The Evolution of a ‘Tragedy of the Commons’ in a Host-Pathogen Metapopulation

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Abstract
Recent studies have suggested that the manner in which hosts of disease-causing organisms move and interact can have profound consequences on the success and evolutionary trajectory of the disease itself. As we use a model host-pathogen system to address the role of such ‘population dynamics’ in determining the outcome of evolutionary outcomes. We describe an experimental system in which interactions between bacterial hosts (Escherichia coli) and their viral pathogen is T4 coliphage (Fig 1). The bacterial host is Escherichia coli and its viral pathogen is T4 coliphage. From knowledge of how isolated populations of bacteria and phage coexist we construct a theoretical framework for explaining how metapopulations (collections of many populations linked by occasional migration) behave. Theoretical predictions are then tested experimentally with metapopulations of bacteria and bacteriophage. The experiments (described below) embed this host-pathogen system inside 96-well microtiter plates, yielding a metapopulation structure for the host-pathogen system.

Introduction
Bacteria and viruses are usually thought of as being completely isolated from one another, and the interactions between them are thought of as being completely independent. However, in nature both bacteria and viruses are frequently found living in close proximity to one another. This close proximity allows for the exchange of genetic material between the two groups, which can have important consequences for the evolution of both groups. Theoretical predictions are then tested experimentally with metapopulations of bacteria and bacteriophage. The experiments (described below) embed this host-pathogen system inside 96-well microtiter plates, yielding a metapopulation structure for the host-pathogen system.

Metapopulation Modeling
We can characterize the state of a microtiter well as being to a set of two states (uninfected or infected with bacteriophage). By performing dilutions and migrations, we empirically determine the transition matrix for our well model (Table 1). We use this matrix to run lattice-based simulations of metapopulations. Our simulations predict coexistence in the metapopulation (Fig 2a). Wells exhibit a kind of ‘rock-paper-scissors’ dynamics: Migration is limited by bacterial density (bacterial movement), and this bacterial movement in turn limits the viral progeny. The host cell lysis) of our evolved phage isolates. We placed each isolate in a common reservoir, thoroughly mixed, and redistributed into a fresh set of wells. The dynamics with spatially restricted migration are more stable than with no migration event (i.e., straight dilution of a focal population). The restricted migration favors prudent pathogens. We believe that there are potential consequences of this work to the evolution of resistance in disease systems, prudent prediction in predator-prey systems, and the evolution of cooperation more generally.

Hypotheses
We tested these theoretical predictions using experiments involving the experimental evolution of interacting species in large relatively small networks. The experiments (described below) embed this host-pathogen system inside 96-well microtiter plates, yielding a metapopulation structure for the host-pathogen system. We find that the bacteria and virus cannot coexist within a single well and therefore prolonged ecological coexistence at the metapopulation scale must rely on extinction in some of the subpopulations and continual colonization through migration.

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Evolutionary Model
We next investigated the latent period (the time from phage adsorption to host cell lysis) of our evolved phage isolates. We placed each isolate in a common reservoir, thoroughly mixed, and redistributed into a fresh set of wells. The dynamics with spatially restricted migration are more stable than with no migration event (i.e., straight dilution of a focal population). The restricted migration favors prudent pathogens. We believe that there are potential consequences of this work to the evolution of resistance in disease systems, prudent prediction in predator-prey systems, and the evolution of cooperation more generally.

Potential Mechanisms
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Conclusions
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Acknowledgments
P3, P1, and P2 are common "marked" phage strains, Fig 6b). At each MOI, phage from the Unrestricted treatment (Fig 6a). Hence, evolution in the failure of hypothesis 3. Rapacious phage fail better in the Unrestricted treatment because: (1) the increased probability of reaching fresh hosts results the likelihood of extinction (1) and (2) the increased probability of mixing types favors the competitive. In the Restricted treatment, wells of the less productive rapacious type "burn out" before spreading very far and prudent type persist for a longer period (Fig 7).

Figure 1: A diagram of an Escherichia coli bacteriophage. The blue, yellow, and red shading indicate the different regions of the bacterium and virus. The purple layer represents the DNA. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage.

Table 1: The Viable Matrix. All entries in rows and columns give the identity of the state of the source well of the metapopulation at time step t and the identity of the state of the destination well of the metapopulation at time step t+1. The values in the matrix are the probabilities of migration between the two states. The matrix is a transition matrix for our well model (Table 1).

Figure 2: A diagram of an Escherichia coli bacteriophage. The blue, yellow, and red shading indicate the different regions of the bacterium and virus. The purple layer represents the DNA. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage.

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Figure 3: A diagram of an Escherichia coli bacteriophage. The blue, yellow, and red shading indicate the different regions of the bacterium and virus. The purple layer represents the DNA. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage.

Figure 4: A diagram of an Escherichia coli bacteriophage. The blue, yellow, and red shading indicate the different regions of the bacterium and virus. The purple layer represents the DNA. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage.

Figure 5: A diagram of an Escherichia coli bacteriophage. The blue, yellow, and red shading indicate the different regions of the bacterium and virus. The purple layer represents the DNA. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage.

Figure 6: A diagram of an Escherichia coli bacteriophage. The blue, yellow, and red shading indicate the different regions of the bacterium and virus. The purple layer represents the DNA. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage.

Figure 7: A diagram of an Escherichia coli bacteriophage. The blue, yellow, and red shading indicate the different regions of the bacterium and virus. The purple layer represents the DNA. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage.

Figure 8: A diagram of an Escherichia coli bacteriophage. The blue, yellow, and red shading indicate the different regions of the bacterium and virus. The purple layer represents the DNA. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage.

Figure 9: A diagram of an Escherichia coli bacteriophage. The blue, yellow, and red shading indicate the different regions of the bacterium and virus. The purple layer represents the DNA. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage. The black square represents the 'body' of the bacteriophage. The yellow layer represents the prdutent phage, while the red layer represents the rapacious phage.