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## COVID-19 Report

### AI and Machine Learning Could Be Saviors

<https://www.business.com/articles/coronavirus-outbreak-ai-and-ml-saviors/> - March 17, 2020

- Scientists, researchers, doctors, and healthcare experts have the option to perform predictive analysis and use this to understand and monitor the COVID-19 pandemic
- Unlike a few years ago during the SARS epidemic, it is now possible to quickly sequence a virus's genome → took only a month to identify the sequence of the genome (January 2020)
- This technology is also being used to track the spread of disease
  - o Microsoft Bing has launched a real-time map of the spread of COVID-19 – showing states related to the several confirmed cases
  - o For this to be useful, a lot of data must be collected and processed
- AI and ML companies are looking into building a strong prediction tool for the coronavirus
- Some companies have come up with tools to help healthcare professionals detect the warning signs of the virus → BlueDot has made an efficient tool based on AI and ML to predict the outbreak of the virus + identify areas that should be no-travel zones because of the spread of the virus
  - o The tool works by researching and collecting a huge amount of information
  - o Data is collected from sources such as websites, social media, new articles, and government reports
- There are other AI and ML tools that can identify places where the virus might hit soon
- A professional at Humboldt University is also making predictions on the coronavirus outbreak and
- China has already started using AI-powered robots for coronavirus patients in some hospitals
  - o These robots can disinfect themselves and carrying out tasks like delivering medicines and changing bed sheets
  - o This helped the hospitals care for more patients in less time with their help
  - o This also eradicated the possibility of cross-infection

<https://www.engineering.com/DesignSoftware/DesignSoftwareArticles/ArticleID/20036/Using-AI-to-Monitor-COVID-19s-Evolution.aspx> - March 16, 2020

- **Graphen** (a startup specializing in AI systems inspired by full brain functionality) has released its AI gene evolution pathway analysis of COVID-19
- The company modeled the spread and severity of COVID-19 by analyzing the variants of each reported whole genome sequencing from more than 30 countries and regions to date
  - o They then used the data to identify the virus' mutations as they spread



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- Their AI-driven analytics visualizes how the virus propagates, mutates, and spreads through the world
  - o This gives us a better understanding of the propagation paths of the pandemic
- By understanding the mutation of each virus and locating where those variants are in its nearly 30,000 genetic locations, the virus' evolution chain and significant clusters can be identified
  - o These patterns can then help pharmaceutical companies better identify targets for drug development, help predict the spreading speed of the virus, or even help predict the harmfulness of specific variants that may cause symptoms beyond those observed from the original strain
  - o Ex. a virus strain isolated from the confirmed case on January 5<sup>th</sup>, 2020 in Wuhan later appeared in Taiwan, Belgium, Australia, and has since evolved into the strain of most initial cases in the State of Washington
- So far, Graphen's data has helped to identify 2 super-spreaders (individuals who infect large amounts of people)

<https://economictimes.indiatimes.com/magazines/panache/this-tech-firm-used-ai-machine-learning-to-predict-coronavirus-outbreak-warned-people-about-danger-zones/articleshow/73697801.cms> - January 29, 2020

- **BlueDot** (A Canadian firm that specializes in infectious disease surveillance) was the first to predict an impending outbreak of COVID-19 on December 31, 2019 using an AI powered system that combs through animal and plant disease networks, news reports in vernacular websites, government documents, and other online sources
- They also used global airline ticketing data to predict that the virus would spread to Seoul, Bangkok, Taipei, and Tokyo, even before any government announcements
- ML and natural language processing techniques were also employed to create models that process large amounts of data in real time
- Once the system spits out automated results, the findings are analyzed by trained epidemiologists who draw inferences and attach a risk factor to each case
  - o This is then turned into a report which is sent to BlueDot's clients

Virtual Medicine Plays Key Role in Addressing Pandemic

[https://www.engineering.com/Hardware/ArticleID/20044/Virtual-Medicine-Plays-Key-Role-in-Addressing-Pandemic.aspx?e\\_src=relart](https://www.engineering.com/Hardware/ArticleID/20044/Virtual-Medicine-Plays-Key-Role-in-Addressing-Pandemic.aspx?e_src=relart) - March 20, 2020

- Virtual medicine (or telemedicine) is one key technology being used to fight the disease
  - o Main reason: can help prevent transmission of the virus between asymptomatic, mildly symptomatic patients, and healthcare providers or other patients at clinics and hospitals
- Virtual medicine can help triage patients, targeting those with evidence of more severe respiratory infections and remotely coordinate eventual in-person care, allowing for proper isolation procedures to be followed

