Modeling virus-host interaction during viral infection of a single cells

Viruses are intracellular parasites, which need cellular components to replicate. While many individual interactions between an infecting virus and cellular host factors have been identified, their all-over complex interplay in terms of dynamics and outcomes are not well understood. The aim of this project is to generate mathematical models, which enable obtaining a quantitative understanding of the outcomes of virus – host factor interactions with respect to virus production per an infected cell. This outcome will potentially allow to identify the step in the virus life cycle, which has the biggest impact in virus expansion, and thus define the best target for antiviral drug interventions (antiviral therapy). Another goal of this project is motivated by the fact that multiple infections of a single cell can lead to reshuffling of viral genomes with the concomitant production of recombinant viral progeny. In this project mathematical modeling shall also be applied to answer fundamental questions about the dynamics of variant generation under different single cell infection conditions.

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Dynamic properties of immune cell populations in response to viral infections

The adaptive immune response is a very efficient mechanism of the body defence again a microbial infection, and the proliferation of lymphocytes, which follows an infection and activation of the immune response, is its key component. Existing experimental methods allow labeling cells using fluorescent dyes and then following the proliferation of these cells by dye dilution with flow cytometry. However, the underlying dynamic properties and mechanisms of the proliferation to a large extend remains a mystery and a major challenge for immunologists. The aim of this project is to develop mathematical tools that enable reliable estimation of fundamental proliferation parameters, such as proliferation rates, death rates and time to first division, and relate those to different outcomes of real-life viral infections.

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Viral evolution and immune responses

Microbial mutation and evolution is probably the most significant single factor accountable for emergence of pathogens and drug-resistant strains, and preventing the development of effective drugs and vaccines. A particular question which this project shall address is about the role of immune selection pressure generated via a number of mechanisms such as neutralizing antibodies or cytotoxic T lymphocytes in natural selection and viral evolution. Another related question is whether and how HIV variation is linked to the development of AIDS. Answering these questions will allow us to better predict the long-term spread of drug resistance and CTL-escape mutations, as well as the likely impact of vaccination. Accordingly, our goal is to develop mathematical models of viral evolution which include immune response and antiviral therapy and which enables us to address these question.

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Virus-induced modulation of cytokine signalling

Cytokine signalling is one of the main effectors of the immune response in our bodies, and as such it serves as the basis for a wide range of therapies against a variety of diseases, by either activating or inhibiting the immune system. An important example of such a disease and a therapy is the use of immune-suppressive drugs, which is used to fight autoimmune disorders such as multiple sclerosis. A common treatment of multiple sclerosis is based on the cytokine known as interferon beta, which activates among others the Jak/Stat pathway. The goal of this project is to examine, by means of a combination of mathematical modelling and experimental studies, how the presence of viral species, such as the Epstein-Barr virus, affects the response of the Jak/Stat pathway to interferon beta, with the goal of shedding light on the large variability observed in the effectivity of that therapy among multiple sclerosis patients.

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