Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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AI-driven drug discovery: A boon against COVID-19?

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ABSTRACT

The COVID-19 is an issue of international concern and threat to public health and there is an urgent need of drug/vaccine design. There is no vaccine or specific drug yet made as of July 23, 2020, for the coronavirus disease (COVID-19). Thus, the patients currently can only be treated symptomatically. A quick identification of the drugs for COVID-19 may act as a potential therapeutic medication which has been used earlier in patients to answer the present pandemic condition before it could get more worse. According to our view, an artificial intelligence (AI) based tool that may predict drugs/peptides directly from the sequences of infected patients and thereby, they might have better affinity with the target and contribute towards vaccine design against COVID-19. Researchers across the world proposed several vaccines/drugs for COVID-19 utilizing AI based approaches, however, testing of these proposed vaccines/drugs will be needed to verify the safety and feasibility for combating COVID-19.

1. Background

Intelligent algorithms in case of machine learning, and in "big data," are considered as support and calculation tools for molecular applications, but not as an objective in and of themselves. The developments and latest advancement that the utilization of the above mentioned approach has grasped in the last few years can extend over areas that are straightly or obliquely linked to the health or food technology, or can even be used to assist in the advancement of industrial applications or pharmaceutical products. But it is important to distinguish between different sectors in the roadmap of the treatment of infectious diseases along with an efficient deployment of AI. The first sector of this roadmap includes proper utilization of AI technique that will lead to the discovery of potential candidates and those putative candidates will probably follow a regular (traditional) long-term pathway of drug development and clinical validation process later. While, other sector may involve the clinical trials on patients in order to explore the efficacy and proper combination of drugs or dosage in designing potential therapy (Ho, 2020). The designing of the drug combination therapy based on AI will prove a crucial approach to identify ideal & effective regimens when a fast intervention is required during pandemics.

Presently, AI has been used extensively for drug research against Coronavirus disease (COVID-19) since AI platform can prove to be more useful for the identification of potential existing drugs with inhibitory human coronavirus (HCoV) activities by utilizing various learning datasets such as (Ke et al., 2020):

- Reported or proven potential active compounds for combating SARS-CoV, SARS-CoV-2, influenza virus, human immunodeficiency virus (HIV) (Ke et al., 2020).
- Inhibitors for known 3C-like protease (main protease of SARS-CoV-2) and other important protein targets translated by the SARS-CoV-2 viral genome (Zhavoronkov et al., 2020).

All the drugs predicted by using AI-based drug discovery could use to combat feline coronavirus in *in-vitro* cell-based assay and the results obtained from these assays will give the feedback to the AI system in order to relearn (Ke et al., 2020). This may further lead to the generation of a modified AI-based model for the searching of existing drugs again.

This beneficial technology is utilized in accelerating drug testing progressively, where standard testing takes a lot of time and consequently assists with quickening this procedure essentially, which may not be conceivable by a human (Vaishya et al., 2020). It has also become an incredible asset for diagnostic testing and development of drugs & vaccines at quite a bit of quicker rate than expected and is additionally useful for clinical trials during the vaccine development. The hypothetical view of this works reports contriving an anti-coronavirus tool based on artificial intelligence to discern anti-coronavirus targets in the embodiment of peptides/drugs. The anti-coronavirus target protein sequences reported from the current outbreak which we can scan against the

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anti-coronavirus target datasets via AI based tools which will provide the precision-based anti-coronavirus peptides/drugs.

2. AI-driven drug discovery

Artificial Intelligence in *Computational Drug Designing* looks for high-quality research related to drug and clinical research on artificial intelligence approaches to exploiting the power of *Computational Drug Designing* by applying Artificial Intelligence and core chemistry (Chan et al., 2019). *Computational Drug Designing* is an evolving area of research related with the designing as well as in testing of molecular properties, interactions, and behavior for assembling better materials, processes, and systems for specific functions.

Computational Artificial Intelligence and molecular chemistry advance in parallel with the rapid progress in drug design methods for COVID-19. This technique is becoming a powerful tool in medicinal chemistry to identify the starting points as hit molecules for COVID-19. This approach reduces the time and cost taken for drug research and development. The applications based on utilizing AI-based approach for designing of drugs are involved precisely with the molecular structure of the drugs. AI based applications crucial retrieve data and information from engines to search novel drug candidates, optimize drug repurposing. Developments in "Artificial Intelligence and *Computational Drug Designing*" techniques are becoming the benchmark for the COVID-19, opening new avenues for drug discovery (Walters and Murcko, 2020). New approaches are needed as the cost of drug development is increasing with decreasing investment returns.

