Investigating Viral Transmission using an Agent-Based Model

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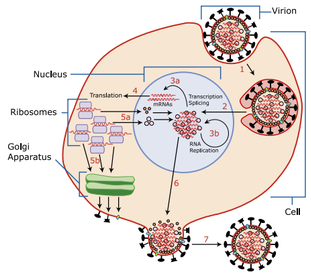
Motivation

- A virus spreads through a body in two known ways, free cell transmission and cell to cell transmission.
  - During free cell transmission, cells make viruses that diffuse throughout the body which may cause any cell that the virus touches to become infected.
  - During cell to cell transmission, a virus spreads to a neighboring cell through an intercellular transfer.
- The different modes of transmission allow viruses to spread at different speeds.
- Cell to cell transmission also protects the virus from dangers outside the cell such as antivirals and components of the immune response.

Background

- A virus enters a cell and begins to to replicate.



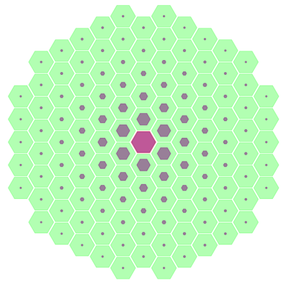
- As more and more viruses are made, the viruses begin to spread throughout the body.

Our Approach

- We will construct an agent-based model to simulate the spread of virus.
- An agent-based model represents each cell independently to examine the collective behavior.

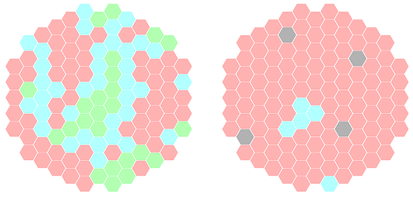
Modeling Virus Spread

- The virus produced by free cell transmission diffuses over the top of the cell layer.
- The virus from cell to cell transmission is not repersented by diffusion, because it is directly transfered from one cell to another.
- The image below is exaggerated for illustrating the diffusion of the virus



Modeling Cell States

The cells can be in one of four states.



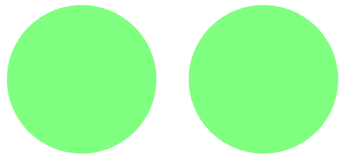
- Green- Healthy cells
- Blue- Infected cells not producing virus (Eclipse cells)
- Red- Virus-producing infected cells
- Black - Dead cells

- Cells become infected either from virus above them or from virus transferred from neighboring cells.
- Cells transition from eclipse to infectious and infectious to dead after periods of time drawn from a gamma distribution.

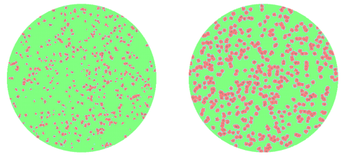
Modeling Infections

- 100969 cells in a hexagonal grid were simulated.
- For the images below a Multiplicity of Infection (MOI) of 10^{-5} was used. MOI determines the initial amount of virus.
- We compared infections using only cell-free transmission and only cell-to-cell transmission.
- Below the first 4 days for cell-to-cell (left) and cell-free (right) transmission are shown.

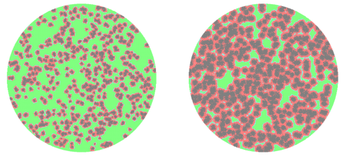
Day 0:



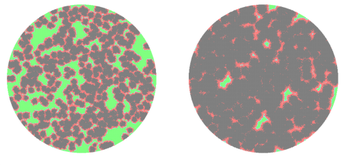
Day 1:



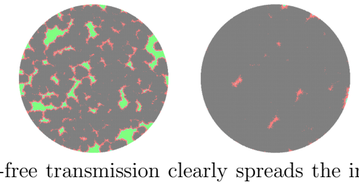
Day 2:



Day 3:



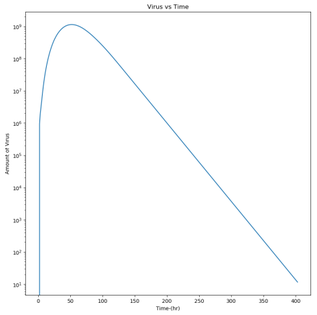
Day 4:



Cell-free transmission clearly spreads the infection faster.

Viral Time Course

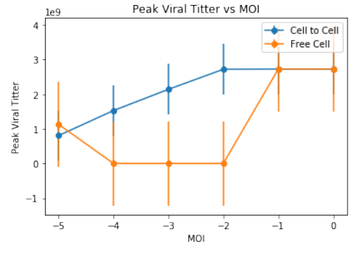
A simulation is performed for a number of MOIs and a virus vs. time graph is recorded for each.



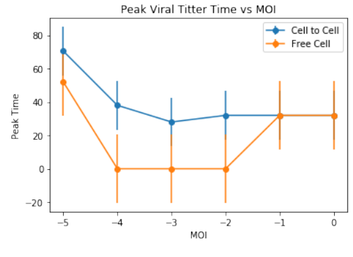
We use different features of the viral time course to assess how transmission mode changes the infection.

Peak Viral Titer

The peak virus amounts and corresponding times vs. MOI:

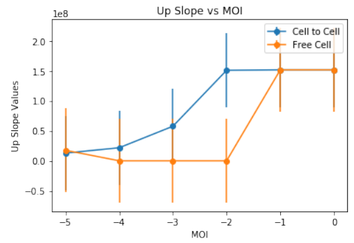


Time of Viral Peak



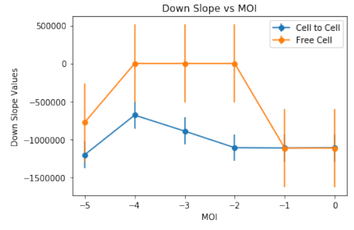
Growth Rate

The slope of the increasing portion of the viral titer curve gives a measure of how quickly the virus spreads.



Decay Rate

The slope of the decreasing portion of the viral titer curve gives a measure of how quickly the virus disappears.



Conclusions

- In general, the infection spreads quicker with cell-free transmission.
- For large MOI, there is little difference in peak viral titer, growth rate, or decay rate for the two transmission modes.
- For small MOI, the viral titer peaks sooner for cell-free transmission.

Future Work

- Simulate more cells — typical experimental wells have one million cells.
- Simulate infections with both modes of transmission.
- Examine the effect of antivirals.