– Master or Diploma Thesis –

Spatiotemporal modeling of viral infection spread in the human respiratory tract

Joint project between AstraZeneca Gothenburg (Sweden) and the Chair of Scientific Computing for Systems Biology, Faculty of Computer Science, Center for Systems Biology Dresden, TU Dresden.

Motivation

Respiratory viral infections are a major cause of Chronic Obstructive Pulmonary Disease and asthma exacerbations. Exacerbations have a significant impact on morbidity in both diseases and, in their most severe form, can lead to death. Therefore, developing drugs with antiviral properties can potentially decrease morbidity and improve patients' quality of life. The mechanism by which viruses trigger exacerbations is poorly understood. A deeper understanding of the temporal and spatial sequence of events from initial infection to exacerbation is essential for the identification and clinical testing of new therapeutic targets for prevention of viral exacerbations.

Infection of respiratory viruses such as Human Rhinoviruses (HRV) starts from the nose, where viruses find the optimal temperature to replicate. Experimental data suggest that the infection can spread from the upper to the lower part of the respiratory tract (from the nose to the lung). The body responds to the viral infection and employs the host defense mechanism to recruit immune cells to the site of infection. In patients with a dysregulated immune system, immune cells and their secreted signaling molecules (so-called cytokines) may accumulate in the lung and cause deleterious effects such as poor lung function and shortness of breath.

Project Objectives

Part 1

We would like to develop a theoretical model to simulate the progression of viral infection in time and space based on physiological parameters such as the surface area of the nasal epithelium, the length of trachea and immune system parameters. In this part, the immune system can be modelled as simply as possible to minimize the number of parameters.

Part 2

The next step is to include the kinetics of different immune cells such as cytotoxic T-cells, natural killer cells and their secreted cytokines. The aim is to simulate how quickly immune cells migrate to the site of infection and how the host defense mechanism prevents the infection spread. Such a platform would allow us to demonstrate the impacts of different types of deficiency in the host defense mechanism, as potential models of altered host response in disease.

Qualifications

We are looking for a motivated master or Diploma student with background in mathematics, physics, engineering or computer science, good programming skills, interest in medical applications, especially in immunology, and experience or knowledge of spatiotemporal simulation algorithms.

The successful candidate will have a chance to interact with experts in mathematical modeling, pharmacokinetics and immunology from the Center for Systems Biology Dresden and AstraZeneca. This joint project with AstraZeneca includes travels to Gothenburg, Sweden, for meetings.

About the Industry Partner AstraZeneca

At AstraZeneca, we discover, develop, manufacture and market small molecules and biologics focused on three key areas – oncology; cardiovascular and metabolic diseases; and respiratory, inflammation and autoimmunity. At AstraZeneca, we believe that the best way we can help patients is to push the boundaries of science. We uncover the ways diseases work and then discover new, targeted medicines that can change lives. Whether you're a scientist, a subject expert or a professional, when you join AstraZeneca, you'll help us to develop life-changing medicines that will make a difference to millions of lives.

References

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They applied reaction-diffusion equations with a delay to show different regimes of infection spreading.

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Presents a crowd-sourcing software framework for computer simulations of viral spread in respiratory tissues and applies it to different viruses.

[5] A. Yakimovich, H. Gumpert, C. J. Burckhardt, V. A. Lütschg, A. Jurgeit, I. F. Sbalzarini, and U. F. Greber. Cell-free transmission of human adenovirus by passive mass transfer in cell culture simulated in a computer model. J. Virol., 86(18):10123–10137, 2012.

Presents a spatiotemporal simulation framework for virus spread in tissues based on particle methods and multi-scale modeling.