COVID-19 Drug Discovery Using Genetic Constrained Graph Variational Autoencoder (GCGVAE)

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Abstract

Variational Autoencoder is an effective and efficient tool while dealing with various generative problems. In this paper, we developed a unique kind of variational autoencoder, which is Genetic Constrained Graph Variational Autoencoder (CGCVAE), to discover the potential drug for Severe Acute Respiratory Syndrome Corona-Virus 2 (commonly known as SARS-CoV-2). After evaluating our results with tools that indicates the effectiveness while inhibiting SARS-CoV-2, we concluded that our results are much more effective than those existing drugs for treating COVID-19. Our model could also be used to generate other drugs given the assays of target protease.

1 Abbreviation

Table 1: Abbreviation List

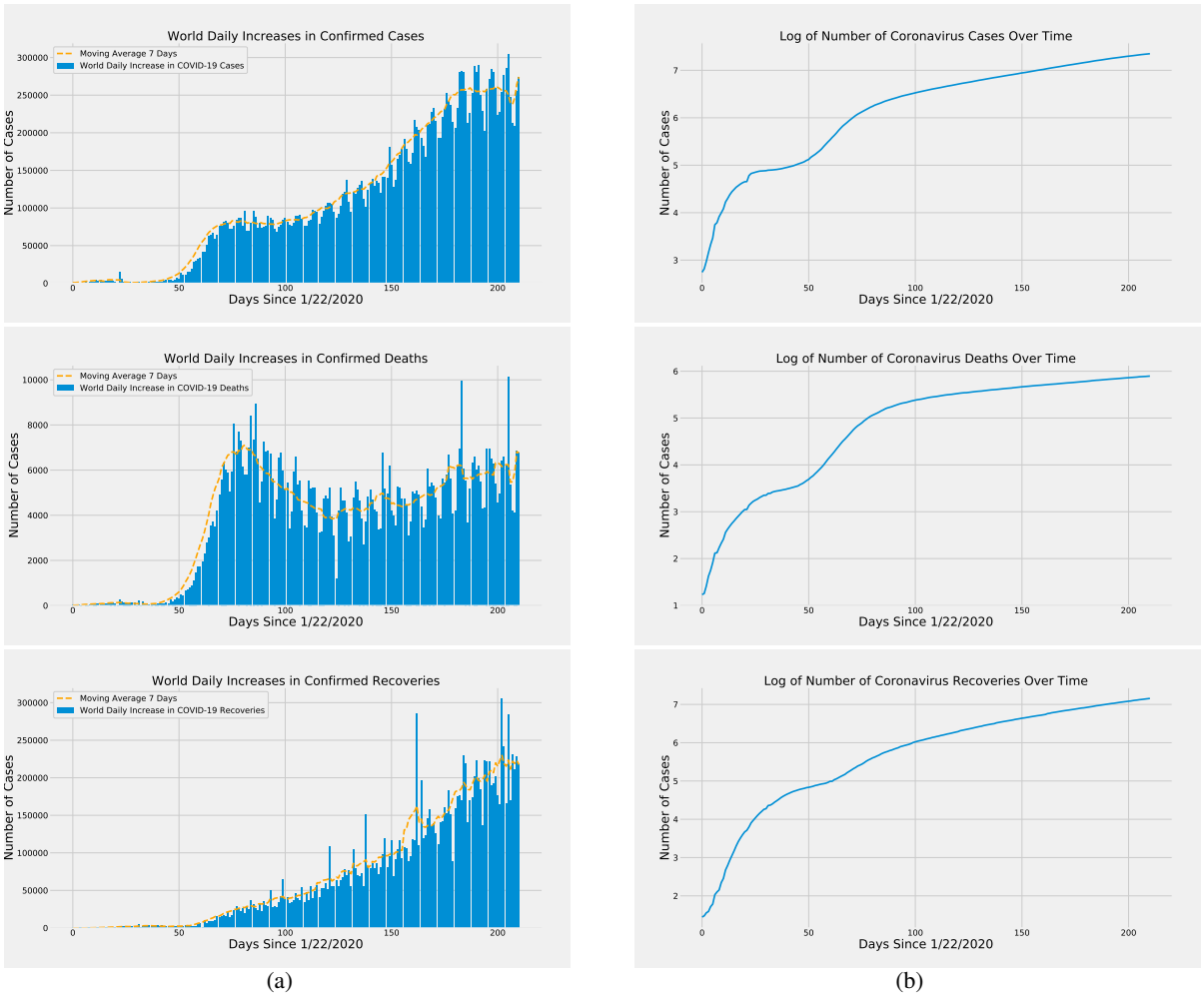
Full Name	Abbreviation
Severe Acute Respiratory Syndrome Corona-Virus 2	SARS-CoV-2
Coronavirus Disease 2019	COVID-19
Genetic Algorithm	GA
Machine Learning	ML
Deep Learning	DL
Edge Memory Neural Network	EMNN
Generative Adversarial Network	GAN
Simplified Molecular Input Line Entry System	SMILES
Variational Autoencoder	VAE
Constrained Graph Variational Autoencoder	CGVAE
Genetic Constrained Graph Variational Autoencoder	GCGVAE
Reinforcement Learning	RL

