2021 WPI Research Experiences for Undergraduates in Industrial Mathematics and Statistics

Modeling SARS-CoV-2 (COVID-19) to Predict its Effect on Patients with End-Stage Renal Disease

Veronica Berger, Williams College
Olivia Tom, Boston University
Yael Yossefy, Wesleyan University



Abstract

With the emergence of **SARS-CoV-2** and its subsequent effect on public health, mathematical models have become vital in gaining a better understanding of the virus, providing insight into its infection and spread, and allowing us to predict how it affects vulnerable populations, e.g., patients with **End-Stage Renal Disease** (ESRD). We therefore developed two models using nonlinear differential equations:

- **The COVID-19 Wave Model**, describing the spread of the disease, is a SEIR model fit to U.S. cumulative mortality data during the third wave (Oct 1, 2020 to Feb 1, 2021). It accounts for mitigation strategies (e.g., social distancing, mask wearing), allowing the model to successfully predict daily infections, and to capture the wave-like behavior of the disease.
- **The Compartmental SARS-CoV-2 Model**, describing in-host dynamics, simulates the interaction between viral particles and immune response cells (e.g., T Cells, antibodies). The model fits viral load measurements as a function of time for infected patients from two different sources.

Given the success of these models in fitting data of otherwise healthy individuals, fitting them to data specific to patients with ESRD can be used to inform treatment protocols.

Background and Research Goals

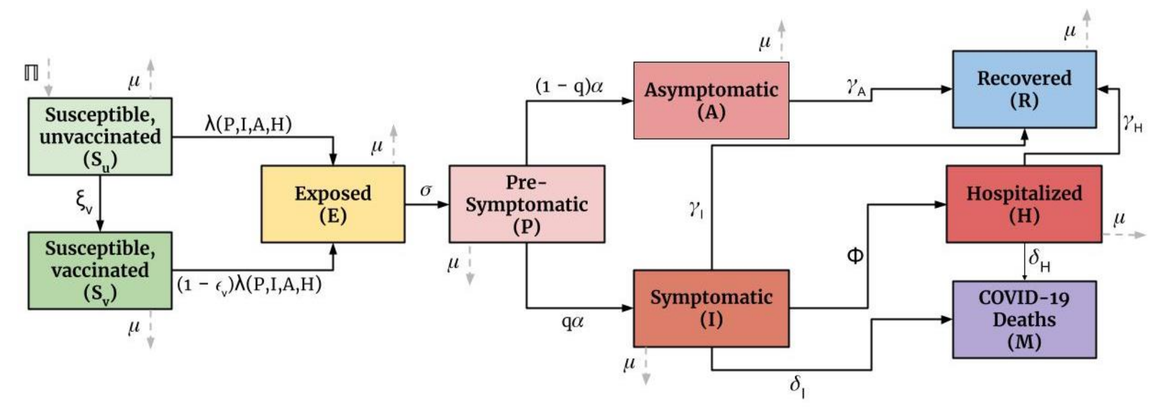
Population Level

Develop a mathematical model to predict the how SARS-CoV-2 spreads throughout the United States.

In-Host Level

Develop a mathematical model that describes the immune responses to SARS-CoV-2 infection.

COVID-19 Wave Model



$$\lambda(P, I, A, H) = \beta_P P + \beta_I I + \beta_A A + \beta_H H$$

$$\frac{d\beta_i}{dt} = -\psi\left(\frac{H^m}{k^m + H^m}\right) \cdot \beta_i + p(\beta_{i0} - \beta_i)$$

$$\text{where } i = \{P, I, A\}$$

Figure 1: The COVID-19 Wave Model is a SEIR model based on the work of Gumel et. al. We implement the transmission rate of each infected class, β_i, as differential equations of sigmoidal form to mimic changing transmission rates due to mitigation strategies. Once hospitalizations pass a certain threshold, the transmission rate decreases, reflecting government shutdowns, causing less infections to occur. Transmission rates are then pushed back up after the fall in infections, reflecting reopening policies.

