is difficult to determine the actual host of the virus -the host may be particularly adapted- and possible origin of the virus

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(12, 13). To overcome this situation, viral genome structures obtained from different animals, possibly hosting betacoronaviruses such as SARS-CoV-2, are obtained and can be trained with deep neural networks. Various computational techniques that can analyze the DNA and RNA sequences of the virus have been developed. Different architectures have been developed to train neural networks by continuously feeding data (14). Some of the ANN (Artificial Neural Network) based viral host prediction approaches are listed below.

• Truncated Back Propagation Through Time (TBPTT) Algorithm: A viral sequence is processed one timestep at a time (k1 timesteps). It minimizes error for the expected output with a given input (Figure 1).

• Recurrent Neural Networks (RNNs): RNNs can be repeatedly trained to predict viral host traits. By using this method, we can obtain the nearest neighbors and neural networks can be built (Figure 2).

• Convolutional Neural Networks (CNNs): The prediction of virus mutation can be studied using CNNs. This can be used to analyze the course of an outbreak. The below image depicts the forecasting of the dynamics of an influenza-like illness. This same process can be applied to SARS-CoV-2 (15-18) (Figure 3).

3.3. Detecting COVID-19 in X-Ray Images with AI Tools

It is possible to detect COVID-19 in X-Ray images of patients using AI tools such as Tensorflow and Keras. Although this method is not a reliable, accurate medical diagnostic method, it still shows how knowledge from computer vision/deep learning can make a big impact on the world of healthcare using AI tools. We just need to obtain the X-ray dataset of patients who have been tested positive for COVID-19. It can be obtained from various open sources. This is followed by sampling of "normal" patients. Finally, a CNN should be trained to detect COVID-19 from the sampled X-Ray images. The below figure shows the dataset of X-Rays of COVID-19 positive and COVID-19 negative patients. These can be trained by neural networks to automatically detect the presence of COVID-19 (19, 20) (Figure 4).

3.4. Exploring SARS-CoV-2 Spike Glycoprotein with Python Tools

Since the discovery of COVID-19, there have been various controversies and debates on its possible origin. The genome of SARS-CoV-2 consists of single, positive-stranded RNA, which is roughly 30K nucleotides long. The genome structure has similarity to other coronaviruses, more specifically the betacoronaviruses. The particular characteristic that makes it similar to other betacoronaviruses is the spike glycoprotein structure. It facilitates the entry of the virus into the cells. In this process, we are going to explore the genome of SARS-CoV-2 from different hosts (21).

3.4.1. Importing Modules

The following modules were imported from BioPython (version 1.76) (22) (Figure 5).

3.4.2. Obtaining Sequences from NCBI

NCBI virus database was used to download the betacoronavirus sequences. The csv and fasta files for the viruses were downloaded. By using the accession number or host, we accessed the subsets (23) (Figure 6).

3.4.3. Getting Subsets of the Sequence

The subsets were obtained after accessing the SARS-CoV-2 betacoronaviruses. It was listed with the species, the host, and the date of collection (24) (Figure 7).

3.4.4. Aligning the Given Sequences

For aligning multiple sequences of betacoronaviruses, we used NCBI Genome Workbench (Multiple Sequence Alignment Viewer) and ClustalX (version 2.1). We can see the Receptor Binding Domain (RBD) and Polybasic Cleavage Site by scrolling across the sequence (25, 26) (Figure 8).

3.4.5. Phylogenetic Tree

We can view the phylogenetic tree using the NCBI Tree Viewer (27) (Figure 9).

3.4.6. Viewing the Structure of Novel Coronavirus Spike Receptor-Binding Domain Complexed with Its Receptor ACE2

For this process, we obtained the SWISS MODELS from Protein Data Bank (PDB). The model chosen was the structure of novel coronavirus spike receptor-binding domain complexed with its receptor ACE2. The structures were downloaded in PDB formats and processed in PyMol environment. By using this tool, we visualized and explored the molecular structure of SARS-CoV-2 spike glycoprotein (28-32) (Figure 10).

