MATH300: FINAL PROJECT PAPER
A quantitative and qualitative analysis of the COVID–19 pandemic model - Reconstruction

Thao Duong

May 3, 2024

1. ABSTRACT

This paper focuses on developing mathematical models to address the spread of COVID-19 and assess healthcare strategies. It introduces an updated model based on differential equations with transmission parameters and conducts computational simulations and sensitivity analyses. The highlighted method involves computing local sensitivities for model parameters using three techniques: non-normalizations, half normalizations, and full normalizations.

The results reveal significant changes in model dynamics based on various key parameters, particularly the transition rates between asymptomatic infected individuals and reported/unreported symptomatic infected individuals. This information aids global efforts to reduce infections and prevent widespread transmission. Additionally, the paper identifies critical model parameters, making it accessible to biologists with limited mathematical knowledge and facilitating future theoretical and practical model improvements.

2. Introduction

The COVID-19 pandemic has presented a formidable global challenge, necessitating a deep understanding of its dynamics and predictions. In 2020, our knowledge about COVID-19 was still evolving rapidly. Researchers were particularly focused on deciphering the disease's epidemiological aspects, including transmission rates and key parameters like the basic reproduction number (R0). At that time, the world was grappling with over 460 million confirmed cases, with hundreds of thousands of deaths reported globally.

Despite extensive research efforts utilizing mathematical models, computational simulations, clinical data, and examination tests, various dimensions of the COVID-19 issue remained to be fully explored. Researchers were actively investigating mathematical epidemiology models to predict disease dynamics, with a notable emphasis on R0. This metric, representing the average number of secondary infections from a primary infection in a susceptible population, played a crucial role in understanding transmission dynamics and identifying critical model parameters.

Studies indicated varying estimates of R0, highlighting the complexity of COVID-19's spread. These investigations utilized diverse modeling approaches, including stochastic epidemic models, compartmental models based on clinical progression, and next-generation matrix approaches. Additionally, researchers examined parameters like the serial interval, aiding in understanding disease transmission dynamics and informing healthcare strategies.

However, gaps persisted, particularly in understanding local sensitivities in computational simulations and fully leveraging sensitivity analysis techniques. To address these gaps, this study proposes a

comprehensive mathematical model to estimate transmissibility and analyze model dynamics through computational simulations. By identifying critical model elements and quantifying their impact, this research aims to provide theoretical insights for biologists and practical recommendations for disease control strategies, ultimately contributing to ongoing efforts to combat COVID-19 effectively.

3. Methods

The concept of chemical kinetic theory is a significant method for comprehending and expressing biological processes through model equations. Model states, parameters, and equations are important assumptions which build up the models since those assumptions can support examining math modeling effectively.
Stoichiometric equation:

$$\sum_{j=1}^{m} a_{ij} x_j \xrightarrow{\alpha_1} \sum_{j=1}^{m} b_{ij} x_j \; i = 1, 2, ..., n \tag{1}$$

Classical theory of mass- action law was applied to build model reaction rates.

$$v_i = \alpha_i \prod_{j=1}^{m} x_j^{a_{ij}}(t), i = 1, 2, ..., n. \tag{2}$$

System of differentials equations with initial components

$$\frac{dx}{dt} = \sum_{i \in J \subset \mathbb{R}} \pi_i v_i, x_i(0) = x_i^0, \tag{3}$$

Form of equation (3)

$$\frac{dx_j}{dt} = h_j(x, \alpha), \tag{4}$$

Main equation of sensitivity

$$s_{ip} = \frac{\partial x_j}{\partial \alpha_p} = \lim_{\Delta \alpha_p \to 0} \frac{x_j(\alpha_p + \Delta \alpha_p) - x_j(\alpha_p)}{\Delta \alpha_p} \tag{5}$$

Differential equations can be solved for sensitivity coefficients as following:

$$\frac{\partial s_{jp}}{\partial t} = \frac{\partial}{\partial t}(\frac{\partial x_j}{\partial \alpha_p}) = \frac{\partial}{\partial \alpha_p}(\frac{\partial xj}{\partial_t}) = \frac{\partial}{\partial \alpha_p}(h_j(x(t), \alpha)). \tag{6}$$

Sensitivity equations

$$\dot{S} = H_{\alpha p} + J.S, p = 1, 2, ..., n \tag{7}$$

4. Updated Models

Classical epidemic disease models typically consist of elements representing individuals and changes in interactions among these elements within a population. To elaborate, in an epidemic network model, individuals are represented as nodes, and the connections between them signify contacts. This framework aids in comprehending infectious disease models through a graphical network perspective. Recent models have been proposed to describe the dynamics of COVID-19, focusing on initial populations and interaction parameters derived mainly from confirmed cases in China. These models revolve around clinical progression, epidemiological factors, and intervention strategies. In

this study, we refine a prior model and expand it to include recovered individuals (R), unreported symptomatic death rates ($\alpha_1 U$), and reported symptomatic death rates (α_2W). The diagram illustrating the model's network and individual interactions is depicted in Figure 1. The COVID-19 model's directed graph is represented as a graph G = (N, L), where G is the model graph, N=(S, I, U, W, R) is the set of nodes representing states, and L = v1, v2, v3, v4, v5, v6, v7 signifies the set of links representing reactions.