Compartmental SARS-CoV-2 Model

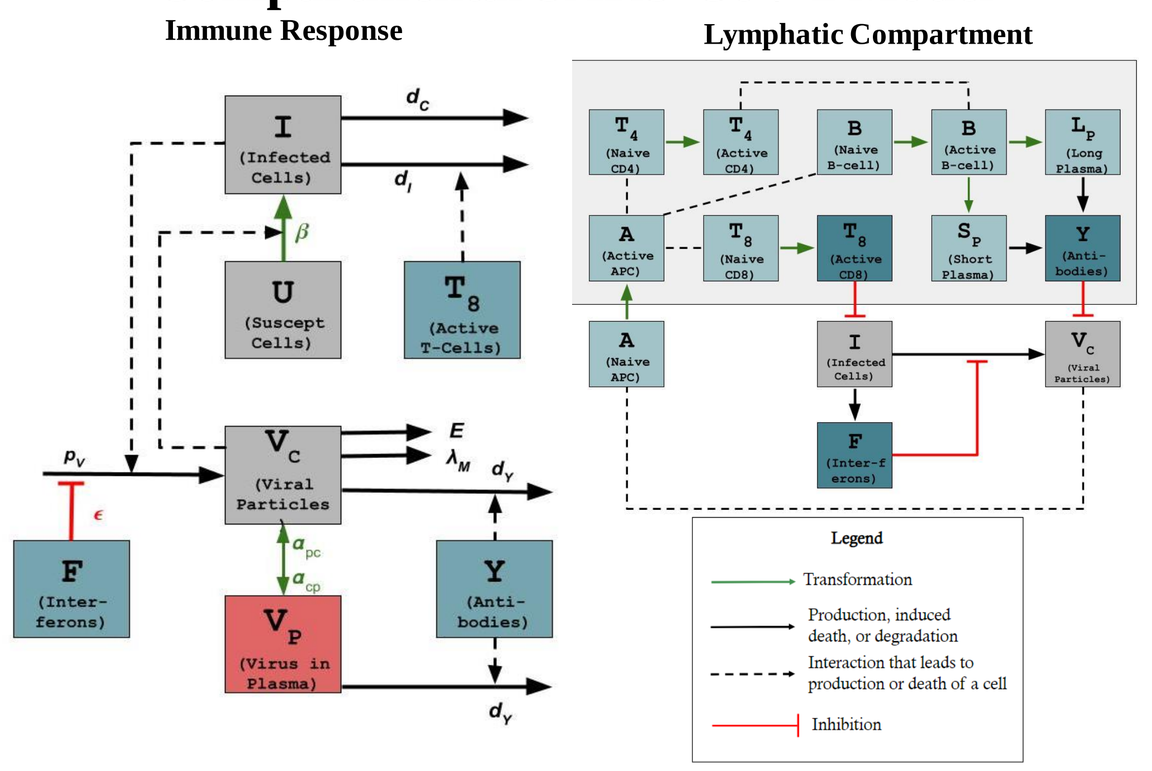


Figure 4: This in host model is based on the work of Dogra et. al, and implements both the innate and adaptive immune responses to SARS-CoV-2 infection in one organ, the plasma, and lymphatic system. CD8 T-Cells, Interferons, and Antibodies (left) directly interact with viral particles and the cells they invade. The Lymphatic Compartment (right) shows how other cells transform into or produce these three direct inhibitors.