- Help healthcare workers avoid unnecessary exposure from less acute patients who can be treated at home
- **Teledoc** is a multinational virtual medicine company based in the U.S – one of the companies that have emerged in recent decades advertising an affordable and convenience alternative to traditional in-person practices
  - They have experienced a spoke in patient daily visit volume by 50% during the second week of March
- Part of the \$8 billion in emergency funding passed by the U.S. Congress will go toward expanding the reach of telehealth coverage to help stem the pandemic
- The Ontario Ministry of Health and Long-Term Care have announced that telemedicine will be used broadly going forward
  - Italy is relying heavily on it
- These services will also help give cognitive-behavioral treatments to people experiencing mental health conditions brought on by self-isolation
  
- **Inovio Pharmaceuticals** used the genetic sequence of the virus, posted by Chinese scientists in a public database on January 10<sup>th</sup> to generate a vaccine candidate
- They plugged the viral sequence into their proprietary machine learning system (SynCon) → it took 3 hours to generate a “fully-designed” DNA-based vaccine, called INO-4800
  - This is now in a preclinical trial, with animal trials expected to start soon
  - They are making preparations to hold a large phase 2 clinical trial in humans later this year
- **Moderna Therapeutics** took a similar approach with its modified messenger RNA (mRNA)-based vaccine for COVID-19 which is also in clinical trial
  - It took the, 2 days to finalize the sequence for their vaccine, mRNA-1273, and 23 days for the vaccine to be ready for a clinical trial
- Scientists say that there are genetic similarities between SARS-COV-2 and other coronavirus like SARS and MERS
  - This makes it easier to potentially repurpose existing drugs to fight the new coronavirus
  - This is what **Gilead Sciences** is doing with remdesivir – an antiviral drug that was originally developed to treat Ebola
    - The company has begun 2 large phase 3 clinical studies to determine its efficacy and dosage – 1 in China and the other managed by the National Institute of Allergy and Infectious Diseases (NIAID)
- A group of scientists from South Korea and the U.S. are using deep learning to investigate the potential for commercially available antiviral drugs to be used to treat COVID-19
  - They developed a system called Molecule Transformer-Drug Target Interaction that's designed to comb through the available literature to predict drug-target interactions across a range of variables
  - This found that atazanavir, an anti-viral medication used to treat HIV.AIDs could be a good candidate for treating COVID-19



### 3 Areas of AI Application

<https://syncedreview.com/2020/03/27/un-who-mila-map-the-ai-vs-covid-19-battlefield/>

- March 27, 2020

- 3 areas of AI application:
  - 1) Medical – individual patient diagnosis and treatment
  - 2) Molecular – drug discovery-related research
  - 3) Societal
- Most clinical applications of AI during the COVID-19 pandemic response has been in medical imaging diagnosis
- Researchers have found that COVID-19 has particular radiological signatures and image patterns which can be observed in CT scans
- Identifying patterns is a time-consuming task even for experienced radiologists
  - o A quick accurate diagnosis can be a lifesaver
- Training data is key to boosting the speed and accuracy of machine learning CT lung scan based diagnosis
- COVID-19 cases present a unique respiratory pattern and thus, some studies have exploited this to develop non-invasive prediction tools that can use for example, Kinect depth camera streams to identify possible infections
- Others have trained Gated Recurrent Unit neural networks to classify abnormal respiratory patterns → can be a useful non-invasive measurement when screening at a large scale
  
- In Spain, 4 robots are automating up to 80,000 COVID-19 tests a day
- On March 26, Microsoft, together with top AI universities in the U.S., launched the C3.ai Digital Transformation Institute and issued a call for AI techniques to mitigate pandemic fallout, with up to \$5.8 million in prizes
- Computer companies and major cloud providers like AWS, Microsoft's Azure, and Google Cloud Platform also joined a consortium to ensure coronavirus researchers don't encounter compute limitations
- Alibaba, Tencent, and Baidu opened up cloud services in China
- Xprize launched the Pandemic Alliance this week to support researchers and provide them with data from launch partner Anthem

### C3.ai Digital Transformation Institute

<https://c3dti.ai>

- Mission: to attract the world's leading scientists to join in a coordinated and innovative effort to advance the digital transformation of business, government, and society
- In addition to cash awards, C3.ai DTI recipients will be provided with significant cloud computing, supercomputing, data access, and AI software resources and technical support provided by Microsoft and C3.ai



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- Unlimited use of the C3 AI Suite and access to the Microsoft Azure cloud platform and access to the Blue Waters supercomputer at the National Center for Supercomputing Applications (NCSA) at UIUC
- 1st call for proposals is open now → deadline is May 1, 2020

