

Persistence for “Kill the Winner” and Nested Infection Lotka-Volterra Models

by

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ABSTRACT

In recent decades, marine ecologists have conducted extensive field work and experiments to understand the interactions between bacteria and bacteriophage (phage) in marine environments. This dissertation provides a detailed rigorous framework for gaining deeper insight into these interactions. Specific features of the dissertation include the design of a new deterministic Lotka-Volterra model with $n + 1$ bacteria, $n/n + 1$ phage, with explicit nutrient, where the j^{th} phage strain infects the first j bacterial strains, a perfectly nested infection network (NIN). This system is subject to trade-off conditions on the life-history traits of both bacteria and phage given in an earlier study Jover *et al.* (2013). Sufficient conditions are provided to show that a bacteria-phage community of arbitrary size with NIN can arise through the succession of permanent subcommunities, by the successive addition of one new population. Using uniform persistence theory, this entire community is shown to be permanent (uniformly persistent), meaning that all populations ultimately survive.

It is shown that a modified version of the original NIN Lotka-Volterra model with implicit nutrient considered by Jover *et al.* (2013) is permanent. A new one-to-one infection network (OIN) is also considered where each bacterium is infected by only one phage, and that phage infects only that bacterium. This model does not use the trade-offs on phage infection range, and bacterium resistance to phage. The OIN model is shown to be permanent, and using Lyapunov function theory, coupled with LaSalle's Invariance Principle, the unique coexistence equilibrium associated with the NIN is globally asymptotically stable provided that the inter- and intra-specific bacterial competition coefficients are equal across all bacteria.

Finally, the OIN model is extended to a "Kill the Winner" (KtW) Lotka-Volterra model of marine communities consisting of bacteria, phage, and zooplankton. The zooplankton acts as a super bacteriophage, which infects all bacteria. This model is shown to be permanent.

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Chapter 1

INTRODUCTION

Bacteriophage are the most populous viruses in the world, and infect bacteria. This interaction plays an important role in ecosystems and in the evolution of bacteria, and is critical for treating many bacterial diseases. What makes bacteriophage so important is that they are usually harmless to both the host that they reside in, and most other (beneficial) bacteria. Currently, their most common use in humans is to treating food poisoning bacteria. As more and more viruses seem to be developing antibiotic resistance, there has been a renewed interest in phage therapy. There are over 10^{31} estimated bacteriophage and the densest location in which they are found is sea water. Getting large data sets for the interactions between bacteria and bacteriophage is expensive and time consuming, and there were no large data sets collected until Moebus and Nattkemper (1981) produced the largest known phage-bacteria infection data set, with 774 bacteria and 298 phage strains from 48 stations across the Atlantic Ocean. They used Phage-host cross-reaction tests to determine the interactions between bacteria and bacteriophage. This was, by far, the largest data set at the time, but it was just a large chart of interactions with organization based on which station the sample was taken. Flores *et al.* (2013) analyzed the data set and came up with a unique subset of 286 bacteria strains and 215 phage strains, with 38 disjoint components. The subset was created by first removing all of the bacteria that had no phage interactions, and then removing what looked to be the same bacteria or phage sampled at different stations. They called this new data set, the MN matrix, which now organized the bacteria and phage by their infection networks and cut into blocks/modules to represent related bacteria/phage. These blocks, when analyzed, were shown to have both partially nested and perfectly nested infection networks (NIN) within the modules of the components.

Now with the data in much smaller and easier-to-manage modules, Jover *et al.* (2013) started with a Lotka-Volterra model to model the nested infection network. His model incorporated both that bacterial growth rates decrease with increasing defense against infection, and that efficiency of viral infection decreases with host range. He hypothesized that if there exists a positive equilibrium with all populations present, and that all boundary equilibrium are unstable to invasion by at least one population, then the system itself would be permanent. The definition of persistence is the following: The system is said to be permanent (persistent) if there exists some positive threshold, independent of initial data for which all populations are present, such that each population exceeds that tolerance for all large times. We use permanence and persistence interchangeably. The famous example of a three-species competition described by May and Leonard (1975) shows the trade-offs mentioned above are not sufficient for permanence.

