

Modelling the host-pathogen interactions of macrophages and *Candida albicans* using Game Theory and dynamic optimization

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Abstract

The release of fungal cells subsequent to macrophage phagocytosis, called non-lytic expulsion, is reported for several fungal pathogens. On one side non-lytic expulsion may benefit the fungus in escaping the microbicidal environment of the phagosome. On the other side the macrophage could profit in terms of avoiding its own lysis and being able to undergo proliferation. To analyse the causes of non-lytic expulsion and the relevance of macrophage proliferation in the macrophage - *C. albicans* interaction, we employ Evolutionary Game Theory and dynamic optimisation in a sequential manner. We establish a game-theoretical model describing the different strategies of the two players after phagocytosis. Depending on the parameter values we find four different Nash equilibria and determine the influence of the systems state of the host upon the game. As our Nash equilibria are a direct consequence of the model parameterisation we can depict several biological scenarios. A parameter region, where the host response is robust against the fungal infection is determined. We further apply dynamic optimisation to analyse whether macrophage mitosis is relevant in the host-pathogen interaction of macrophages and *C. albicans*. For this, we study the population dynamics of the macrophage - *C. albicans* interactions and the corresponding optimal controls for the macrophages, indicating the best macrophage strategy of switching from proliferation to attacking fungal cells.