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Mathematical models of SARS

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Abstract. The COVID-19 pandemic ignited renewed efforts in quantitative analysis of the impact of pathogens on human health. The mathematical models were critical in understanding the outbreaks for future preventive and reactive approaches to similar outbreaks. This paper intends to explore and provide an understanding of the SARS-CoV-2 infection process, especially its kinetics. Additionally, the paper aims to provide an overview of the immune system's response to infection, especially the immune system's response to infected cells. This paper relates the symptoms of influenza to the observed symptoms of COVID-19, a disease caused by the coronavirus. The research method employed in this study involves the utilization of differential equations and computational simulations to model infection dynamics. This assumption provides the basis for the majority of the models. The paper also highlights some of the benefits of modelling SARS-CoV-2 and makes recommendations for future studies. Mathematical models provide insights into the dynamics of SARS-CoV-2 infection, aiding in the development of more effective preventive and therapeutic strategies. Further research should explore the integration of real-world data into models to enhance their accuracy.

Keywords: SARS-CoV-2, Mathematical Modeling, Immune Response, Influenza Comparison, Infection Kinetics.

1. Introduction

Infectious pathogens pose an incredible threat to humanity. The COVID-19 pandemic was a contemporary example of the damage to humanity caused by infectious pathogens. The COVID-19 pandemic was caused by the novel coronavirus SARS-CoV-2. The pandemic began in 2019 in Wuhan, China, and spread to the rest of the world, causing a global pandemic. Despite efforts from the country of origin, China, to contain the virus, it spread rapidly beyond immediate containment measures.

The coronavirus is a member of the Coronaviridae family, composed of the subfamily Orthocoronavirinae. The Orthocoronavirinae are split into four genera: Gammacoronavirus, Alphacoronavirus, Deltacoronavirus, and Betacoronavirus [1]. The coronaviruses are covered in viruses with positive single-stranded RNA genomes. There are 7 known coronaviruses known to infect humans. These viruses belong to the Alpha and Beta genera and they trigger pathologies similar to the flu or common cold and life-threatening respiratory infections.

Coronaviruses have existed in various species of animals, with studies attempting to identify and isolate viruses in animals dating back to the 1940s. The viruses are found in animals such as camels and bats. Coronaviruses can advance to infect humans through respiratory droplets. Prior to the COVID-19 Pandemic, the Middle East respiratory syndrome (MERS-CoV). MERS-CoV broke out in Saudi Arabia

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in 2012 and lasted until 2020, when the last case was reported. It had 2506 cases reported and caused 862 deaths (CDC, 2020). Prior to MERS, there was Severe Acute Respiratory Syndrome (SARS-CoV). This was reported in Asia in 2003 and had a fatality rate of 11%. There were 8422 reports.

At the onset of the pandemic, there was a widespread lack of vaccines or antiviral drugs formidable against COVID-19. There was a consensus approach to preventive and managerial measures aimed at curbing the spread by preventing new infections. The initial approach relied heavily on individual behavior such as self-isolation and social distancing, and other preventive measures such as handwashing. Other measures included covering coughing and global advocacy for face masks. Additionally, different nations took diverse approaches in the form of policies including travel restrictions, and communal and private quarantines.

During the pandemic, Epidemiological models were developed to discuss transmission and de-confinement strategies. However, there was a significant lack of models to understand the virus's replication cycle effects of drugs, and the interaction of the virus with the human immune system. There was intensified research into developing models to discern within-host viral dynamics. The need to develop infection and pathogenesis models increased within the scientific community.

Therefore, this paper will focus on mathematical models that provide an understanding of coronavirus dynamics. The models sought to highlight the virus's replication cycle, the effects of drugs, and its interaction with the human immune system.

Additionally, it will highlight models for understanding coronavirus growth kinetics, infection biology, and tropism. Of key interest will be the in-host dynamics of the coronavirus as modeled mathematically. The paper will focus on the mathematical models used by Wolfel as the basis for analysis [2].

2. The Mathematical Models

The models utilize Differential Equations to explain the dynamics of coronaviruses.

This will be particularly useful in analyzing the kinetics of SARS-CoV-2. Wolfel used viral load data, measured on a Log10 scale, obtained from swab cultures and consisting of samples from 9 individuals from a hospital in Munich. The report captured the viral load kinetics for these cases and was captured 2-4 days after the onset of symptoms. The parameters were estimated using the parameter identification process. This was intended to reduce the errors between model predictions and experimental data. The reduction is achieved by reducing the RMSLE (Root Mean Squared Logarithmic Error) between the predictions and experimental data, using the function:

$$\mathrm{RMS} = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(\log(yi)) - \log(\bar{yi}))^2} \tag{1}$$

The solutions adopted by Wolfel (2021) solve the problems from previous modeling works， such as those achieved by (Hernandez-Vargas et al., 2014b)[2, 3]. Wolfel adopted the Differential evolution (DE) algorithm as an optimization tool to tackle nonlinear optimization problems. Due to the existence of several mathematical models capable of providing the same results if provided with the same experimental data, there is a need to choose the model that fits best. One such approach is through the use of the AIC (Akaike information criterion): In the AIC, N represents the number of data, M represents the parameters, and RSS represents the sum of fitting squares [4].

$$\mathrm{AICc} = N\log\left(\frac{\mathrm{RSS}}{N}\right) + \frac{2MN}{N - M - 1} \tag{2}$$

The Target Cell Limited Model.