4. Discussion

4.1. Current Scenario in the Use of AI/ML Technologies in Vaccine Development for COVID-19

In the present circumstances, AI technologies are not widely employed by all researchers during vaccine and drug development. Only fewer machine learning models have been implemented for the spread of coronavirus. AI can forecast the rate in which an infection spreads in a

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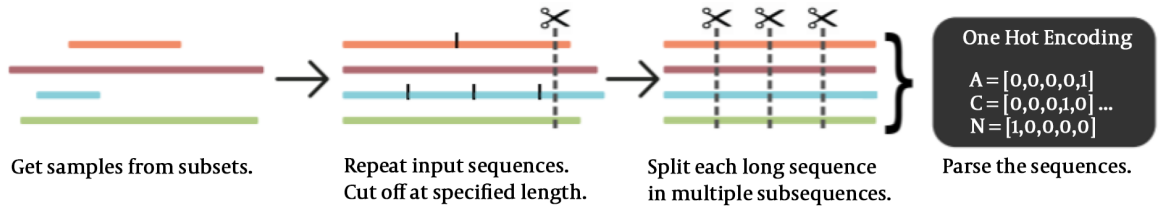


Figure 1. TBPTT Algorithm (courtesy: Mr. Florian Mock-VIDHOP, A viral host predicting tool)

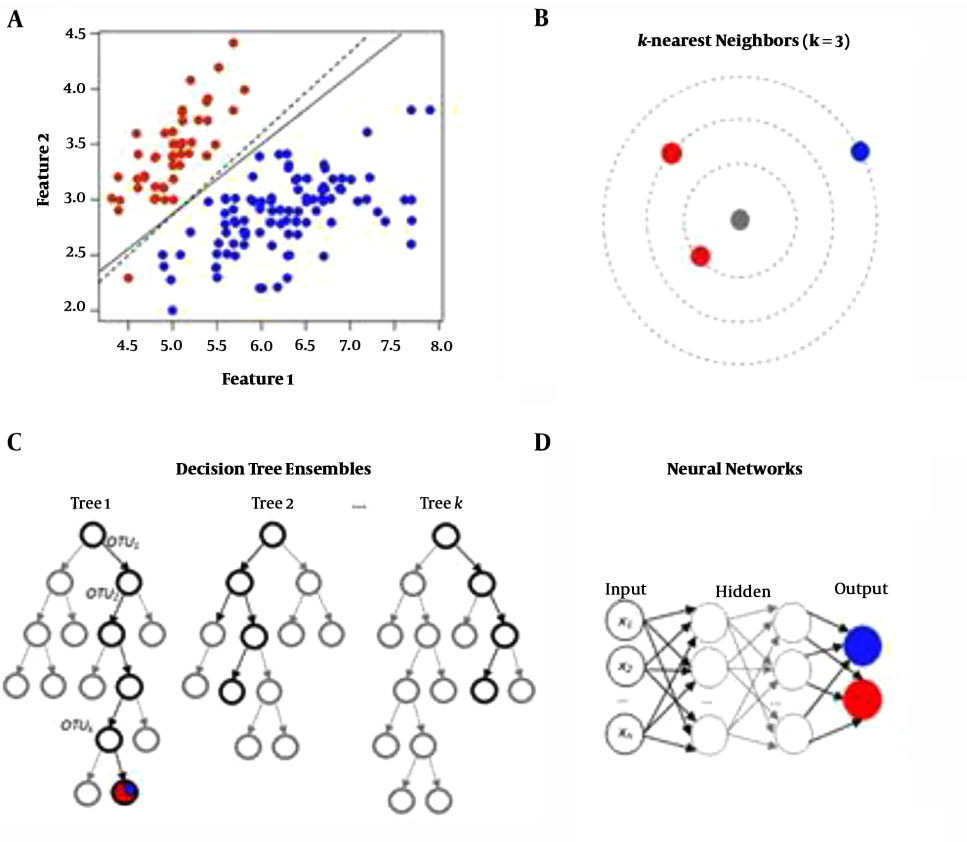


Figure 2. Recurrent Neural Networks (courtesy: Frontiers in Genetics)

particular region. This data can be further processed to help provide health officials the situation of a particular pandemic, thereby aiding the coronavirus response. However, there are many barriers involved such as availability of datasets, limited trained professionals, and resources. In AI and ML, every model is trained so that the solution to the problem is achieved. This is the basis of AI/ML-based researchers and scientists. We believe that this field could have an enormous impact on the current highly accelerating pandemic, COVID-19, that is taking over the world (33-37).

4.2. Applications of Artificial Intelligence and Accounts of Successful Trials

• Deep Learning-Based Drug Screening for Novel Coronavirus: This method was created by researchers in China using DenseNet to predict the interactions between proteins and ligands. This helps predict which drug combinations work preferably well in response to the virus (38-40).

