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A mathematical model for coupling within-host and between-host dynamics in an environmentally-driven infectious disease

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ABSTRACT

This work presents a new model for the linking of within- and between-host dynamics. We use this as a conceptual model for the dynamics of *Toxoplasma gondii*, in which the parasite's life cycle includes interactions with the environment. We postulate the infection process to depend on the size of the infective inoculum that susceptible hosts may acquire by interacting with a contaminated environment. Because the dynamical processes associated with the within- and between-host occur on different time scales, the model behaviors can be analyzed by using a singular perturbation argument, which allows us to decouple the full model by separating the fast- and slow-systems. We define new reproductive numbers for the within-host and between host dynamics for both the isolated systems and the coupled system. Particularly, the reproduction number for the between-host (slow) system dependent on the parameters associated with the within-host (fast) system in a very natural way. We show that these reproduction numbers determine the stability of the infection-free and the endemic equilibrium points. Our model may present a so-called backward bifurcation.

1. Introduction

For most infectious diseases there are two key processes in the host-parasite interaction. One is the epidemiological process associated with the disease transmission, and the other is the immunological process at the individual host level. Viral dynamic models (e.g., [1,3,7,11]) consider the within-host dynamics independent of the interaction at the population level, whereas epidemiological models of population dynamics (e.g., [1,9] and references therein) consider the interaction between susceptible and infected hosts without an explicit link to the viral dynamics within the hosts. There are, however, questions that can only be studied by using models that explicitly link the two processes. Such questions include: (i) How does the within-host dynamics influence the transmission of a pathogen from individual to individual? (ii) What is the effect of population dynamics of disease transmission on the viral dynamics at the individual level? (iii) Will the model predictions in terms of the virulence and basic reproduction number of the pathogen be altered if the two process are dynamically linked [5]? Gilchrist and Sasakiz [6] have used a nested model to evaluate the direction of natural selection (in the study of evolution of virulence) at the within- and between-host levels. In this nested model, the within-host system is independent of the transmission dynamics at the population level.

In this paper, we propose a framework that explicitly links the epidemiological and immunological dynamics through an environmental compartment. Our approach is based on the idea of separating biological time scales, a fast time scale associated with the within-host dynamics, an intermediate time scale associated with the epidemiological process, and a slow time scale associated with the environment. In a simpler case the processes associated with epidemiology and environment can be merged. We demonstrate our framework by using as a simplified model system for the infection by *Toxoplasma gondii*. *Toxoplasma* is an infectious disease for which contamination of the environment plays a major and determinant role in transmission. One of the advantages of this modeling approach (relative to other approaches for modeling within-host between-host transmission processes) is that the explicit linkage between the two processes can be established through environmental contamination, and it allows to postulate an 'inoculum' size related to the degree of infectiousness of the contaminated environment. To the best of our knowledge, all existing models that attempt to couple immunological and epidemiological dynamics confront the difficult and controversial question as to how to model the influence of the epidemiological dynamics on the within-host cellular infection. We propose, as a first step in that direction, the study of infectious diseases where the environmental component is important.

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