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Coupled within-host and between-host dynamics and evolution of virulence

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ABSTRACT

Mathematical models coupling within- and between-host dynamics can be helpful for deriving trade-off functions between disease transmission and virulence at the population level. Such functions have been used to study the evolution of virulence and to explore the possibility of a conflict between natural selection at individual and population levels for directly transmitted diseases (Gilchrist and Coombs, 2006). In this paper, a new coupled model for environmentally-driven diseases is analyzed to study similar biological questions. It extends the model in Cen et al. (2014) and Feng et al. (2013) by including the disease-induced host mortality. It is shown that the extended model exhibits similar dynamical behaviors including the possible occurrence of a backward bifurcation. It is also shown that the within-host pathogen load and the disease prevalence at the positive stable equilibrium are increasing functions of the within- and between-host reproduction numbers ($\mathcal{R}_{w0}$ and $\mathcal{R}_{b0}$), respectively. Optimal parasite strategies will maximize these reproduction numbers at the two levels, and a conflict may exist between the two levels. Our results highlight the role of inter-dependence of variables and parameters in the fast and slow systems for persistence of infections and evolution of pathogens in an environmentally-driven disease. Our results also demonstrate the importance of incorporating explicit links of the within- and between-host dynamics into the computation of threshold conditions for disease control.

1. Introduction

It has been shown that models that couple the disease dynamics at the population level and the cell-pathogen dynamics within hosts can generate new insights into host-pathogen interactions (e.g., [1,7,8,10–12,15]). Gilchrist and Coombs demonstrated in [11] that nested models can be used to derive the functional relationships between disease transmission and virulence at the population level, and these functions are helpful for studying the evolution of virulence. Particularly, based on the assumptions about the dependence of between-host transmission and disease-induced host mortality on the within-host variables (e.g., pathogen load and cell density), they illustrated the possible occurrence of a conflict between natural selection at the individual and population levels.

The examples considered in [11] also provide specific functional forms for describing the trade-off relationships between disease transmission and pathogen virulence. In one of their examples, the disease transmission rate at the population level β is assumed to be a power function of the within-host pathogen load V, i.e.,

$$\beta(V) = a_1 V^z, \quad z > 0, \tag{1}$$

where a_1 is a positive constant, while the disease-induced host mortality (virulence) α is assumed to be a function of the average density of target cells T within a host given by

$$\alpha(T) = a_2\left(\frac{1}{T} - \frac{1}{T_0}\right), \tag{2}$$

where T_0 is the density of target cells at the infection-free steady state and a_2 is a positive constant. Under the assumption that the within-host dynamics occur on a much faster time scale than the between-host dynamics, the variables V in Eq. (1) and T in Eq. (2) can be replaced by their values at the positive steady state, which leads to the following relationship between α and β:

$$\beta(\alpha) = a_1\left(\frac{\Lambda\alpha}{a_2 k}\right)^z, \tag{3}$$

where Λ and k are parameters associated with the within-host system. Because the qualitative behavior of the function in Eq. (3) can be

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