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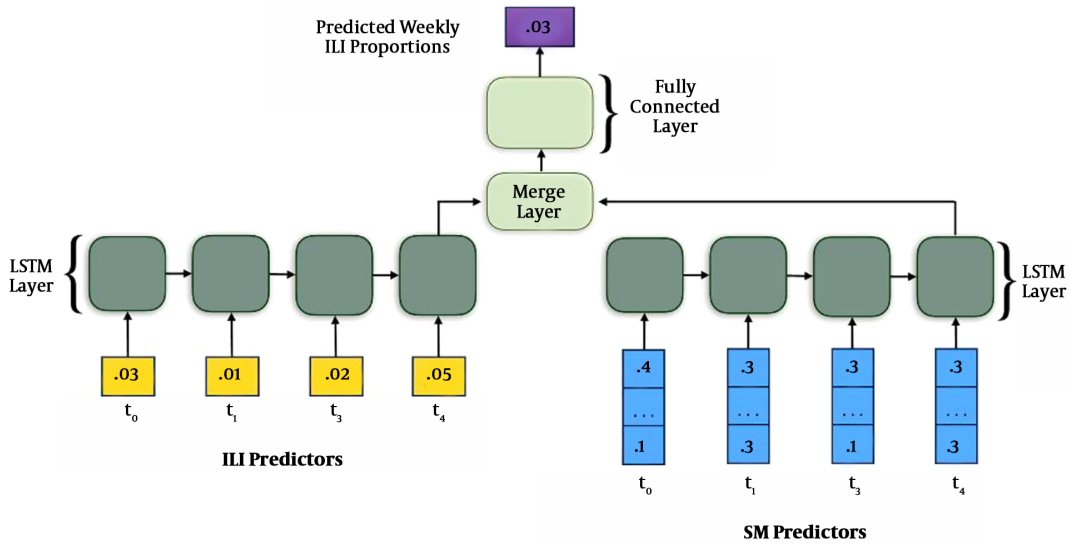


Figure 3. Convolutional Neural Networks (courtesy: Semantic Scholar)

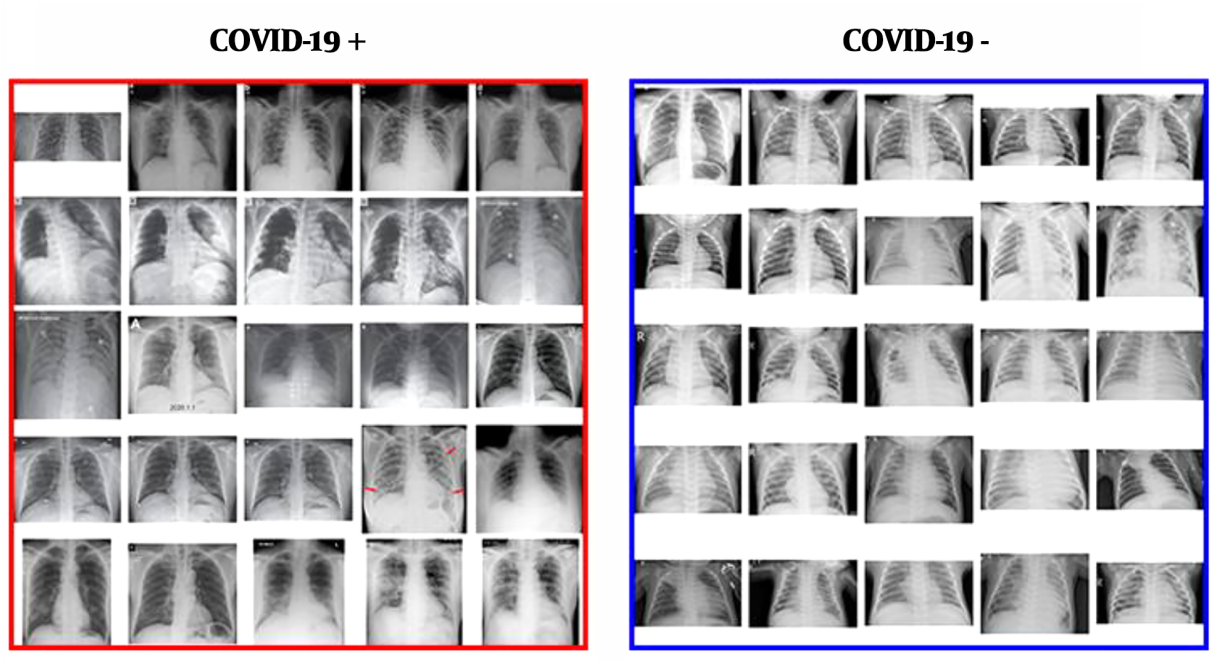


Figure 4. X-Ray dataset samples of COVID-affected and non-affected patients (courtesy: Pylmage)

• Predicting Antiviral Drugs that are Available Commercially to Control COVID-19: Here, a specific method called Molecule Transformer Drug Target (MT-DTI) is used (41).