Therefore, let's examine human populations categorized into five distinct groups:

1 The Susceptible group (S): Comprising healthy individuals.

2 The Asymptomatic group (I): Consisting of infected individuals in the early stage of infection who do not exhibit symptoms but can spread the virus through droplets or direct contact with susceptible individuals.

3 The Symptomatic unreported group (U): Comprising individuals who have been infected, show symptoms of COVID-19, but have not been identified by the government as suspects of COVID-19.

4 The Symptomatic reported group (W): Consisting of individuals who have been infected, display symptoms of COVID-19, and have been identified by the government, either through rapid testing or voluntarily reporting to a hospital. It is assumed that all individuals in this category will receive specific treatment and monitoring, whether through supervised isolation or hospital treatment.

5 The Recovered group (R): Comprising individuals who have recovered from COVID-19 and have temporary immunity.

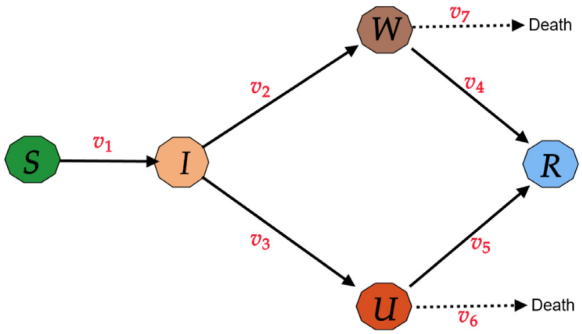


Figure 1. The model interaction individuals for the COVID–19 epidemic outbreak with reaction rates.

The transmission diagram in Fig.1 shows how different groups interact. In this developed model, there are six parameters for computational simulations. These parameters represent the rate constants of interactions between groups of individuals. The interactions between states (individuals) are as follows: Susceptible individuals (S) become infected (I) at a rate of (βS(I+U)) when they are asymptomatic. Then, asymptomatic individuals (I) transition to reported symptomatic individuals (W) at a rate of (γI) or to unreported symptomatic individuals (U) at a rate of (δI). Both W and U groups transition to recovered individuals (R) at rates (ηW) and ηU), respectively. Additionally, some

infected individuals, both reported and unreported, may die at rates (α_1U) and (α_2W), respectively. Below are the reactions of the model along with their respective rates.

$$S \xrightarrow{v_1} I, I \xrightarrow{v_2} IW, I \xrightarrow{v_3} U, U \xrightarrow{v_4} R, U \xrightarrow{v_5}, U \xrightarrow{v_6} Death, W \xrightarrow{v_7} Death, \tag{8}$$

where $v_1 = \beta S(I+U), v_2 = \gamma I, v_3 = \delta I, v_4 = \eta W, v_5 = \eta U, v_6 = \alpha_1 U, v_7 = \alpha_2 W.$

Table 1 describes six constant parameters and five initial states of the model along with their definitions. Using Equations (2) through (4), the model's behavior is described by the following system of nonlinear ordinary differential equations. There are five non- linear ordinary differential equations:

$$\begin{aligned}
&\text{Equation 1}: \frac{dS}{dt} = -\beta S(I+U),\\
&\text{Equation 2}: \frac{dI}{dt} = \beta S(I+U) - (\gamma+\delta)I,\\
&\text{Equation 3}: \frac{dU}{dt} = \delta I - (\eta+\alpha_1)U,\\
&\text{Equation 4}: \frac{dW}{dt} = \gamma I - (\eta+\alpha_2)W,\\
&\text{Equation 5}: \frac{dR}{dt} = \eta W + \eta U.
\end{aligned} \tag{9}$$

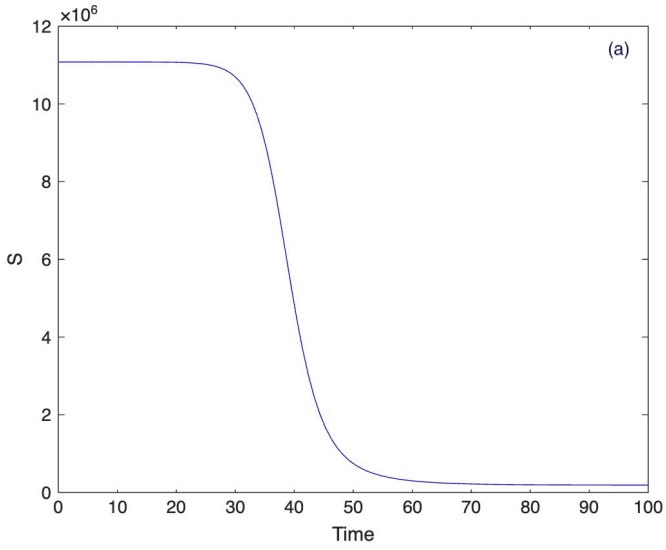
The initial populations of the model are represented by the following equation.