Since the initial stages of the coronavirus 2 outbreak, human airway epithelium (HAE) cells, which had been suggested for other coronaviruses, have been used. These cells played a critical role in isolating and identifying coronavirus 2 shortly after it appeared in Wuhan. These cells provide an effective

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platform for understanding coronavirus 2 interactions. The TCL (Target cell limited) model for coronavirus is used to represent the cell dynamics. The TCL writes as follows:

$$\frac{dU}{dt} = -ßUV \tag{4}$$

$$\frac{dI}{dt} = ßUV - \partial I \tag{4}$$

$$\frac{dV}{dt} = pI - \tag{5}$$

The first equation elaborates on the susceptibility of the ARS-CoV-2 virus. The second equation represents how the infected cells change denoted by I while the last equation represents the viral dynamics and is denoted by (V). These mathematical computations are based on the assumption that coronavirus infections take place in the respiratory epithelial cells as highlighted by Zhu et al [4].

3. The Interaction Between Immune System and SARS-CoV-2

The immune system is a hierarchical biological system composed of two subsystems, the innate system and the adaptive system. The innate system detects foreign pathogens through a barrier of cells and molecules. On the other hand, the adaptive system functions to clear the identified pathogens. The T-cell is a component of the immune system critical to eliminating the influenza virus. The model adapted for the analysis of immune responses assumes a symptomatic resemblance to influenza. The model represents the relationship between the immune system and influenza [5]. Additionally, the model assumes that the infection causes the proliferation of T-Cells. The model is as follows:

$$\frac{dV}{dt} = pV\left(1 - \frac{V}{K}\right) - c_T VT - cV \tag{6}$$

$$\frac{dT}{dt} = s_T + rT\left(\frac{V^m}{V^m + k_T^m}\right) - \partial_T T \tag{7}$$

The first equation models the viral replication of coronavirus using a logic function with a maximum load capacity of K. The function also has a replication rate of K represents the load capacity of each patient in the Wolfel et al. report. The original viral concentration (V0), as provided by Wolfel et al., is 0.31 ml. c represents the viral clearance rate [2]. The rate at which the immune system cells kill the infected cells is represented by the expression cTVT. The second equation represents the response of the T cells to SARS- CoV-2. The expression sT=8tT(0) indicates the homeostasis of T-cells. ST, on the other hand, represents half of the T-Cells. Based on the previous assumption, the T cells can proliferate at the rate of r.

4. Discussion

The two mathematical models extensively dissect the complexity of the coronavirus 2 infectious process. The initial models also provide a preliminary understanding of the model selection process and parameter establishment. These are particularly important in understanding how one mathematical model is chosen over another. It takes into account the robustness of the model and its ability to accurately represent biological processes. Understanding how coronavirus 2 infects cells and its progression is key to taking a preventive approach to the virus.

However, understanding only the viral dynamics is insufficient for a full-scale approach to SARS-CoV-2. As such, the immune response models provide a much needed illustration of in-host behaviour during and post-infection. The information provided by these models forms the basis for the development of drugs aimed at maiming the virus or providing symptomatic relief to infected patients. It provided an in-depth understanding of the shortcomings of the human immune system that require strengthening to enable self-defense against the virus.

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However, despite this progress in scientific and mathematical modeling, there is still a need for a broader perspective on these models. The two mathematical models highlight the gap in the scientific research spectrum aimed at studying SARS-CoV-2. That is, research sidelines immune mathematical modeling and only incorporates, on a small scale, its response. This paper, therefore, intends to deeply explore the SARS-CoV-2 mathematical model and the relationship between the immune models and SARS-CoV-2 responses.

5. Conclusion

In conclusion, the mathematical models discussed in this paper offer an extensive understanding of SARS-CoV dynamics. This comprehension is invaluable for future preparedness in the event of the reemergence of similar viral strains or new pathogens. However, there remains a need for further research to refine these models, especially in terms of cell selection and understanding the post-epidemic immune system's response to previous exposures and responses. Despite the progress made in understanding coronavirus dynamics through mathematical modeling, it's essential to acknowledge the limitations of these models. They are built upon simplifications and assumptions, which may not always fully capture the complexity of real-world scenarios. Therefore, future research should aim to incorporate more real-world data and refine the models to enhance their accuracy and practical utility.

The models provide an elaborative overview of the SARS-CoV dynamics. This understanding provides a basis for future responses in the event of a recurrence or the emergence of new strands. Furthermore, additional research is necessary on the models for cell selection and post-epidemic immune system responses to previous exposures and responses.

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