Remdesivir may be the most promising COVID19 drug

<https://www.drugtargetreview.com/news/58608/remdesivir-most-promising-covid-19-drug-say-researchers/> - March 27, 2020

- Researchers suggest that the most effective therapeutic drugs will directly target the SARS-CoV-2 virus that causes COVID-19
- Other approaches listed in an article published in Antimicrobial Agents and Chemotherapy include blocking SARS-CoV-2 from entering cells, disrupting viral replication, antivirals vaccines and suppressing overactive immune response
- The article suggests that SARS-CoV-2 is easily transmissible because Spike (S) proteins in the surface of the virus bind exceptionally efficiently to the angiotensin-converting enzyme 2 (ACE2) on the surfaces of human cells
- There is 1 clinical study underway, testing if recombinant ACE2 can act as a decoy, binding the S proteins and preventing SARS-CoV-2 infecting cells in patients with severe COVID-19
- The article suggests the most promising COVID-19 antiviral is *remdesivir*
  - Remdesivir inhibited SARS-CoV-2 replication in laboratory studies and was tested in 1 patient with COVID-19 in US
  - The patient's symptoms improved following intravenous remdesivir administration
  - However, more clinical data is required before the drug can be approved for use
- *Tilarone* is a broad-spectrum antiviral that may also be active against SARS-CoV-2
  - This is used in some countries to treat several viruses like influenza and hepatitis
- A further treatment option being explored is a *transfusion of blood from a recovered COVID-19 patient into someone with an active viral infection*
  - Primarily been used for patients in critical condition due to lack of high quality randomized clinical trial data to back up its efficacy
- The expert opinions is that it will take approximately 12-18 months for a vaccine candidate to get to the market

Stem Cell Therapy being developed in Iran

<https://ifpnews.com/iran-scientist-developed-coronavirus-drug> - Marhc 28, 2020

- Iranian professor Dr Masoud Soleimani says that what he and his team are developing for treatment of coronavirus is a stem cell "therapy" NOT a drug as claimed in media report
- They are using mesenchymal stem cells to modify the immune response in corona patients

- Research is being conducted with the support of the health ministry at Shariati and Masih Daneshvari hospitals and results of the first phase of its clinical trail is to be announced soon by the health ministry

Russia claims to have developed COVID-19 treatment based on anti-malaria drug  
<https://www.dailysabah.com/life/health/russia-says-it-developed-covid-19-treatment-based-on-anti-malaria-drug> - March 28, 2020

- On March 28, Russia's Federal Biomedical Agency said it had developed a drug for the treatment of COVID-19 using mefloquine – a drug used to prevent or treat malaria
- According to the agency's statement, the drug prevents virus replication in cells and stops the inflammatory processed caused by the virus
  - o Wil treat patients with various degrees of the infection
- They say that Mefloquine has to be combined with antibiotics for the maximum effects – increases the concentration of antiviral agents in blood plasma and lungs

Potential COVID-19 therapeutics currently in Development

<https://www.europeanpharmaceuticalreview.com/article/115842/potential-covid-19-therapeutics-currently-in-development/> - March 26, 2002

- **Favilavi** – 1st approved coronavirus drug in China
  - o Reportedly shown efficacy in treating COVID-19 safely in a clinical trial involving 70 patients
- **Inovio Pharmaceuticals** plans to begin human clinical trials on their vaccine, **INO-4800** in April
  - o Results are expected to be available in Septembe 2002
  - o They aim to produce 1 million doses of the vaccine by the end of 2020 to perform additional clinical trials and/or emergency use of the vaccine
- **Regeneron's** potential vaccine **REGEN3048** and **REGEN3051** will be ready for human clinical trials by early summer
  - o Large scale manufacture could start by middle of April
- **Gilead's Remdesivir (GS-5734)** has undergone clinical trials in China
  - o Trials are being performed on 761 patients in a randomized, placebo-controlled, double-blind study at multiple hospitals in Wuhan
- **Moderna's MRNA-1273** vaccine is undergoing a Phase I clinical study in April with support from the US NIH and they are preparing for a Phase II study
  - o Vaccine targets the Spike )S\_ protein of the coronavirus
- Roche's **Actemra** has been approved in China for the treatment of severe complications related to coronavirus
  - o Drug is being evaluated in a clinical trials in China – with 188 coronavirus patients
  - o Will go on until May 10
- Many clinical trials are underway with **Chloroquine**
  - o As face and efficacious drug for malaria