3. Why we need artificial intelligence

The number of FDA-approved drugs is declining with the number of new molecular entities (NMEs). The reasons noted are adverse side effects and reduced efficiency of many potential compounds. The delay in NME manufacturing plagues the pharmaceutical industry. Besides this, the assumed effects of the drug on disease are becoming more and more complex. Artificial Intelligence and *Computational Drug Designing* provides a new direction to the system-centric idea for R&D leading to future drugs, which starts with the identification of the scope of a new drug.

4. Pertinent topics that could be potential hypothesis in AI in drug discovery

- Implementation of artificial intelligence in drug discovery and drug target identification for COVID-19
- Implications for artificial intelligence in modulating drug targets for COVID-19
- Influence of COVID-19 compounds/peptides in the era of artificial intelligence
- Artificial intelligence for future therapies against COVID-19
- Artificial intelligence for molecular structure generation
- Artificial intelligence for new sampling techniques in molecular/quantum simulations
- Artificial intelligence for molecular data (to recognize reactivity based on differences in spectra from original reagents which classifies reaction mixtures as either reactive or unreactive)
- Artificial intelligence for biological function of COVID-19
- One of AI and chemistry's grand challenges: to find a function for every known-unknown metabolite in present scenario

5. Race to find cure for COVID-19 already started

Now a days, AI is being used by several companies for the identification and screening of existing drugs that could be repurposed for the treatment of COVID-19, aid clinical validation, sift through trial data, and scour through patient electronic medical records (EMRs). Companies like TCS' Innovation Lab in India, where a team of TCS scientists identified 31 potential hits that might act as inhibitors for COVID-19 (TCS Scientists Hone in On, 2020). Similarly, a startup named Benevolent AI, that has raised $292 million to apply AI-based COVID-19 drug discovery, came up with an already approved drug through AI-based drug discovery approach for COVID-19 as an effective treatment (Potential new treatment, 2020). UK-based company Exscientia already team-up with Diamond Light Source (UK's national synchrotron science facility) to utilize its AI drug discovery platform for identifying potential compounds against COVID-19 (AI technology to screen, 2020). The *Molecule. one*, a European AI-centered startup has released its patented syntheses planning platform for free access to the scientific fraternity, in an effort to help researchers rapidly synthesize and test potential candidate molecules against COVID-19. IBM has also utilized its AI generative frameworks to three COVID-19 drug targets and has generated 3000 novel potential hits or molecules (Roy, 2020). The list of companies those are using AI-based drug development against COVID-19 has been mentioned in Table 1 (How AI is fighting, 2020).

6. Role of AI in vaccine research

The Harvard T.H. Chan School of Public Health and the Human Vaccines Project have declared the Human Immunomics Initiative, a joint effort which will make use of artificial intelligence models for accelerating the development of vaccines (Human Immunomics Initiati, 2020). This Initiative aimed at proper utilization of state-of-the art techniques in epidemiology, immune monitoring, network biology, AI and machine learning to explain effective immunity in old-aged populations, and use these data to speed up the development of successful vaccine and therapeutic.

7. AI vs non- AI scenarios

Utilizing data in order to make better predictions and automation is something that we already know; what AI approach brings is a capacity to manage new degrees of scale and data intricacy. Various methods for statistical calculations usually work inside the imperatives of already built-in or fixed assumptions, yet AI can be potentially effective in a broad scenario where it will help in finding out whether a molecule fits this criterion or not. AI can potentially contribute to the battle against COVID-19 in discovering possible treatments and vaccines. Indeed, even some time before the COVID-19 outburst, AI was notable for its immense capability to contribute towards novel drug discovery (Coldeway, 2019; Fleming; Segler et al., 2018; 6 Things We Learned about AI, 2020). In this pandemic situation, several data centers and research labs have already revealed that they are implementing AI to hunt for treatments including both vaccine and drugs against COVID-19. The expectation is that AI may speed up both the progressions of discovering new drugs and repurposing existing (old) drugs. On the other hand, in the context of a Non-AI scenario, we can identify putative existing drugs with inhibitory coronavirus activities by utilizing *in-silico* or *in-vitro* techniques. Conventionally, the process of drug discovery is very lengthy (usually it may take 9–10 years to bring the drug into market), complex and costly. Hence, AI might perform an essential component by accelerating the whole test process from years to months by assessing various scenarios across different parameters at once. Drug screening methods based on AI may prove to be more helpful in understanding the vital part of the virus (such as viral protein structure) in order to determine how the functioning inside viral cell will play an important role in quicken the developments of drugs and vaccines to combat COVID-19.

For COVID- 19, AI has not been proved so impactful yet. Its potential usage has been hindered due to paucity of available data. To overcome these limitations, a careful balance is required between data privacy and public health, and thorough human-AI interaction (Naudé, 2020).

Table 1
List of companies applying AI for the development of treatment against COVID-19.