Time-varying Rate of Transmission

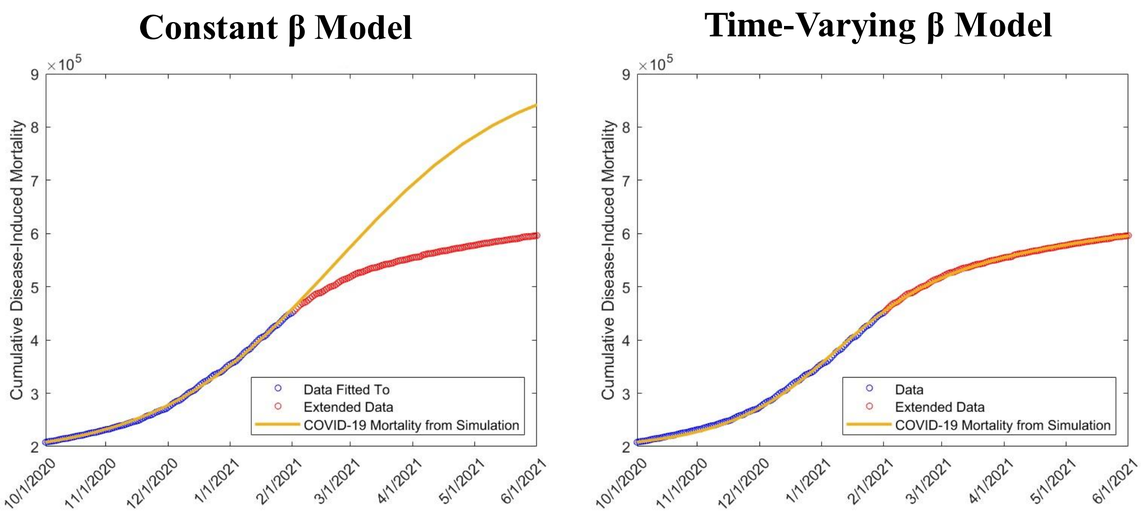


Figure 2: The mortality class (yellow) is fit to cumulative disease-induced mortality data from the third wave (blue) using MATLAB optimization package fminsearch. With the constant beta model (left), cumulative mortality overestimates data after the third wave (red), as it does not take into account the mitigation strategies responsible for lowering transmission rates. Using a time-varying beta (right) proves more predictive, which is why we chose to develop this model over the constant beta model.

Viral Load and Active Cell Counts Among Patients

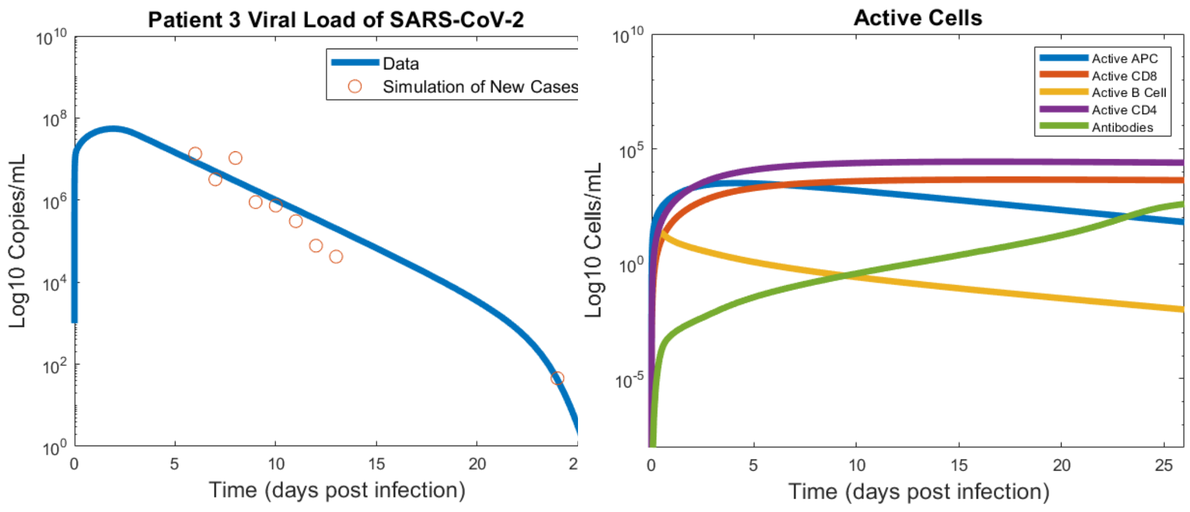


Figure 5: Clinical data of viral swabs from untreated COVID-19 patients averaged from Vetter et al. with an incubation period of 6 days.