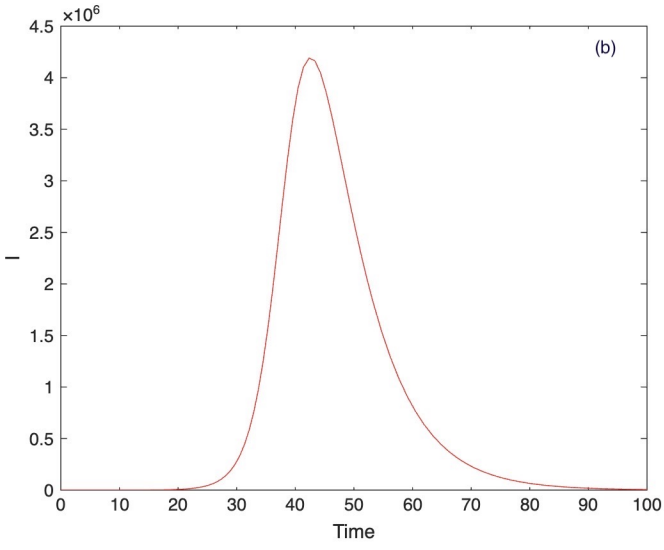
$$S(0) = S_0 > 0, I(0) = I_0 > 0. U(0) = U_0 > 0, W(0) = W_0 > 0, R(0) = R_0 \geq 0 \tag{10}$$

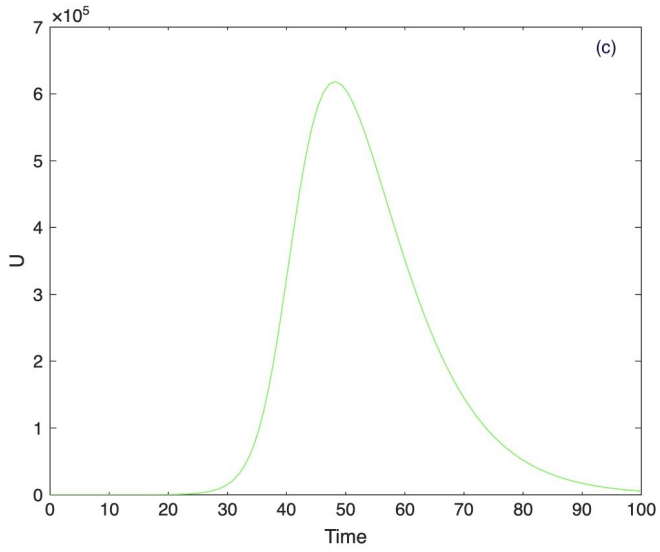
Table 1
The model reaction constants (parameters) and initial individual populations for COVID–19 epidemic outbreak with their biological definitions, all data are confirmed cases in China presented in [55].

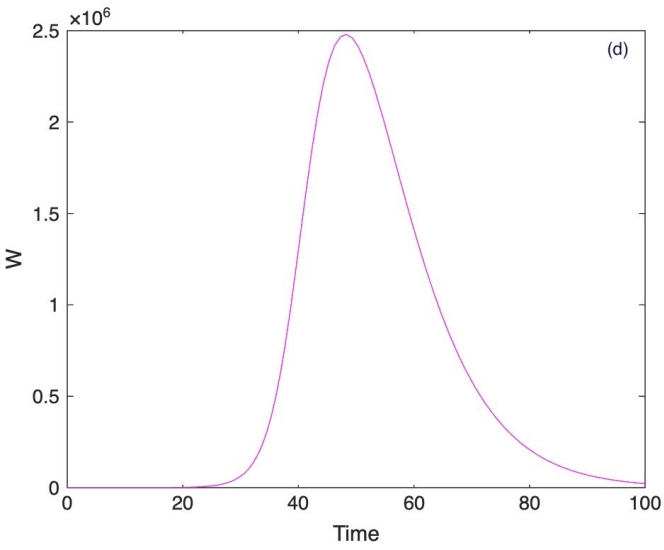
Symbols	Biological definitions	Estimated values
$S(0)$	Initial susceptible individuals	11.081×10^6
$I(0)$	Initial asymptomatic infected individuals	3.62
$U(0)$	Initial unreported symptomatic infected individuals	0.2
$W(0)$	Initial reported symptomatic infected individuals	4.13
$R(0)$	Initially recovered individuals	0
β	Transmission rate between susceptible individuals and asymptomatic infected individuals	4.44×10^{-8}
γ	Transition rate between asymptomatic infected and reported symptomatic infected	0.1142
δ	Transition rate between asymptomatic infected and unreported symptomatic infected	0.0285
$1/\eta$	Average time symptomatic infectious have symptoms	1/7
α_1	The unreported symptomatic death rate	1.5×10^{-4}
α_2	The reported symptomatic death rate	1.7826×10^{-5}