• DeepMind and AlphaFold: DeepMind uses the AlphaFold library to predict the protein structures of COVID-19 (42, 43).

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```
In [12]: import os,sys,glob,random,subprocess
         from importlib import reload
         import pandas as pd
         pd.options.display.width=180
         import pylab as plt
         from Bio import SeqIO
         from Bio.Seq import Seq
         from Bio.SeqRecord import SeqRecord
         from Bio import Phylo, AlignIO
         from bokeh.io import show, output_notebook, output_file
         output_notebook()
```

BokehJS 1.3.4 successfully loaded.

Figure 5. Importing modules

```
In [13]: ncbidata = pd.read_csv('ncbi_betacoronavirus_25-02-20.csv')
         print (len(ncbidata))
         print (ncbidata.columns)
         ncbidata['Release_Date'] = pd.to_datetime(ncbidata.Release_Date)

         print (ncbidata.Host.value_counts()[:10])
         #put sequences into a set of SeqRecord objects with Biopython
         seqrecs = SeqIO.to_dict(SeqIO.parse('ncbi_betacoronavirus.fasta','fasta'))
```

```
7875
Index(['Accession', 'Release_Date', 'Species', 'Genus', 'Family', 'Length', 'Nuc_Completeness', 'Genotype', 'Genome_Region',
'Segment', 'Authors', 'Publications', 'Geo_Location',
       'Host', 'Isolation_Source', 'Collection_Date', 'BioSample', 'GenBank_Title'],
      dtype='object')
Homo sapiens                2427
Bos taurus                   614
Camelus dromedarius          482
Eidolon helvum               341
Bos grunniens                139
Rhinolophus sinicus          130
Camelus                      127
Chiroptera                   123
Rhinolophus ferrumequinum     82
Rousettus leschenaultii       76
Name: Host, dtype: int64
```

Figure 6. Obtaining sequences

