Modeling SARS-CoV-2 Interactions with the Immune System in COVID-19

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Abstract

We propose and analyze a mathematical model for the interaction of immune cells and SARS-CoV-2 infected cells using a system of ordinary differential equations with the goal of understanding immune-mediated viral clearance in COVID-19. We numerically explore parameter sets which yield qualitatively different behavior, such as viral clearance, viral persistence, and rebounding infection. We apply equilibrium and bifurcation analysis to the model, and discuss results in the context of the biological pathways the model represents. Additionally, we develop an agent-based model which includes a spatial component to complement our dynamical systems approach.

Acknowledgements

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Differential Equation Analysis

We use a system of differential equations that describes the change in population of immune response cells (z) and infected cells (y) with respect to time shown below.

Pathway	Description
a	constant source of infected cells
b	natural death of infected cells
c	killing of infected cells by CTLs
d	proliferation of CTLs by antigen from infected cells
e	death and exhaustion of CTLs

$$\frac{dy}{dt} = \overbrace{\gamma}^{a} - \overbrace{\delta_y y}^{b} - \overbrace{\rho yz}^{c}$$

$$\frac{dz}{dt} = \overbrace{\kappa yz}^{d} - \overbrace{\delta_z z}^{e}$$

Results of ODE Analysis

A bifurcation analysis of of δ_y shows how the natural death infected cells affects the system (Fig. 1). Each curve shows how the system's equilibria change as we increase δ_y. Notice that there is one equilibrium point that will always have an infected population of two, regardless of the rate that infected cells die at. However the other equilibrium, shown by the curve, shows that the population of infected cells will shrink as δ_y increases.

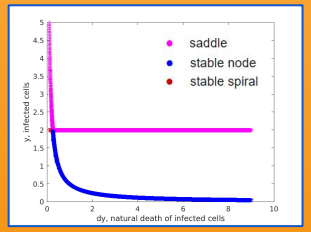

Figure 1: Bifurcation analysis of δy showing transitions between saddles, stable nodes, and stable spirals

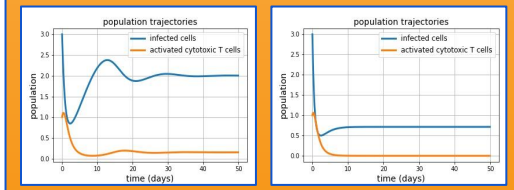

Figure 2: Population versus time graph for both infected cells (blue) and immune response cells (orange). We see that for δy =0.1 (left), the infected population in blue remains large but is significantly reduced when δy=0.7 (right) indicating a successful immune response.

Agent Based Model Analysis

To supplement our ODE analysis we use NetLogo to simulate infection spreading inside the lungs. In the simulation, white patches represent healthy lung cells, green patches are infected cells that are not yet infectious, red patches are infected and infectious, while black patches represent dead cells. As the infection spreads, an immune response is triggered by infected cells releasing IFNγ which attracts macrophages that destroy infected cells.

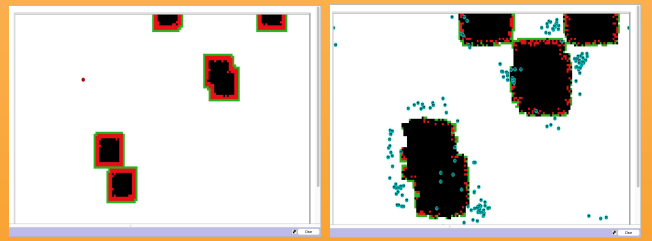

Figure 3: The image to the left shows six infected cells immediately after beginning to spread the infection with a single red macrophage. The image to the right shows how the infection spread after 24 hours. Notice the macrophages have now multiplied and surrounded the infection sites, turning green after destroying an infected cell.

Results of ABM Analysis

The simplified simulation demonstrates the importance of macrophage signalling. Increasing the macrophages ability to detect IFNγ resulted in the infection being destroyed much faster indicating that treatments focused on macrophage signaling could be successful.