5. Results


×10^6
(a)
S
Time


×10^6
(b)
I
Time


×10^5
(c)
U
Time


×10^6
(d)
W
Time

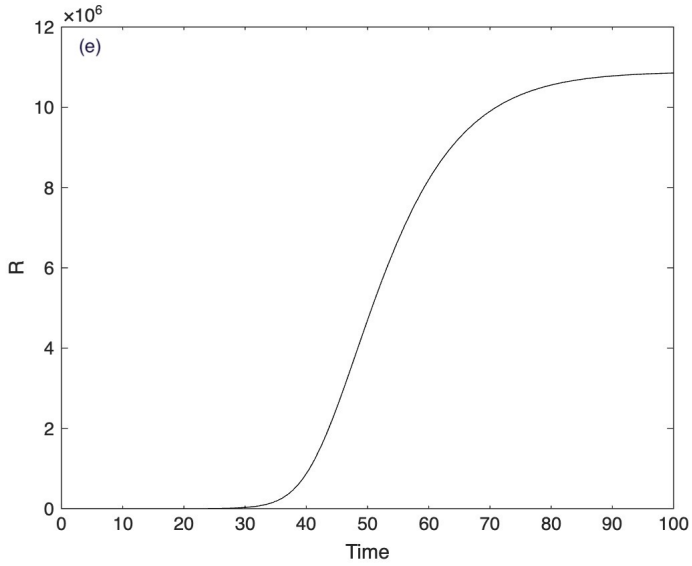

×10^6
(e)
R
Time

Fig. 2. Simulations using MATLAB are performed to model the dynamics described in system (9) of COVID-19. These dynamics encompass susceptible individuals (a), asymptomatic infected individuals (b), unreported symptomatic infected individuals(c), reported symptomatic infected individuals (d), and recovered individuals (e).

