Host-based Viral Evolution and Mutation

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***Short Abstract* — We discuss our model of viral-host interaction, and the dynamics that is induced by the multiple forces acting on the virus in that system. Cell permissivity and system immune response result in two opposing strategies for viruses, the former which requires a high "match" to the cells for infection, and the latter which then more easily recognizes the virus from past infections. These cell-based interactions, together with the other forces on viral population, give rise to a rich phase diagram. We find a first-order phase transition with three main phases, dividing three viral infection modes (acute, chronic, and opportunistic).**

***Keywords* — Viruses, dynamics, mutation, evolution, quasispecies, infection, therapeutics**

I. INTRODUCTION

We use computational modeling [1,2] to study within-host viral infection and evolution. In our model, viruses exhibit variable binding to cells, with better infection and replication countered by a stronger immune response and a high rate of mutation. By varying host conditions (permissivity to viral entry and immune clearance intensity) for large numbers of cells and viruses, we study the dynamics of how viral populations evolve from initial infection to steady state and obtain a phase diagram of the range of cell and viral responses. The opposing dynamics in this model gives rise to a rich phase diagram.

II. RESULTS

We find a first-order phase transition as a function of increasing cell permissivity at fixed immunity, featuring bi-modal quasispecies distributions at the phase boundary. In addition, we find a cross-over region and higher-order transitions in other areas of phase space as a function of varying immunity at fixed cell permissivity. These phase transitions delineate three main phases, with an order parameter corresponding to the match of virus to cell. We calculate the evolution of the viral load inside and outside cells, as well as the mutation of the viral quasispecies distribution, both as a function of time.

The dynamics reveals two time scales of viral infection in our model, one portraying fast onset and the other of varying length to steady state. We find three distinct replicative strategies corresponding to three physiological classes of viral infections: acute, chronic, and opportunistic. We show similarities between our findings and the behavior of real viral infections such as common flu, hepatitis, and SARS-CoV-2019.

Our simulations also reveal a wide range of physical phenomena, including metastable states, periodicity, and glassy dynamics. Lastly, our results suggest that the resolution of acute viral disease in patients whose immunity cannot be boosted can only be achieved by significant inhibition of viral infection and replication.

With time permitting, we will discuss our modeling of the effects of viral therapeutics on the viral load, with unexpected results for one or more therapeutic types.

III. METHODS & FINAL REMARKS

The cells in our model have a match region of 50 AA, each position being able to take a range of 26 different values. The viruses have a corresponding section 100 AA long, with each position also taking 26 different possible values. The virus tries all possible alignments of virus to cell, and the alignment with maximum match to cell we term the match number for that virus. Given the 26^100 different viruses in our model, a beyond-astronomical number, we are in the thermodynamic limit, and thus a phase transition is not unexpected. It is certainly an emergent property, in that it cannot in any way be predicted from initial conditions.

REFERENCES

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