Chao *et al.* (1977) showed that starting with a single bacterium (specifically *escherichia coli*) and bacteriophage (specifically virulent virus T7), a mutation can occur in the bacterium, making a new bacterium that is immune to the bacteriophage. In this new system, the bacteriophage can mutate into a new bacteriophage that now infects the original bacterium and the mutated bacterium. In this new system, the most recently created bacterium can mutate into a new bacterium which is immune to both the original bacteriophage and the mutated bacteriophage. This process can continue indefinitely, producing a family of nested infection networks, where the number of bacteria is equal to the number of bacteriophage, or the number of bacteria is one more than the number of bacteriophage. This process shows how the infection network that Jover *et al.* (2013) found from the Moebius and Nattkemper (1981) data can be formed naturally in the environment. Therefore, the goal is not simply to show that a specific nested infection network is permanent, but to show

that the entire family of infection networks is permanent. Chao *et al.* (1977) further showed that the newer (and more resistant) bacteria were inferior competitors, relative to their more susceptible counterparts, which is one of the trade-off conditions Jover *et al.* (2013) used in all of the NIN systems.

Wolkowicz (1989) showed that, for a Lotka-Volterra based infection network where each competitor species could be predated on by multiple predator species, there were only two different types of equilibria; one where each nonzero concentration competitor species is predated on by exactly one nonzero concentration predator species, and another where each competitor species with nonzero concentration, except the one with the largest relative break-even concentration which has no nonzero concentration predator predated on it, is predated on by exactly one nonzero concentration predator species. Furthermore, if there were n nonzero concentration competitor species at equilibrium, then they would be the first n competitor species, and if there were only two populations of each species then the coexistence equilibrium is the only solution. Butler and Wolkowicz (1987) showed that, for the case of $n = 3$, if j competitors persisted, they would similarly be the first j . This is exactly how the equilibria in both the NIN and OIN behave (and this work was done prior to this dissertation). Furthermore, Wolkowicz (1989) used a Lyapunov function to establish the asymptotic stability of the system considered, and in the case where there were at most two predator species, showed global asymptotical stability of the coexistence equilibrium. Wolkowicz (1989) even conjectured that the coexistence equilibrium would be globally asymptotically stable even for higher dimensions, but was unable to prove that at the time. The Wolkowicz papers were found after most of the chapters for this dissertation were completed.

In each of the models that will be discussed there is a single nutrient, explicit or implicit depending on model, which is able to support n different bacteria which are predating on the nutrient. Without any bacteriophage, this shouldn't be possible, because of competitive

exclusion, where if you have at least two competitors competing for the exact same resource, in this case nutrient, the competitors cannot stably coexist. In these models without bacteriophage, the bacterium with the largest growth rate, usually the first bacterium, would out compete the other bacterium, and eventually become the winning bacterium, causing all of the other bacterium to go extinct. Even though the bacteriophage are predating on the bacterium, the bacteriophage are helping the bacteria survive due to the bacteriophage helping to kill off/control the growth of any winning bacterium. This dissertation then looks at three different models, one with two infection networks, where the bacteriophage and bacteria interaction does lead to permanence.

Outline of this Dissertation

Chapter 2 of this dissertation addresses the following question: since the trade-off conditions on the life-history traits Jover *et al.* (2013) does not always guarantee persistence, what other trade-offs might be needed to make their system persistent? Since the assumptions are being investigated, it is important to go back to the basics and find the fewest additional requirements possible, to be able to show persistence. In other words, instead of looking at the Lotka-Volterra model, consider a chemostat model, that uses the trade-offs from the Lotka-Volterra model. The resulting model monitors the dynamics of a community of bacteria and bacteriophage, where the bacteria compete with each other for nutrient, and the bipartite infection network is perfectly nested. The goal is to see if this model will be persistent on its own, or if it requires additional trade-offs Jover *et al.* (2013) to guarantee persistence. Additionally, inspired by Chao *et al.* (1977), it is also of importance to see if, starting with a single bacterium and bacteriophage, it is possible under mutations of both the bacterium and bacteriophage to end up with a perfected nested system. If it is possible, then it is of importance to see if this entire family of infection networks are themselves permanent. Sufficient conditions are found to have an arbitrary size bacteria-phage

community arise through the succession of permanent subcommunities each with a nested infection networks. This arbitrary size community is shown to be permanent.