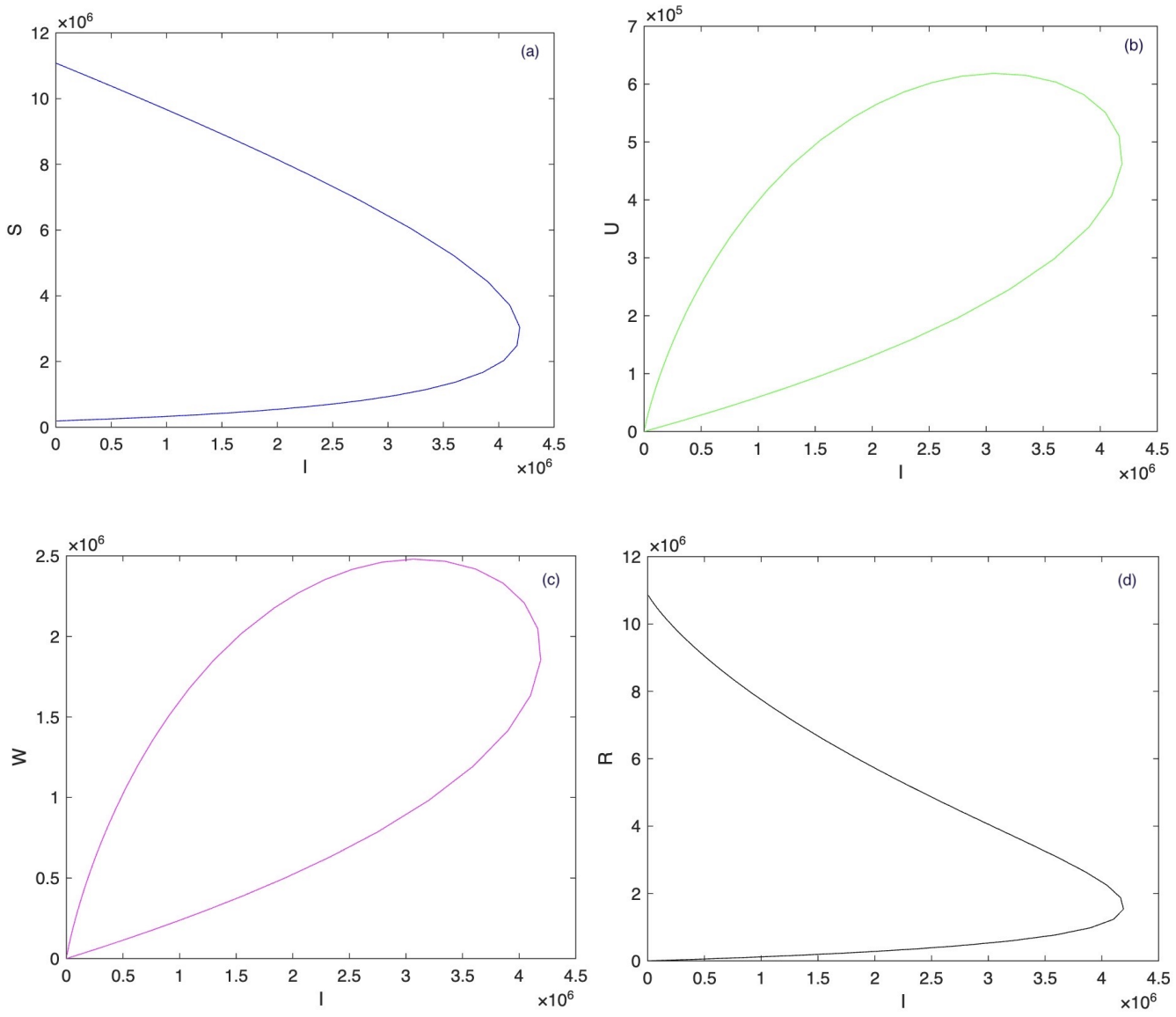


Figure 3. displays computational simulations depicting the model states outlined in system (9) of COVID-19, conducted through MATLAB. It illustrates the connections between asymptomatic infected individuals and (a) susceptible individuals, (b) unreported symptomatic infected individuals, (c) reported symptomatic infected individuals, and (d) recovered individuals.

The parameter values and initial populations used in this research are sourced from the WHO situation report as detailed in [55] and the National Health Commission of the Republic of China. Figures 2-6 illustrate various model dynamics based on initial population model states and estimated parameters. Computational numerical simulations are conducted across two-dimensional planes to

analyze model parameters and initial populations.

Figure 2 illustrates the dynamics of susceptible, asymptomatic infected, reported symptomatic, and unreported symptomatic individuals. The count of susceptible individuals steadily declines and stabilizes after 60 days, while the number of recovered individuals rises and levels off after the same period. Notably, the number of infected individuals in both asymptomatic and symptomatic categories experiences significant changes between days 40 and 80.

Additionally, Figure 3 above explores the connections between infected individuals and other groups within COVID-19. It shows consistent dynamic relationships for reported and unreported symptomatic states, while the dynamics differ slightly for susceptible and recovered groups.

