Frequency of multiply infecting bacteriophage in natural environments exposed by spatial models

Bradford P. Taylor[1], Catherine Penington[2], and Joshua S. Weitz[3,1]

***Short Abstract* — It is generally assumed that multiple infections of microbes by viruses is rare. This assumption stems, in part, from the use of mean field models of virus-microbe population dynamics. Here, we investigate an explicitly spatial model of interactions and assess the frequency of multiple infections given biophysically relevant rates of interaction and movement. We find that multiple infection are significantly more common than in mean field models, and we investigate how such infections can alter ecological dynamics and virus-microbe coexistence.**

***Keywords* — Viruses, Bacteria, Multiple infections, Spatial Models, Multiscale Models**

I. Purpose

Viruses are able to directly interact when coinfecting a host cell. This direction interaction benefits the viruses by allowing recombination leading to quicker adoption of positive mutations in the population [1]. However, coinfection allows direct competition leading to within-host niche specialization by viruses and the emergence of cheaters for shared viral products due to the modular structure of viruses [2]. Investigations of these phenomenon are in vitro settings mediated by high multiplicity of infection (MOI) inoculants. The relevance of coinfection in vivo settings is poorly understood. We address this gap in understanding via simulation. The goal of this project is to quantify the rate and magnitude of multiple infections within a stochastic individual based spatial model (IBSM).

Previously, IBSM have resolved apparent paradoxes in viral ecology such as the tragedy of the commons [3]. In addition, ecological IBSM feature increased ranges of coexistence [3]. These results stem from the spatial correlations between hosts and viruses and the existence of density dependent effects. Meanwhile, experimental effects of coinfection include delayed lysis and altered burst size [4,5]. Hence, coinfection is a phenomenon that affects dynamics across multiple scales. Our approach demonstrates what condition coinfection is amplified or tempered due to multi scaled feedback.

[1]Department of Physics, Georgia Institute of Technology, Atlanta, GA, USA. E-mail: bradfordptaylor@gmail.com

[2]Department of Mathematics, Queensland University of Technology, Queensland, Australia. E-mail: catherine.penington@qut.edu.au

[3]Department of Biology, Georgia Institute of Technology, Atlanta, GA, USA. E-mail: jsweitz@gatech.edu

II. Results

By considering the dynamics of viruses and three classes of hosts (susceptible, infected, and coinfected) in an individual based stochastic spatial model. We consider parameter space corresponding to viral-host dynamics involving in autotrophs marine environments such as prochloroccocus. We demonstrate coinfection occurs frequently across parameter space. In addition we quantify the distribution of MOI across the host population. We show that coinfection occurs frequently and that high intracellular MOI can be achieved even when population level virus to bacteria ratio is low. Spatial correlation between host and virus populations account for this increased level of coinfection as compared to an analogous mean field model. We implicitly model intracellular effects due to coinfection by including parameter dependence on individual MOI. We characterize how altered lysis times and burst sizes affect the rates of coinfection within and coexistence of the virus host populations.

III. Conclusions

Coinfection and its effect on viral-host dynamics phenomenon is inherently multiscaled affecting intracellular decision-making to population level evolution. By demonstrating increased frequency of coinfection in a spatial environment as compared to a mean field model, we argue that modelers and experimentalists alike should consider multiple infections a more common phenomenon.

References

[1] Turner PE, Chao L (1998) Sex and the Evolutuion of Intrahost Competition in RNA Virus phi6. *Genetics*. **150** 2 523-532

[2] Huang AS (1973) Defective Interfering Viruses *Annu. Rev. Microbiol*. 27:101-118

[3] Heilmann S, Sneppen K, Krishna S (2012) Coexistence of phage and bacteria on the boundary of self-organized refuges. *PNAS* **109**. 12828-12833.

[4] Bode W (1967) Lysis inhibition in *Escerichia coli* infected with bacteriophage T4. *J. Virol.* **1**(5) 948-955

[5] Gadagkar R, Gopinathan KP (1980) Bacteriophage burst size during multiple infections. *J Biosci*. **2** 3 253-259