Chapter 3 extends the work in Chapter 2 by showing the Lotka-Volterra model by Jover *et al.* (2013) is persistent with one additional requirement. Additionally, for the community of bacteria and bacteriophage, a one-to-one infection network is designed, where each bacteriophage specializes on infecting a unique single host strain, so no two bacteriophage are infecting the same bacteria. The goal is permanence for both infection networks, and once permanence is obtained, the global dynamics for both infection networks. Both infection networks are shown to be permanent, and global dynamics for both infection networks are found. Additionally, in the special case where the perfectly nested Lotka-Volterra model has identical inter- and intra-specific bacterial competition coefficients, the coexistence equilibrium is shown to be globally asymptotically stable.

In Chapter 4, the methodology from the previous two chapters is extended to show permanence for a KtW model based on of the work of Thingstad and Lignell (1997). This model is referred to as a KtW model, because the increased reproduction of any winning bacteria results in increased predation by some virus. The KtW mathematical model for this scenario is a Lotka-Volterra system of equations for bacteria, bacteriophage, and zooplankton, and uses the following assumptions: (1) all microbes compete for a common resource, (2) all microbes, except for one population, are susceptible to virus infection, (3) all microbes are subjected to zooplankton grazing, and (4) viruses infect only a single type of bacteria. The system is shown to be permanent and its global dynamics are established.

Finally Chapter 5 is a concluding chapter summarizing the findings in each of the earlier chapters.

Chapter 2

HOW NESTED INFECTION NETWORKS IN HOST-PHAGE COMMUNITIES COME TO BE

Introduction

We show that a chemostat community of bacteria and bacteriophage in which bacteria compete for a single nutrient and for which the bipartite infection network is perfectly nested is permanent, a.k.a uniformly persistent, provided that bacteria that are superior competitors for nutrient devote the least to defence against infection and the virus that are the most efficient at infecting host have the smallest host range. This confirms earlier work of Jover *et al.* (2013) who raised the issue of whether nested infection networks are permanent. In addition, we provide sufficient conditions that a bacteria-phage community of arbitrary size with nested infection network can arise through a succession of permanent subcommunities each with a nested infection network by the successive addition of one new population.

This work is inspired by the recent paper Jover *et al.* (2013). Noting that empirical studies strongly suggest that the bipartite infection networks observed in bacteria and virus communities tend to have a nested structure characterized by a hierarchy among both host and virus strains which constrains which virus may infect which host, they identify key tradeoffs between competitive ability of the bacteria hosts and defence against infection and, on the part of virus, between virulence and transmissibility versus host range such that a nested infection network can be maintained. They find that “bacterial growth rate should decrease with increasing defence against infection” and that “the efficiency of viral infection should decrease with host range”. Their mathematical analysis of a Lotka-Volterra

model incorporating the above mentioned tradeoffs strongly suggests that the perfectly nested community structure of n -host bacteria and n -virus is permanent, sometimes also called persistent, or uniformly persistent Han and Smith (2012); Smith and Thieme (2011); Thieme (1993). Indeed, they establish several necessary conditions for permanence: (1) a positive equilibrium for the system with all host and virus populations at positive density exists, and (2) every boundary equilibrium of the $2n$ -dimensional ordinary differential equations, where one or more population from the nested structure is missing, is unstable to invasion by at least one of the missing populations. They also note that while equilibrium dynamics are rare for such systems, invasability of boundary equilibria can imply invasability of general boundary dynamics provided permanence holds according to results of Hofbauer and Sigmund (1998). However, permanence of a perfectly nested infection network is not established in Jover *et al.* (2013). The famous example of three-species competition described by May and Leonard (1975) shows that the necessary conditions mentioned above are not sufficient for permanence.