Strategy	Name of the Company	Status
Repurposing Existing Drugs	Benevolent AI	The firm based in UK (recognized in the AI based drug discovery) came up with 6 most putative molecules with Baricitinib for possible treatment. Eli Lilly already got in touch with this firm because of their exciting finings and has already started clinical validation process.
	Innoplexus	Indo-German company become successful in proposing three combination therapies against COVID-19 and right now these combinations are in validation process both *in-vitro* & *in-vivo*: (a) Combination of chloroquine and tocilizumab. (b) Combination of chloroquine and Remdesivir. (c) Combination of hydroxychloroquine with clarithromycin or plerixafor
	Deargen	A firm from Korea, in collaboration with Dankook University, came up with an antiviral drug named atazanavir (a drug known for HIV treatment) with high efficacy. However, its clinical trials are currently going on.
	Gero	Nine drugs have been identified by this Singaporean company using its AI platform. Out of which, niclosamide and nitazoxanide are the most potent molecules.
	Cyclica	6700 molecules including FDA approved drugs and molecules in Phase I human trials are currently being screening by the Canadian company by utilizing their AI based drug repurposing platform MatchMaker.
	Healx	A company based in UK is also trying to discover combination-based therapy of already approved drugs against this deadliest virus
	VantAI	A company based in New York is currently heading towards a systems or network biology approach to study the interplay between viral and human proteins during the progression of this infection.
Designing New Drugs	Insilico Medicine	A company based in Hong-Kong came up with the seven promising molecules against COVID-19 and already synthesized two molecules out of them for testing.
	Exscientia	A company based in UK, in association with the Diamond Light Source, UK's synchrotron facility, screened 15,000 clinically proven molecules from Scripps Research Institute in California, US and also heading towards the study of mechanism of the functioning of the SARS-CoV-2 virus through data modeling with the help of AI.
	Iktos and SRI international	The French AI based firm named Iktos works in designing new potent molecules and has teamed-up with SRI Biosciences (based in US) for synthesizing and testing the molecules via utilizing their fully automated system based on synthetic chemistry.

8. Sustainability and scale-up of AI based drug discovery techniques

Numerous significant factors are needed to come up with an effective public health response to an outburst of a new infection (McCall, 2020), which include transmissibility and risk populations, infection, incubation period and mortality rate, characterizing causative organism, epidemiological modeling (McCall, 2020). This strategy worked for SARS and may also be beneficial for COVID-19 as the data can be used to train and prime the AI application for its dedicated task (McCall, 2020). AI can accomplish cost reduction and increase effectiveness; predictive maintenance and improved resource deployment; and assurance in terms of quality (Reddy, 2020). Artificial Intelligence is the innovation that empowers machines to take care of issues similarly we do as human beings. For decades, computer programs were coded manually to give a specific outcome from a certain input. By utilizing AI technique, computers may examine the complete data to identify significant patterns for making useful predictions (How AI can make your marketing, 2020).

Underneath the enormous potential of AI, there are various rationalities associated with a proper deployment of AI which additionally should be comprehended. Every single AI deployment may require practical understanding of the planned future usage in the real scenarios and should be run by individuals who could possibly comprehend the data and the associated fundamental issue in order to resolve it. Most of the AI-based solutions can be custom built to come up with a solution to specific problems and may get trained on your own data while few niche softwares or tools with limited applications can be just simply plugged into an organization. The AI ought to be vigorous by configuration, choosing or making the right algorithms and tools calculations for the specific task. At the last, these AI-based drug discovery models should undergo an efficient ongoing monitoring via a skilled operations unit, with sufficient long-term support, reorientation processes and controls for model drift over time.

9. Infrastructure investment required

As far as infrastructure facility is concerned, high-end workstations/servers (with inbuilt GPUs, large storage & tesla card) and high-speed connectivity are required to carry out such drug discovery process based on AI. Scaling of this infrastructure is essential in terms of high-throughput screening, optimization of leads, & manufacturing). Protein dynamics simulation is also one of the fundamental and computationally intensive tasks to be carried out. Factors such as speed, energy consumption and cost involved in computing decides the further progress of such processes. Therefore, we must drive the boundaries of computing power up to reach our desired output in terms of creating new potential mechanisms and linkages to facilitate drug development. The equipment's mentioned above could be utilized for carrying forward the COVID-19 project in terms of getting both new drugs as well as repurposed drugs using AI technique.

10. Conclusion

In summary, we can conclude that AI might prove impactful in treatment & cures against COVID-19. These AI-based tools can be used for scanning of peptides/drugs against COVID-19 from their own targets. Nevertheless, when it comes to medicine, AI as of now, has a demonstrated reputation for being a rapid and cost-effective method but clinical trials are required for the validation purpose.

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