```
In [14]: accessions = ['KY417146','MN908947','MN996532','AY278741','MK211376']
         subset = ncbidata[ncbidata.Accession.isin(accessions)]
         cols= ['Accession','Species','Host','Collection_Date']
         subset[cols]
```

Out[14]:

	Accession	Species	Host	Collection_Date
278	MN908947	Severe acute respiratory syndrome-related coro...	Homo sapiens	2019-12
813	MK211376	Coronavirus BtRs-BetaCoV/YN2018B	Rhinolophus affinis	2016-09
2554	KY417146	Severe acute respiratory syndrome-related coro...	Rhinolophus sinicus	2013-04-17
7646	AY278741	Severe acute respiratory syndrome-related coro...	NaN	NaN

Figure 7. Obtaining subsets

• Prediction of Critically Ill Patients in Wuhan Using ML Models: Artificial Intelligence scientists in Wuhan developed this method to identify the intensity of infections with factors such as age, gender, etc.

• Data based screening and Kalman filters for analysis of data.

• Further predictions of infection in a particular region (44-46).

4.3. Conclusions

Artificial Intelligence and Machine Learning is still subject to many criticisms, and many people are questioning its capacity to solve real-world problems. In other words,

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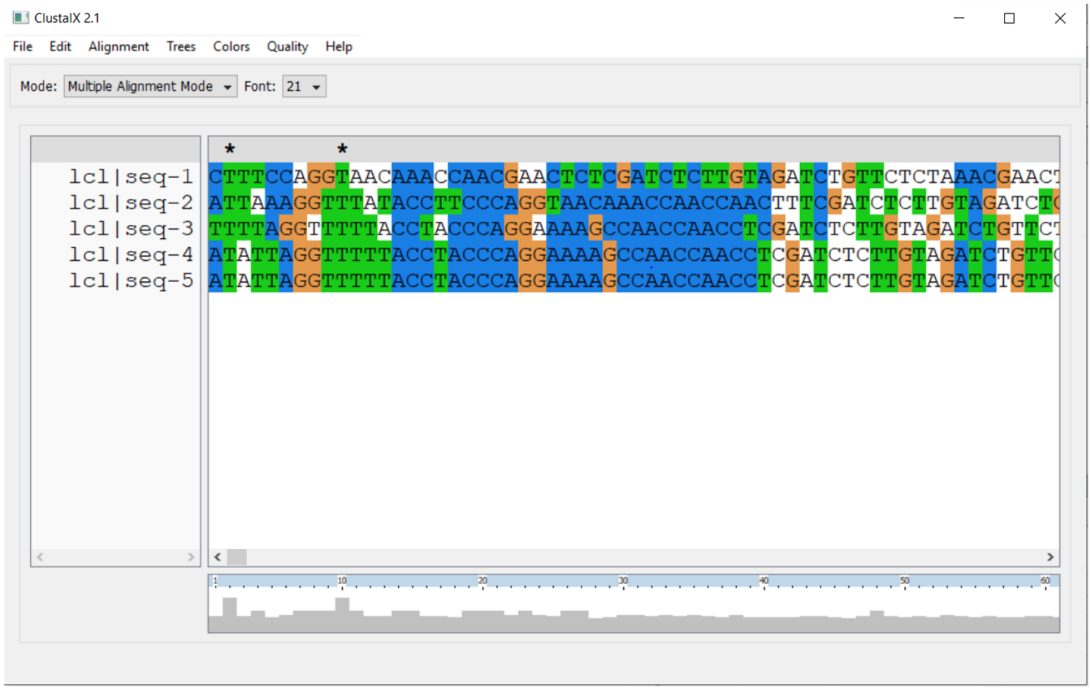


Figure 8. Alignment using Clustal

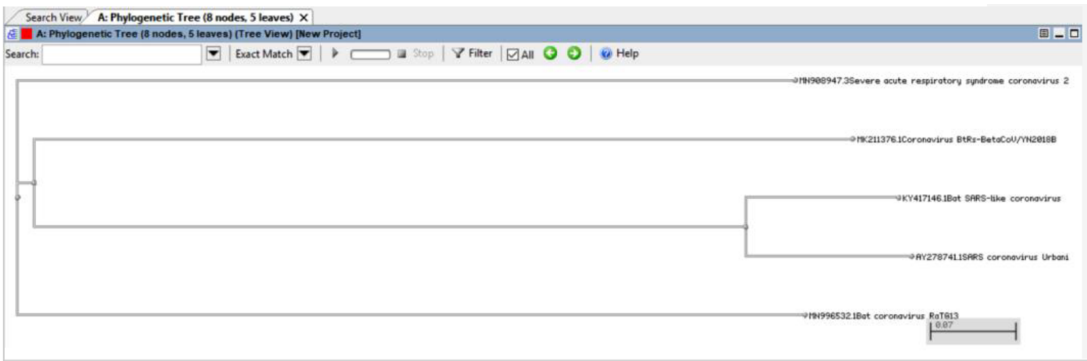


Figure 9. Phylogenetic Tree

it is still an underutilized area in healthcare systems that needs to be developed to benefit millions of people. The main reason is that people prefer to handle every situation in a manual way. For instance, a hospital will prefer to handle its X-Ray or CT data in a manual way by doctors rather than train a model using CNNs to analyze the data. But if this technology is used to the maximum, it has the potential to create a revolution in the field of vaccine and drug development and benefit the whole of mankind.

Footnotes

Authors' Contribution: Study concept and visualization: Shantani Kannan; acquisition of data: Kannan Subbaram; analyzing and interpretation of the data: Sheeza Ali and Hemalatha Kannan.

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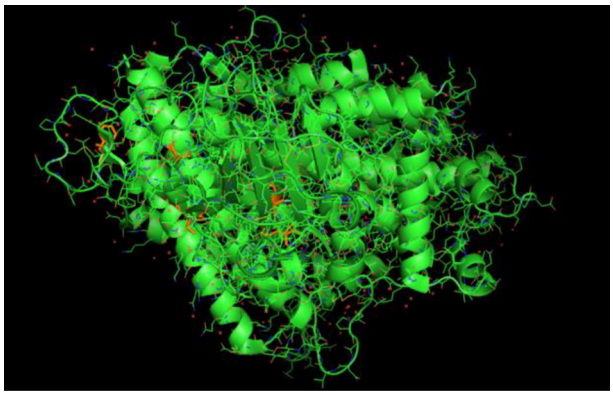


Figure 10. Spike glycoprotein structure of SARS-CoV-2

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