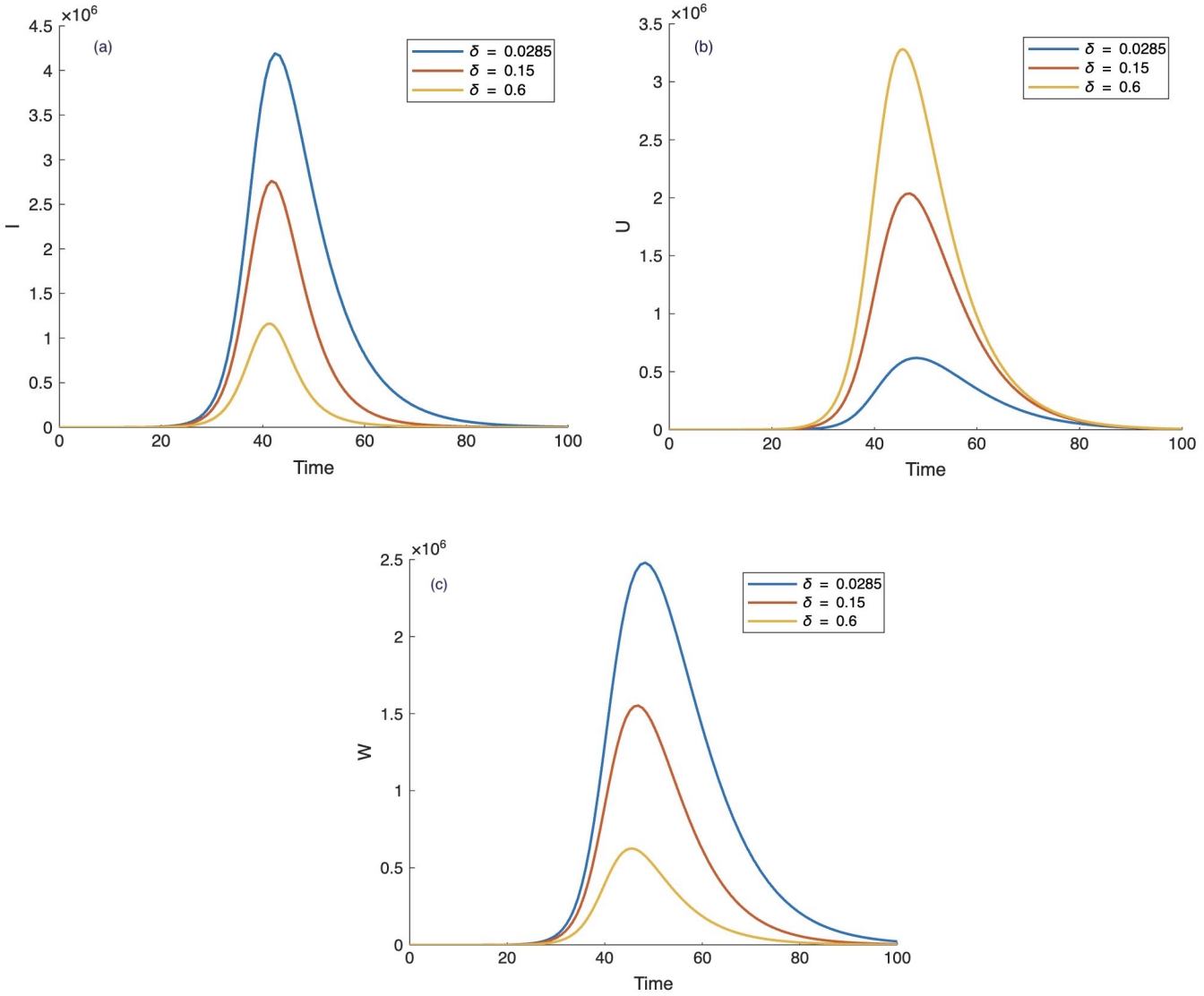


Figure 4. The effect of transition rate δ has shown on (a) asymptomatic infected individuals, (b) unreported symptomatic infected individuals, (c) reported symptomatic infected individuals, in computational simulations using MATLAB parameters used $\delta = 0.0285, 0.15, 0.6$ respectively.

Figure 4 illustrates the influence of the transition rate δ on asymptomatic infected, reported symptomatic infected, and unreported symptomatic infected individuals. This parameter has a direct

impact on the variables I, U, and W. For instance, increasing the value of δ from 0.0285 to 0.6 results in a significant increase in the number of unreported symptomatic infected individuals, as shown in Fig. 4(b). Conversely, reducing the values of the transition rate δ leads to a rise in asymptomatic infected and reported symptomatic infected cases, as showed in Figs. 4(a) and 4(c).

