# Spatiotemporal dynamics of phage-biofilm interactions

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Short Abstract— Bacteriophage ('phage') - viruses that infect and lyse bacteria - can be deployed therapeutically to treat infections caused by bacterial pathogens. However most reported studies of the therapeutic potential of phage neglect the spatial heterogeneity in bacterial communities, e.g., in microcolonies and biofilms. Here, we present experiments, theory, and simulations that investigate the spatiotemporal dynamics arising from interactions between P. aeruginosa and phage. Time-dependent high resolution confocal imaging is used to examine how phage propagate through spatial domains of bacteria. Together with a three dimensional multi-scale modeling approach, our results shed light on how phage shape the emergence and collapse of microcolonies and biofilms.

Keywords— Biofilm, Bacteriophage, Phage therapy, Antibiotic resistance, Pseudomonas aeruginosa, Pattern formation

## I. INTRODUCTION

Bacteriophages are ubiquitous in natural systems and provide an alternate cure for infections caused by antibiotic-resistant strains of bacteria. Infections in cystic fibrosis and wound patients often contain clusters of bacteria which secrete a protective exopolymeric substance creating a biofilm-like environment [1]. Though the non-linear population dynamics between planktonic bacteria and phage is well studied, the interactions between phages and spatially organized bacterial aggregations are underexplored. Mean-field dynamics need not recapitulate spatial dynamics, particularly given that local aggregates modulate the strength of phage diffusivity [2], latent period of phage incubation, and other physiological properties of bacteria. Therefore, it is essential to understand the emergent spatial structure and reorganization of bacteria in biofilms in the presence of phage in order to better understand the therapeutic potential of phages [3].

## II. RESULTS

Using fluorescent strains of Pseudomonas aeruginosa and its phage PeV2 as model organisms, we observe their spatial evolution through spinning disk confocal microscopy. We quantify the characteristics of the biofilm such as density, volume of live and dead bacteria, size and abundance of bacterial clusters and zones of bacterial elimination, and typical inter-cluster distances through the evaluation of pair-correlation function. We compare these findings with the results of our simulation of bacteria-phage dynamics, based on an individual-based molecular dynamics framework.

## III. CONCLUSION

Through theory, experiments, and simulation, we investigate the nature of interactions in phage-biofilm systems. The complex non-linear population dynamics gives rise to various emergent spatial patterns which is dependent on the initial conditions of phage exposure.

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