2 Introduction

2.1 Motivation

COVID-19 firstly been found at Wuhan, a city in China. The virus that caused COVID-19 is designated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was also previously known as 2019-nCoV. The most common symptoms of COVID-19 are fever, tiredness, and dry cough. Some patients even have aches and pains, nasal congestions, runny nose or sore throat. These symptoms are usually mild and begin gradually. Even though most people will recover from COVID-19, some still have serious illness, especially for people aged over 60. According to WHO (World Health Organization), around 1 in every 5 people who are infected with COVID-19 develop difficulty in breathing and require hospital care.

Although different countries carried out policies to stop the virus and cure the sufferers, many people are still exposed to sever threats. People over 60 often have underlying medical conditions such as diabetes, heart diseases, respiratory disease or hypertension, which exposes them at greater risk if they had been infected by the virus. In Indonesia, the 2018 Riskesdas basic health survey data show that cardio vascular disease and diabetes are among the highest disease burdens of the country. Nearly 11 % of Indonesian adults have high blood sugar levels and 1.5% suffer from heart disease – making these groups vulnerable to developing severe COVID-19 symptoms if they become exposed to the disease. Moreover, the same Riskesdas data show that nearly 63% of adult men in Indonesia smoke. This number is among the highest prevalence of smokers in the world.



(a) (b)

Figure 1: The statistics of COVID-19 since January

Thus, it is necessary to find ways to develop new strategies to stop the virus and cure the infected. Many countries had put a lot of efforts in developing vaccines to enable the majority to be immune to the virus. Even though vaccines

is effective for most developed nations, in most developing countries, new vaccines could be extremely difficult to develop. Since developing countries have more risk of suffering from COVID-19, it is necessary to design a drug that could cure the infected effectively. Since mass producing drugs for COVID-19 is much cost-effective than developing vaccines, our results is useful for countries that urgently need drugs to cure the coronavirus.

When coming to sorting out all drugs in current database, ML algorithms performs much more effective and efficient than humans. Since there are millions of ligands and protease in the National Center for Biotechnology Information (NCBI) database, it can be extremely difficult for humans to find and develop drugs for COVID-19. In this paper, we developed a generated model called GCGVAE that could automatically sort all useful data from the database and generate useful moleculCres to bind with SARS-CoV-2 protease. Since its performance (measured by binding affinity) is much better than those existing drugs, including Remdesivir, Ribavirin, Umifenovir, Favipiravir, Lopinavir, etc., our generated molecules have great potentials to save more infected people around the globe.

2.2 Challenges

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2.3 Significance

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3 Related Work

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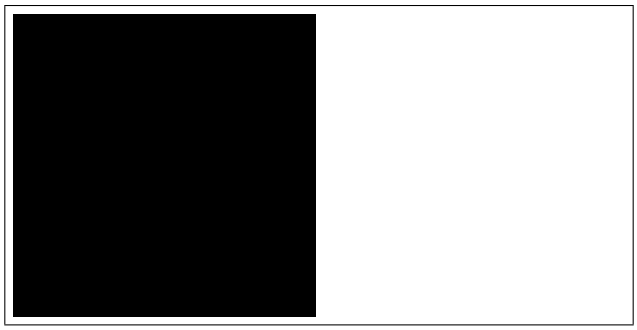

Figure 2: Sample figure caption.

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4 Methods

4.1 Generative Model

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4.2 EMNN and QED prediction

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4.3 GGNN model

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[1] Sample of the first footnote.

Table 2: Sample table title

	Part	
Name	Description	Size (μm)
Dendrite	Input terminal	$\sim$100
Axon	Output terminal	$\sim$10
Soma	Cell body	up to 10^6

4.4 Graph-Based Genetic Algorithm

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References

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