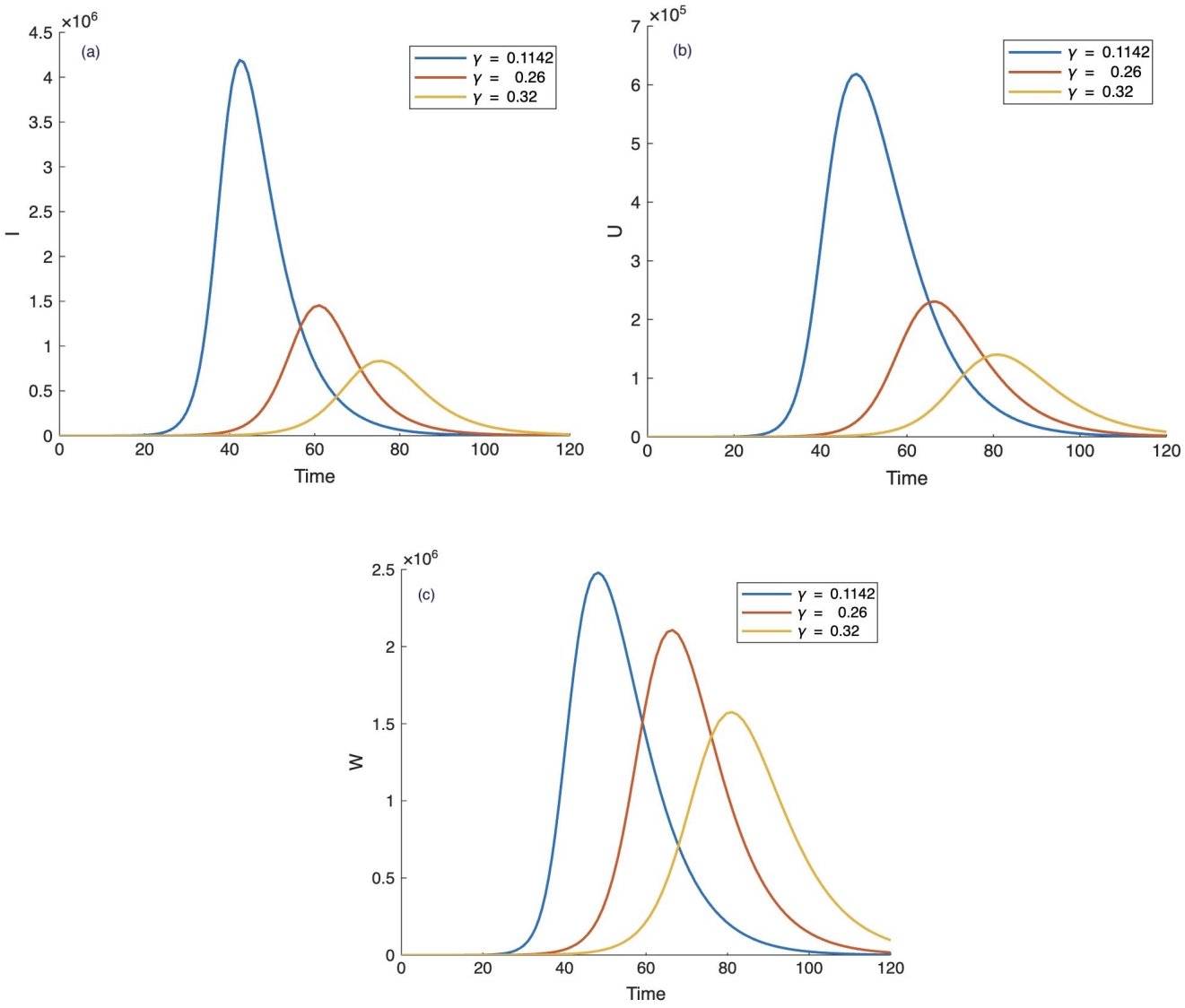


Figure 5. The effect of transition rate γ on (a) asymptomatic infected people, (b) unreported symptomatic infected people, (c) reported symptomatic infected people, in computational simulations using MATLAB parameters used $\gamma = 0.1142, 0.26, 0.32$ respectively.

Figure 5 shows how increasing the transition rate γ flattens the dynamics of asymptomatic, reported symptomatic, and unreported symptomatic infected individuals. This parameter's effect is evident on the variables I, U, and W. Notably, the model dynamics for these states exhibit a flatter trend as γ increases. This aspect is crucial for disease control strategies.