Permanence of bacteriophage and bacteria in a chemostat has been established for mathematical models of very simple communities consisting of a single virus and one or two host bacteria in Smith and Thieme (2012); Han and Smith (2012).

A nested infection network of three bacterial strains and three virus strains has the structure described in the infection table below. An ‘x’ in the matrix means that the host below is infected by the virus on the left while a blank entry indicates no infection; for example, the second column of three x’s indicates that bacteria H_1 is infected by virus V_1, V_2 and V_3 . Host H_1 is the least resistant to infection while H_3 is the most resistant; virus V_1 specializes on a single host while V_3 is a generalist, infecting all host.

V_3	x	x	x
V_2	x	x	
V_1	x		
	H_1	H_2	H_3

This community may have evolved by the sequential addition of one new population following a mutational event or the selection of a rare variant. Below, going back in time, we list in order the communities from which the one above may have evolved from an ancestral community consisting of a single bacteria and a single virus on the right.

V_2	x	x	
V_1	x		
	H_1	H_2	H_3

V_2	x	x
V_1	x	
	H_1	H_2

V_1	x	
	H_1	H_2

V_1	x
	H_1

Other possible evolutionary trajectories starting from the ancestral pair at the bottom are highly unlikely. Obviously, a new virus cannot evolve without there being a susceptible host for it; however, a new bacterial strain resistant, or partially resistant, to some virus may evolve. Obviously, the three-host, three-virus network need not be the end of the evolutionary sequence. A fourth bacterial strain may evolve resistance to all three virus.

Just such a sequence of mutational or selection events is observed in chemostat experiments starting from a single bacteria population and a single virus population and leading to a nested infection network. Chao *et al.* (1977) describe such a scenario in their experimental observations of *E. Coli* and phage *T7*. A bacterial mutant resistant to the virus is observed to evolve first. Resistance is conferred by a mutation affecting a receptor on the host surface to which the virus binds. Subsequently, a viral mutant evolves which is able to infect both bacterial populations. Eventually, another bacterial mutant arises which is resistant to both virus. Similar evolutionary scenarios are noted in the review of Bohannan

and Lenski (2000). Thus, a nested infection structure can evolve as an arms race between host and parasite.

Our goal in this chapter is to show that a nested infection network consisting of n bacterial host and n lytic virus is permanent given the trade-offs identified in Jover *et al.* (2013). Recall that permanence means that there is a positive threshold, independent of positive initial conditions of all populations, which every bacteria and virus density ultimately exceeds.

However, we replace the Lotka-Volterra model used by Jover *et al.* (2013) by a chemostat-based model where bacterial populations compete for nutrient and virus populations compete for hosts as in Chao *et al.* (1977); Han and Smith (2012); Smith and Thieme (2012); Weitz *et al.* (2005), although we ignore latency of virus infection. Aside from the additional realism of including competition for nutrient, our model avoids the non-generic bacterial dynamics of the Lotka-Volterra model which possesses an $n - 1$ -dimensional simplex of virus-free equilibria.

Chemostat-based models of microbial competition for a single nutrient are known to induce a ranking of competitive ability among the microbes determined by their break-even nutrient concentrations for growth, here denoted by λ but often by R^* in the ecological literature. The competitive exclusion principle applies: a single microbial population, the one with smallest λ , drives all others to extinction Tilman (1982); Smith and Waltman (1995) in the absence of virus. In our model of a nested infection network, this host can be infected by every virus strain and as the λ value of host strains increases (i.e., it becomes less competitive for nutrient) it is subject to infection by fewer virus strains. Virus populations are ranked by their efficiency at infecting host. The most efficient strain specializes on the host with smallest λ and as infection efficiency decreases host range increases so that the virus strain of rank k infects the k most competitive host strains.

Our permanence result is a dramatic example of predator-mediated coexistence. In the absence of phage, only a single bacterial strain can survive. However, the addition of an equal number of phage to our microbial community with infection efficiency versus host range tradeoff as noted above lead to the coexistence of all populations.

