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Severe First and Mild Later: Temporal Strategies in Pathogen Evolution

Because pathogens replicate within hosts and transmit between them, selection takes place on multiple levels. There has been ongoing interest for more than two decades in trying to understand the conditions favoring the evolution of acute, highly transmissible infections, focusing on trade-offs such as the transmissibility-virulence trade-off and the invasion-persistence trade-off. Studies have shown that these types of trade-offs lead to intermediate pathogen attack rates. These earlier studies typically consider the evolution of a single trait under a defined trade-off. However, for some pathogens, the course of infection within the host is likely to be more complex, determined by more than a single dimension, opening the door for more complicated strategies related to disease severity. The protozoa *Plasmodium falciparum* (Pf), which causes the most severe type of malaria in humans, is one example of such a pathogen. During the course of an infection, Pf has the ability to express up to 60 different variants of surface proteins (PfEMP1) encoded by a family of var genes, which are recognized by the host immune system and which also act as virulence factors.

In this talk we examine the role of temporal variation of life history traits during the course of an infection, and we ask whether the addition of a temporal dimension can assist in reducing the burden arising from multiple selective pressures. We allow the life history traits of different stages to evolve independently, and as a case study, we assume there is a trade-off between transmission and duration. To capture multiple selective pressures acting on the parasite, we consider invasion persistence trade-offs in terms of critical community size of hosts. We demonstrate that a composite strategy that is ordered in time and consists of a more transmissible stage at first, followed by a less transmissible one later, confers a higher fitness than any single, constant, strategy. These results are relevant to ordered expression in *P. falciparum* of severe vs. mild var genes, as well as for acute infections that are followed by milder symptoms in some bacterial pathogens.