- Coronavirus patients administered with the Chloroquine Phosphate drug achieved a better drop in fever and shorter recovery time in clinical trials being conducted in Chinese hospitals
- An intranasal COVID-19 vaccine is being developed by US-based clinical-stage biopharmaceutical company, **Altimune**
  - Animal studies are being progressed

Below are other candidates at different stages of the drug development lifecycle

Company/research	Drug/vaccine candidate	Development stage
MIGAL	Infectious Bronchitis Virus (IBV) vaccine	Pre-clinical trials
APEIRON Biologics	APN01	Phase I
Tonix Pharmaceuticals	TNX-1800	Initial evaluation
Innovation Pharmaceuticals	Brilacidin	Initial evaluation
Clover Biopharmaceuticals	S-Trimer vaccine	Pre-clinical trials
Vaxart	TBC	Pre-clinical trials

CytoDyn	Leronlimab	Phase II for HIV and fast tracked for COVID-19
Applied DNA Sciences and Takis Biotech	Linear DNA Vaccine	Pre-clinical trials
BIOXYTRAN	BX-25	TBC
Novavax	MERS coronavirus vaccine	Phase I in 2020
Biocryst Pharma	Galidesivir	Advanced animal testing
Takeda	H-IG therapy	TBC
Heat Biologics	gp96 vaccine	Early development
Pfizer and BioNTech	mRNA vaccine, BNT162	Clinical programme development with Fosun in China

Generex	li-Key immune system activation	Clinical programme development in China
Vir Biotechnology/Wuxi	MABs binding to virus	TBC
Vir Biotechnology/Alnylam	siRNA candidates	
Janssen Pharmaceuticals	PREZCOBIX® HIV medication (darunavir/cobicistat)	TBC

- While there are many vaccines in the works, it will take some time to establish the complete safety and efficacy of the successful candidates

#### AI Companies who are stepping up to combat COVID-19

<https://www.forbes.com/sites/tomtaulli/2020/03/28/ai-artificial-intelligence-companies-that-are-combating-the-covid-19-pandemic/#34a2afb958f8> - March 28, 2020

- Competitions are being setup to stir innovation
  - o Kaggle's COVID-19 Open Research Dataset Challenge – in collaboration with the NIH and White House
    - 1<sup>st</sup> contest was to help provide better forecasts of the spread of COVID-19 across the world
  - o Decentralized Artificial Intelligence Alliance is putting together Covidathon – an AI hackathon to fight the pandemic coordinated by SingularityNET and Ocean Protocol
    - They have more than 50 companies, labs, and nonprofits
  - o MIT Solve established the Global Health Security & Pandemic Challenge
    - A member of this organization, **Ada Health**, developed an AI-powered COVID-19 personalized screening test
      - Ada's core system connects medical knowledge with intelligent technology to help people actively manage their health and medical professionals to deliver effective care
      - #1 medical app for 140 countries
      - Global launch was in 2016
- AI companies that are eliminating their fees to help
  - o NVIDIA – providing a free 90 day license for Parabricks – allows for using AI for genomics purposes

- Also provides free support from Oracle Cloud Infrastructure and Core Scientific (a provider of NVIDIA DGX systems and NetApp cloud-connected storage)
- DataRobot is offering its platform for no charge
- Run:AI is offering its software for free to help with virtualization layers for deep learning models
- DarwinAI has collaborated with the University of Waterloo's VIP Lab to develop COVID-Net
  - A convolutional neural network that detects COVID-19 using chest radiography
  - They are now making this technology open source
- **Biofourmis** created a remote monitoring system that has a biosensor for a patient's arm and an AI application to help with the diagnosis → to help reduce infection rates for doctors and medical support personnel
- **Vital** uses AI and Natural Language Processing to manage overloaded hospitals
  - Founders are Aaron Patzer (creator of Mint.com) and Justin Schrage (an ER doctor)
  - They are now devoting all its resources to create **C19check.com** – The app, which was built in a partnership with Emory Department of Emergency Medicine's Health DesignED Center and the Emory Office of Critical Event Preparedness and Response, provides guidance to the public for self-triage before going to the hospital
  - So far, it's been used by 400,000 people
- **AliveCor** launched **KardiaMOBile 6L** – an AI-enabled platform, which measures QTc in COVID-19 patients
  - Helps detect sudden cardiac arrest
- **CLEW** launched the **TeleICU**, which uses AI to identify respiratory deterioration in advance

Using plasma from recovered COVID-19 patients as potential treatment

<https://bc.ctvnews.ca/plasma-from-recovered-covid-19-patients-in-canada-could-be-studied-as-potential-treatment-1.4872544> - March 28, 2020