In fact, we will show that the n -bacteria, n -virus community can arise through a succession of permanent sub-communities just as described in the infection tables above for the case $n = 3$, starting with an ancestral community of one susceptible bacterial host and one virus. This is important because it ensures that the intermediate communities are sufficiently stable so as to persist until a fortuitous mutational or colonization event allows further progression. Permanence is not a guarantee of long term persistence since environmental stochasticity may intervene to cause an extinction event, especially when a population is in a low part of its cycle. See Figure 2.1 below. However, our permanence result implies that should an extinction event occur, the resulting community is likely to be a permanent one and therefore recovery is possible.

We also show that time averages of species densities are asymptotic to appropriate equilibrium levels. Solutions of our chemostat-based model are highly oscillatory, apparently aperiodic, just as those observed for the Lotka-Volterra system of Jover *et al.* (2013). See Figure 2.1.

Perhaps it is interesting to note that the mathematical justification used to establish our results is to exploit the evolutionary sequence noted in the infection tables above by way of the principle of mathematical induction, establishing permanence in a given sub-community in the successional sequence by appealing to the permanence hypothesis of its predecessor in the sequence.

The competitive exclusion principle is critical to our approach. We will show that two virus strains cannot share the same set of bacterial hosts (i.e. cannot have the same host range) since one of the virus will be more efficient at exploiting the host and drive the other

to extinction. Similarly, two bacterial strains cannot suffer infection by the same set of virus because the weaker competitor for nutrient will eventually be excluded. Therefore, the competitive exclusion principle drives the evolution of communities towards a nested infection structure.

As noted in Jover *et al.* (2013), perfectly nested infection networks are generally only observed for very small host-virus communities. Because natural host-virus communities have strong tendency to be approximately nested in their infection structure, it is worthwhile to consider how the idealized nested network may have evolved. Mathematical modeling is especially useful for exploring these idealized scenarios. Furthermore, permanence, or persistence in mathematical models is known to be robust to model perturbations under appropriate conditions Schreiber (2000); Garay and Hofbauer (2003); Hirsch *et al.* (2001) and therefore it should continue to hold for small deviations from a nested infection structure.

A Chemostat-based Host-Virus Model

The standard chemostat model of microbial competition for a single limiting nutrient Smith and Waltman (1995) is modified by adding lytic virus. Our model is a special case of general host-virus models formulated in Chao *et al.* (1977) which include viral latency. Let R denote the nutrient which supports the growth of bacteria strains H_i ; it is supplied at concentration R_0 from the feed. V_i denote the various virus strains that parasitize the bacteria. Bacteria strain H_i is characterized by its specific growth rate $f_i(R)$ and its yield γ_i . For simplicity, we assume that the yield is the same for all bacterial strains: $\gamma_i = \gamma$ is independent of i . At this point, we assume only that the specific growth rates f_i are increasing functions of nutrient R , vanishing when $R = 0$. Following Jover *et al.* (2013), we assume that virus strain V_i is characterized by its adsorption rate ϕ_i and its burst size β_i ,

both of which are assumed to be independent of which host strain it infects. D denotes the dilution rate of the chemostat.

The community of bacterial strains $H_1, H_2, \dots, H_n$ and virus strains $V_1, V_2, \dots, V_n$ is structured as follows. Virus strain V_i parasitizes all host strains H_j for $j \leq i$. Thus, strain V_1 specializes on host H_1 while strain V_n is a generalist, infecting all host strains. As i increases, virus strain V_i becomes more generalist, less of a specialist; the index i is indicative of the number of host strains V_i infects. This structure is referred to as a nested infection network in Jover *et al.* (2013).

