Project: A Simulation of Viral Spread

Umbrella Corporation: Tao Luo, Lu Qiao, I-Shu Wang, Howard Wu

Current progress:

We realized that the equations listed in our proposal only describe the simulation at a macro level **(Equation 1)** and lacked the description of the behavior of individual cell activity. Thus, we found a new paper that would complement our previous model **(Equation 2)**. We decided to adopt the mathematical models from the following equations (Citation: Modeling Viral Spread - PMC (nih.gov)):

$$\begin{cases} \frac{dT}{dt} = \lambda - \omega IT - d_T T \\ \frac{dI}{dt} = \omega IT - \delta I \end{cases} \quad \textbf{(Equation 1)}$$

Equation 1: Describe the concentration of uninfectious target cell (***T***) and infected cells (***I***) over time. Target cells (T) are produced at a constant rate $\boldsymbol{\lambda}$ and have an average lifetime of ***1/dT***. Infected cells, ***I***, die with rate $\boldsymbol{\delta}$ per cell. Viruses from infected cells have a cell-to-cell transmission rate constant $\boldsymbol{\omega}$. (Citation: Accounting for Space—Quantification of Cell-To-Cell Transmission Kinetics Using Virus Dynamics Models - PubMed (nih.gov))

$$\frac{dR_{i,j}}{dt} = \alpha R_{i,j}\left(1 - \frac{R_{i,j}}{R_{\text{cap}}}\right) - \gamma R_{i,j} - \rho R_{i,j} \quad \textbf{(Equation 2)}$$

Equation 2: Describe the RNA expression level (***Ri,j***, proportional to viral concentration in cell) in infected cells over time, where virus replication with a maximal replication rate α and a carrying capacity of ***Rcap*** for each cell. Positive-strand RNA is degraded with rate γ and exported from the cell with an export rate ρ.

For the simulation of treatment, we looked for available antiviral drugs from literature. (Citation: Lan, Jie et al. "Cell-to-cell transmission of HIV-1 from provirus-activated cells to resting naïve and memory human primary CD4 T cells is highly efficient and requires CD4 and F-actin but not chemokine receptors." *Journal of medical virology* vol. 94,11 (2022): 5434-5450. doi:10.1002/jmv.28005) Currently three major classes prevent the spread of virus through interfering with its ability to enter target cells, converse into double stranded DNA in host cells and maturation of the virion. We summarized the second and third mechanisms as a disturbance of viral replication, then manipulation of two variables $\boldsymbol{\omega}$(cell-to-cell transmission rate) and α (maximal replication rate) could simulate the effect of these drugs.

In reality, different types of drugs could be used together to "increase therapy efficacy, overcome problems of tolerance, and decrease emergence of viral resistance". We might be able to simulate this cocktail treatment as well.

Project schedule:

Progress	Expected Due Date
Walk through project models, define equations we would use	10/29/2022 (done)
Make a plan for following works	11/01/2022 (done)
Plan overall structures of the project and distribute individual tasks Create GitHub project	11/08/2022 (Start working on draft of code)
Working on codes and discuss any difficulties	11/15/2022
Finalize code and draft essay and the outline of final presentation	11/22/2022
Turn in final essay draft	11/28/2022 (Optional Rough Draft Due)
Turn in final presentation	11/29/2022 (Final Presentation Slides Due)
Finalize code and essay	12/06/2022
Turn in final report and code	12/13/2022 (Day after final exam)
Final due date & end of semester, enjoy winter break!	12/16/2022 (Final Code & Essay Due)