Analyzing a Mathematical Model for Virus Propagation in the Trachea

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Introduction

During a viral respiratory infection, ciliated cells lining the trachea known as epithelial cells push virus up and out of the trachea through mucous layers in a process called mucociliary clearance (MCC). This process is an example of physical motion called advection. Researchers have established that MCC affects viral dynamics in the respiratory tact, however we have yet to quantify this process.. We are using a system of partial differential equations to simulate spatial and time-dependent behaviors of virions in a medium with advection. We intend to show that advection manages viral infection by preventing virus from entering the lower respiratory tract.

The Model

The model describes dynamics between various stages of a viral infection. Cells start as uninfected, but vulnerable target cells (T). Target cells turn into inactive infected cells during an eclipse phase (E). After the eclipse phase, cells turn into infectious, virus producing cells (I). During this entire process, the concentration of virus is changing (V).

$$\partial_t T = -\beta TV$$
$$\partial_t E = \beta TV - \frac{E}{\tau_E}$$
$$\partial_t I = \frac{E}{\tau_E} - \frac{I}{\tau_I}$$
$$\partial_t V = pI - cV + D\partial_x^2 V + v\partial_x V$$

Parameters:

- τ_E: duration of eclipse phase
- τ_I: productively infected cell lifespan
- c: virus clearance rate
- β: infection rate of cells by virus
- p: virus production rate
- D: diffusion coefficient
- v: advection speed

Viral Dynamics for Human Respiratory Tract (HRT):

Virus concentration, $V(x,t)$, in the periciliary fluid, PCF

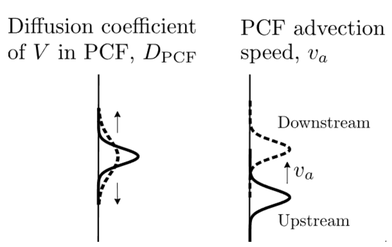

Figure 1: Diagram depicting diffusion of concentration of virions (left) and special effects of advection (right). *(From Quirouette et.al Quantitative Biology, 2019)*

Mathematical Analysis

Fourier Series Expansion: To solve this system, each function is expanded as a spatial Fourier Series with functions of time as our constants. This method, known as a spectral method, converts partial differential equations into ordinary differential equations.

$$\boldsymbol{T} = \sum_{n_T} c_{T,n}(t)e^{-in_T x} \qquad \boldsymbol{E} = \sum_{n_E} c_{E,n}(t)e^{-in_E x}$$

$$\boldsymbol{I} = \sum_{n_I} c_{I,n}(t)e^{-in_I x} \qquad \boldsymbol{V} = \sum_{n_V} c_{V,n}(t)e^{-in_V x}$$

Analyzing each derivative the virus equation:

$$\partial_x^2 V = \sum_{n_V} -n_V^2 c_{V,n}(t)e^{-in_V x} \qquad \partial_x V = \sum_{n_V} -in_V c_{V,n}(t)e^{-in_V x}$$

Substituting our derivatives into our virus equation:

$$\frac{\partial}{\partial t} C_{V,n}(t) = pC_{I,n}(t) - c * C_{V,n}(t) - n_V^2 DC_{V,n}(t) - in_V vC_{V,n}(t)$$

Computational Solutions

The spatial Fourier series expansion converted our partial differential equation into a *solvable* ordinary differential equation. Now, the spatial changes of our virus are encoded into the coefficients of the Fourier series expansion $c_V(t)$. The initial conditions determine the coefficients of expansions through an inverse Fourier series expansion. Then, the system is advanced by a small timestep using a Runge-Kutta to obtain a new distribution of virus. The coefficients of the series expansion will change with the timestep, so they are determined through another inverse Fourier Series expansion. This process is repeated for every time step.

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During a viral infection, the concentration of virus and their location are constantly changing over time, making the infection very difficult to understand. However, mathematics has tools to describe these changes. We use these tools to simulate how viruses spread down the human throat. We believe our simulations will reveal important information on when and why a viral infection becomes dangerous.

Results

Our model shows definite stages of viral infection. Initially, virus concentration rapidly grows around the area of exposure until all the target cells become infected. After this phase, the fraction of infected cells decays over time, resulting in lower viral concentration at the area of exposure. The process is repeated everywhere else in the respiratory tract at different rates. The overall effect is a travelling wavefront of virus in the respiratory tract. The wavefront changes with advection speeds.

Viral Kinematics *(no advection)*:

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Viral Kinematics of Various Advection Speeds

Table of TEIV with 3 different advections speeds

Future Work

- Find a critical advection speed that prevents virus from entering the lower respiratory tract
- Modify the model to include other biological behaviors present in the respiratory tract: cell heterogeneity, regeneration, immune response
- Model damage to mucociliary clearance and examine how this affects viral kinematics.

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