Our model is described by the following differential equations:

$$\begin{aligned} R' &= D(R_0 - R) - \sum_i \frac{1}{\gamma} f_i(R) H_i \\ H_i' &= H_i(f_i(R) - D) - H_i \sum_{j \geq i} \phi_j V_j \\ V_i' &= \beta_i \phi_i V_i \sum_{j \leq i} H_j - D V_i, \quad 1 \leq i \leq n. \end{aligned} \tag{2.1}$$

Non-dimensional quantities are identified below:

$$N = R/R_0, \quad B_i = H_i/(\gamma R_0), \quad DP_i = \phi_i V_i, \quad \tau = Dt$$

Again using prime for derivative with respect to τ , we have the equations

$$\begin{aligned} N' &= 1 - N - \sum_i g_i(N) B_i \\ B_i' &= B_i(g_i(N) - 1) - B_i \sum_{j \geq i} P_j \\ P_i' &= s_i^{-1} P_i \left(\sum_{j \leq i} B_j - s_i \right), \quad 1 \leq i \leq n. \end{aligned} \tag{2.2}$$

where

$$s_i = \frac{D}{\beta_i \phi_i \gamma R_0}, \quad g_i(N) = f_i(R_0 N)/D.$$

Now, each virus strain is characterized by a single parameter s_i which reflects its burst size β_i and its adsorption rate ϕ_i . Clearly, smaller s_i translates to stronger ability to exploit the host.

Following Jover *et al.* (2013), we assume that a virus with larger host range (generalist) has weaker ability to exploit its hosts than a specialist virus with small host range:

$$s_1 < s_2 < s_3 < \cdots < s_n \quad (2.3)$$

Assume that the specific growth rate g_i is a strictly increasing function of nutrient concentration and that there exists the break-even nutrient concentration $\lambda_i < 1$ for strain B_i defined by the balance of growth and dilution: $g_i(\lambda_i) = 1$. We assume that the bacterial species are ordered such that

$$0 < \lambda_1 < \lambda_2 < \cdots < \lambda_n < 1. \quad (2.4)$$

This implies that in the absence of virus, B_i dominates B_j if $i < j$ but that each bacteria is viable in the absence of the others. Indeed, classical chemostat theory Smith and Waltman (1995); Tilman (1982) implies that B_1 would eliminate all B_j , $j > 1$ in the absence of the virus. In particular, the superiority rank of a bacterial strain is inversely related to the number of virus strains that infect it. Strain B_1 is the best competitor in virus-free competition for nutrient but it can be infected by all the virus strains, while strain B_n is the worst competitor for nutrient but can be infected only by virus strain P_n .

System (2.2) enjoys the usual chemostat conservation principle, namely that the total nutrient content of bacteria and virus plus free nutrient

$$T = N + \sum_i B_i + \sum_i s_i P_i$$

must come into balance with the input of nutrient:

$$T' = 1 - T.$$

On the exponentially attracting invariant set $T = 1$ we can drop the equation for N from (2.2) and replace N by $1 - \sum_i B_i - \sum_i s_i P_i$.

As a final model simplification, linear specific growth rates $g_i(N) = r_i N$ are used where, by (2.4), we must have

$$1 < r_n < r_{n-1} < \cdots < r_2 < r_1. \quad (2.5)$$

Then $\lambda_i = 1/r_i$. The result is the system with Lotka-Volterra structure

$$\begin{aligned} B'_i &= r_i B_i \left(1 - \frac{1}{r_i} - \sum_i (B_i + s_i P_i) \right) - B_i \sum_{j \geq i} P_j \\ P'_i &= s_i^{-1} P_i \left(\sum_{j \leq i} B_j - s_i \right) \end{aligned} \quad (2.6)$$

$U = \sum_i (B_i + s_i P_i)$ represents the nutrient value of the bacteria and virus. It satisfies

$$U' = W - (1 + W)U, \quad W = \sum_i r_i B_i \quad (2.7)$$

We consider the dynamics of (2.6) on the positively invariant set

$$\Omega = \{(B_1, \dots, B_n, P_1, \dots, P_n) \in \mathbb{R}_+^{2n} : \sum_i (B_i + s_i P_i) \leq 1\} \quad (2.8)$$

Equilibria

It is well-known that in the absence of virus, there are only single-population bacterial equilibria for chemostat systems. See Smith and Waltman (1995). Let $E_i = (1 - \lambda_i)e_i$ denote the equilibrium where host strain B_i is alone. Here, e_i is the unit vector with all components zero except the i th which is one. In the absence of virus, E_1 attracts all solutions with $B_1(0) > 0$.

