Dynamics of Virus and Immune Response in Multi-Epitope Network

The host immune response can often efficiently suppress a virus infection, which may lead to selection for immune-resistant viral variants within the host. For example, during HIV infection, an array of CTL immune response populations recognize specific epitopes (viral proteins) presented on the surface of infected cells to effectively mediate their killing. However HIV can rapidly evolve resistance to CTL attack at different epitopes, inducing a dynamic network of interacting viral and immune response variants. We consider models for the network of virus and immune response populations, consisting of Lotka-Volterra-like systems of ordinary differential equations. Stability of feasible equilibria and corresponding uniform persistence of distinct variants are characterized via a Lyapunov function. We specialize the model to a ``binary sequence'' setting, where for $n$ epitopes there can be $2^n$ distinct viral variants mapped on a hypercube graph. The dynamics in several cases are analyzed and sharp polychotomies are derived characterizing persistent variants. In particular, we prove that if the viral fitness costs for gaining resistance to each epitope are equal, then the system of $2^n$ virus strains converges to a ``perfectly nested network'' with less than or equal to $n+1$ persistent virus strains. Overall, our results suggest that immunodominance, i.e. relative strength of immune response to an epitope, is the most important factor determining the persistent network structure.

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