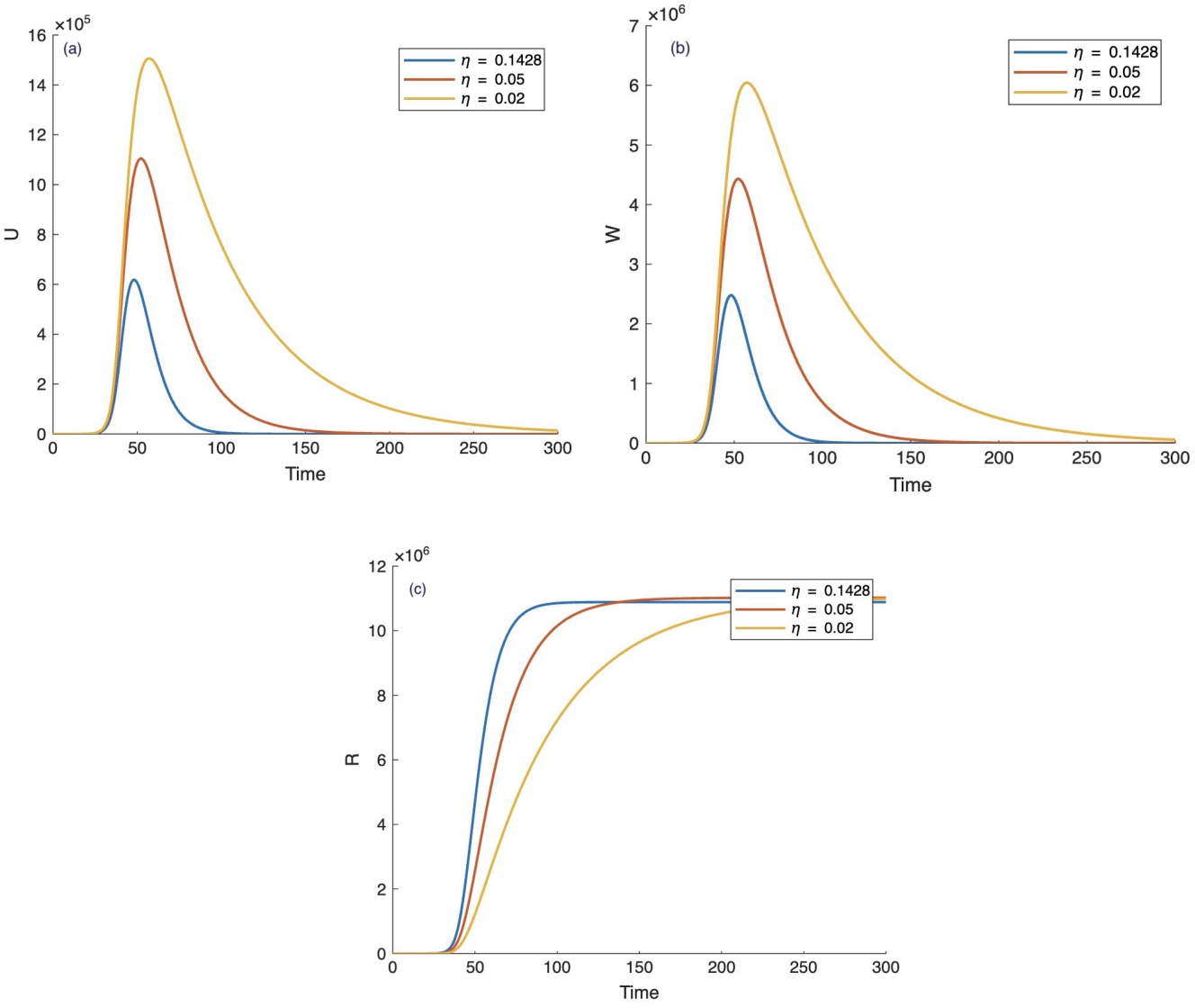


Figure 6. The impact of parameter η on (a) unreported symptomatic infected individuals, (b) reported symptomatic infected individuals, and (c) recovered individuals. The MATLAB simulations utilized parameter values of $\eta = 0.1428$, 0.05, and 0.02.

Figure 6 illustrates how the parameter η, representing the average time infected individuals exhibit symptoms, affects the dynamics of unreported symptomatic, reported symptomatic, and recovered individuals. In Figs. 6(a) and 6(b)Smaller showed that values of η lead to a notable increase in both unreported and reported infected cases. Conversely, larger values of η result in rapid and stable growth in the dynamics of recovered individuals, as seen in Fig. 6(c):

1 Using MATLAB's System Biology Toolbox (SBedit), simulations analyze COVID-19 dynamics for susceptible, asymptomatic, reported/unreported symptomatic, and recovered individuals, highlighting consistent dynamics for symptomatic states and unique dynamics for susceptible and recovered groups.

2 The impact of the transition rate δ on asymptomatic infected, reported symptomatic infected, and unreported symptomatic infected individuals is studied, emphasizing its significant role in the

dynamics of these variables (I, U, and W).
3 Similarly, the transition rate δ is observed to influence the dynamics of asymptomatic infected, reported symptomatic infected, and unreported symptomatic infected individuals, with higher values of γ resulting in flatter model dynamics, a crucial aspect for disease control.
4 Decreasing values of η lead to a substantial increase in both unreported and reported infected individuals, while larger values of η cause rapid and stable growth in the dynamics of recovered individuals.
5 Sensitivity analysis using three techniques —non-normalizations, half normalizations, and full normalizations— identifies critical model parameters, particularly noting the sensitivity of transmission parameters and the average symptomatic period in simulations of model variables.

6. Discussion

Upon reflecting on my experience with recreating the results from the chosen paper, I initially encountered challenges in grasping the author's concepts and methodology. However, through diligent review of the paper and constructive discussions with Professor Tom Stojsavljevic, I gained a comprehensive understanding of their approach. This facilitated the successful recreation of the results.

The parameter values outlined in Table 1 of the original paper played a crucial role in comprehending their significance within the equations and models. Nevertheless, I encountered difficulties stemming from the sensitivity of model states to these parameters. Inaccurate assignments of parameter values could lead to substantial alterations across various models, underscoring the necessity for meticulous parameter selection in the modeling process.
The parameter values, denoted by Greek symbols and documented using LaTeX. Mistakes in typing the LaTeX codes could lead to incorrect parameter assignments, potentially resulting in significant deviations across various models.
Additionally, I utilized MATLAB to recreate the code base for the models in the original paper. However, I encountered challenges due to the sheer volume of models that needed to be recompiled. This resulted in a lengthy process, as each part in the function files required considerable time and effort to complete.

7. Conclusion

My experience in following the modeling process in this manner closely parallels my journey in the math modeling course. The course assignments, including homework and lab exercises, provided me with the necessary skills to code in MATLAB and understand the workings of logistic and discrete equations. This foundational knowledge proved invaluable in approaching the original research papers.
One major idea from our course that resonated with the original research papers is the concept of modeling states and their dynamics. Through the course, we delved into how to formulate equations to describe various biological groups and their interactions. This knowledge greatly facilitated my understanding of the papers' content, particularly in deciphering the model states and the relationships between them in real life applications.
Additionally, the flow diagrams used in the papers were reminiscent of what we learned in the early weeks of the semester. We were taught by Professor Tom Stojsavljevic how to construct flow diagrams and write equations to represent biological systems. Seeing these concepts applied in the papers reinforced the relevance and practicality of the course material.
Overall, my experience in the modeling process mirrored the key ideas from our course, emphasizing the importance of understanding model states, dynamics, and utilizing visual aids like flow diagrams to describe complex systems (Coronavirus disease (COVID-19) in this case)—a true reflection of the

essence of Math Modeling.

8. References

[1] Sarbaz H.A. Khoshnaw, Muhammad Shahzad, Mehboob Ali, Faisal Sultan, A quantitative and qualitative analysis of the COVID–19 pandemic model, Chaos, Solitons Fractals, Volume 138, 2020, 109932, ISSN 0960-0779, https://doi.org/10.1016/j.chaos.2020.109932.