- Researchers in Canada are looking at using blood product from recovered COVID-19 patients as a potential treatment for others who are sick with the virus
- Canadian Blood Services are working with a group of clinical investigators who are designing a national clinical trials to see if convalescent plasma could help treat COVID-19 patients
  - Convalescent plasma = plasma that is collected from patients who have recovered from a virus → means they have developed antibodies necessary to fight the virus
  - In theory, these antibodies could be the basis of a treatment
- However, the Canadian Blood Services has stated that there is not yet enough data to prove it is a successful treatment



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- Dr. Srinivas Murthy, and associate professor at UBC's Department of Medicine, has received funding from the Canadian Institutes for Health Research for a study on how best to treat COVID-19
  - o He has said that while he is involved in a few initiatives to use convalescent plasma, he too states that there is no real science yet to say it is useful
    - Attempts have been made with other diseases but have not shown to be that effective
  - o He goes on to state how sometimes, it could cause significant harm
- This method is also being looked at in the U.S.

B.C. Canada experimenting with malaria and Ebola medication for COVID-19

<https://www.cbc.ca/news/canada/british-columbia/malariaa-medication-covid-1.5513899> - March 28, 2020

- HIV and malaria medications are being used to treat patients with COVID-19 in B.C.
  - o Hydroxychloroquine and Remdesivir
- These drugs are currently being tested on patients inside at least 1 facility in B.C.

<https://science.sciencemag.org/content/367/6485/1412> - March 27, 2020

- On March 20, the World Health Organization (WHO) announced a major study to compare treatment strategies in a streamlined clinical trial design that doctors around the world can join → SOLIDAIRTY
- The study, which could include many thousands of patients in dozens of countries, has emphasized simplicity so that even hospitals overwhelmed by an onslaught of COVID-19 patients can participate
- WHO's website will randomize patients to local standard care or one of the 4 drug regimens, using only ones available at the patients' hospital
  - o Physicians record the day the patient left the hospital or died, duration of hospital stay, and whether the patient required oxygen or ventilation
- Design is not blinded – patients will know they received the drug candidate → could cause placebo effect → doing so in the interest of speed
- Agency hopes to start to enroll patients this week
- Rather than developing and testing compounds from scratch, WHO is focused on repurposing drugs that are already approved for other diseases and have acceptable safety profiles
  - o Also looking at experimental drugs that have preformed well in animal studies against SARS and MERS
- For the study, WHO chose an antiviral called remdesivir, chloroquine, a combination of the HIV drugs lopinavir and ritonavir, and that combination plus interferon-beta, and immune system messenger that can help cripple viruses
- In 2017, researchers showed in test tube and animal studies that Remdesivir can inhibit the SARS and MERS viruses

- Remdesivir, which is given intravenously, has been used in hundreds of COVID-19 patients in the US and Europe under the compassionate use, which requires Gilead to review patients records
- Some doctors reported anecdotal evidence of benefit, but no hard data
- 5 other clinical trials are underway in China and the U.S are testing it and may have preliminary results soon
- A coronavirus researcher, Stanley Perlman states that remdesivir may be more potent if given early but this is a challenge as it is expensive, needs to be administered intravenously, and 85/100 people with COVID-19 don't need it
- Chloroquine and hydroxychloroquine have received attention due to positive results from small studies and an endorsement from President Trump
  - The drugs decrease acidity in endosomes, compartments that cells use to ingest outside material and that some viruses co-opt during infection
  - However, SARS-CoV-2's uses so-called spike protein to attach to a receptor on the surface of human cells and studies in cell culture have suggested that while chloroquine can cripple the virus, the doses needed are usually high and could cause severe toxicity
  - Researchers have tried to drug on other viruses and it has never worked out in humans
  - Results from COVID-19 patients are murky
    - No hard evidence thus far
    - French microbiologist Didier Raoult and colleagues published a study of hydroxychloroquine in 20 COVID-19 patients that concluded the drug had reduced viral load in nasal swabs BUT trial was not randomized and it didn't report clinical outcomes such as deaths
  - Hydroxychloroquine can in some cases harm the heart and there are reports of chloroquine poisoning in people who self-medicated
- Many coronavirus researchers are also skeptical of the lopinavir-ritonavir combination
  - When doctors in Wuhan have 199 patients standard care with or without lopinavir-ritonavir, the outcomes did not differ significantly (reported in The New England Journal of Medicine)
  -
- Interferon-beta may be risky for patients with severe COVID-19
  - If given too late, it could lead to worse tissue damage
- Some researchers have high hopes for camostat mesylate, a drug licensed in Japan for pancreatitis
- The best way to test the drugs would be to administer it to people in early stages of the disease who doctors think are most likely to get worse