Figure 6: The number of active cells grows as naïve cells transform. Active B cell count, however, falls as it is transformed into Antibodies.

Time-Varying β Predicts Other Data

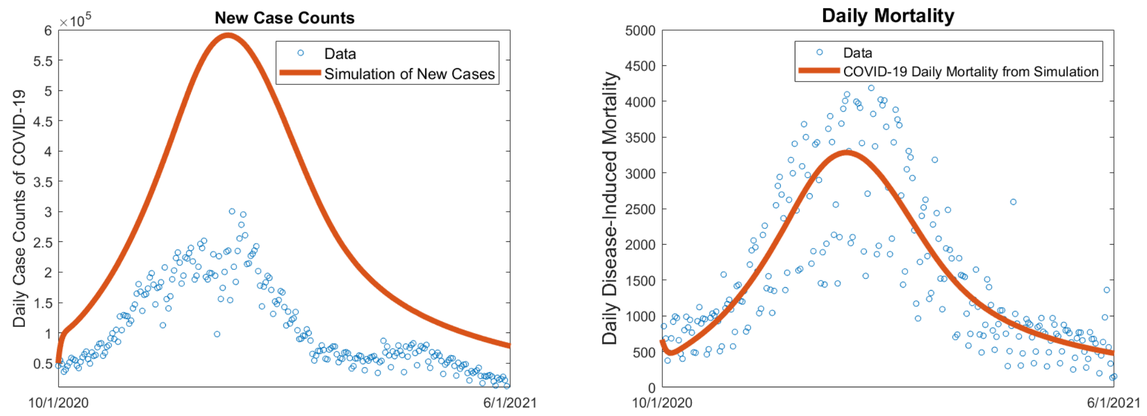


Figure 3: With the time-varying beta, we capture the behavior of other data sets. The simulation for new cases (left) follows the shape but overshoots the data; this is expected, because the data only accounts for those who test positive, while the model accounts for anyone who has the virus. The simulation for daily mortality (right) resembles both the shape and magnitude of the data. By matching data sets without being explicitly fit to them, our model is shown to be more credible and likely to fit to more data.

Summary and Future Work

In summary, the models can be used in tandem to understand how SARS-CoV-2 spreads through populations and within the body. These models serve as a foundation that can be built upon to include more biological complexities. Fitting the models to **data specific to patients with ESRD** can give insight into the transmission, rate of viral elimination, and other important parameters that differ between healthy individuals and those with ESRD. For the population-level model, we **recommend using the time-varying β** as it can match the time scale of pandemic waves, and with more tuning can predict the timing and height of future waves. The second recommendation would be to **add vaccinations as a function of time**. For the in-host level model, we recommend the **implementation of cytokine storms**.

Selected References

Gumel, Abba B. et al. "Towards achieving a vaccine-derived herd immunity threshold for COVID-19 in the U.S." medRxiv 2020.12.11.20247916

Dogra, Prashant et al. "Innate Immunity Plays a Key Role in Controlling Viral Load in COVID-19: Mechanistic Insights from a Whole-Body Infection Dynamics Model." ACS pharmacology & translational science 4.1 (2021): 248–265. Web.

Vetter, Pauline et al. "Daily Viral Kinetics and Innate and Adaptive Immune Response Assessment in COVID-19: a Case Series." mSphere 5.6 (2020): n. pag. Web.

Acknowledgments

- Renal Research Institute Liaisons: Dr. Alhaji Cherif
- WPI Department of Mathematical Sciences
- National Science Foundation Award DMS-1757685

Advisors: Dr. Sam Walcott
Dr. Duncan Wright

Sponsor: Renal Research Institute