Next we consider equilibria where all or nearly all host and virus are present.

Proposition 2.0.1. *There exists an equilibrium E^* with B_i and P_i positive for all i if and only if*

$$\frac{r_n}{1 + Q_n} > 1 \quad (2.9)$$

where $Q_1 = r_1 s_1$ and

$$Q_n = s_1(r_1 - r_2) + s_2(r_2 - r_3) + \cdots + s_{n-1}(r_{n-1} - r_n) + s_n r_n, \quad n > 1.$$

In fact,

$$\begin{aligned} B_1^* &= s_1, \quad B_j^* = s_j - s_{j-1}, \quad j > 1, \\ P_j^* &= \frac{r_j - r_{j+1}}{1 + Q_n}, \quad j < n, \quad P_n^* = \frac{r_n}{1 + Q_n} - 1. \end{aligned} \tag{2.10}$$

The positive equilibrium E^* is unique and $\sum_i B_i = s_n$. Summing by parts yields $Q_n = \sum_{i=1}^n r_i B_i^*$.

(2.9) also implies the existence of a unique equilibrium $E^\dagger$ with all components positive except for $P_n = 0$. In fact,

$$\begin{aligned} B_j^\dagger &= B_j^*, \quad 1 \leq j < n, \\ B_n^\dagger &= B_n^* + \left(1 - \frac{1 + Q_n}{r_n}\right), \\ P_j^\dagger &= P_j^* \left(\frac{1 + Q_n}{r_n}\right), \quad j < n, \quad P_n^\dagger = 0. \end{aligned} \tag{2.11}$$

Remark 2.0.2. (2.9) is equivalent to

$$s_1\left(\frac{r_1 - r_2}{r_n}\right) + s_2\left(\frac{r_2 - r_3}{r_n}\right) + \cdots + s_{n-1}\left(\frac{r_{n-1} - r_n}{r_n}\right) + s_n < 1 - 1/r_n, \tag{2.12}$$

implying that $s_n < 1$. To see that (2.5), (2.3), and (2.9) can be satisfied simultaneously, note that if the r_i are chosen satisfying (2.5), then one could choose s_n such that $s_n r_1 < r_n - 1$. This implies that (2.12) holds with all $s_i = s_n$. In order to satisfy (2.3) it suffices to re-choose the s_i , $i < n$, smaller so that (2.3) holds. Then (2.12) will remain valid with the new s_i .

Remark 2.0.3. $Q_n = Q_{n-1} + r_n B_n^*$ which together with (2.5) implies that $\frac{r_k}{1+Q_k} > \frac{r_n}{1+Q_n}$ for $1 \leq k < n$. Therefore, (2.9) implies the existence of a unique family of equilibria E_k^*

with $B_j, P_j = 0$, $j > k$ described by (2.10) but with Q_k replacing Q_n . Another family of equilibria, $E_k^\dagger$, exists with $B_j = 0$, $j > k$ and $P_j = 0$, $j \geq k$ described by (2.11) but with Q_k replacing Q_n .

Remark 2.0.4. Not surprisingly, the density of B_i at the positive equilibrium E^* is less than the density of B_i at its equilibrium E_i . More explicitly, $s_1 < 1 - \frac{1}{r_1}$ and $s_i - s_{i-1} < 1 - \frac{1}{r_i}$, $i > 1$. This can be seen by rewriting (2.12) as $s_1 r_1 + r_2(s_2 - s_1) + \cdots + r_n(s_n - s_{n-1}) < r_n - 1$ and using (2.5). Note also that $P_j^\dagger < P_j^*$, $B_j^\dagger = B_j^*$ for $j < n$ and $B_n^\dagger > B_n^*$.

Remark 2.0.5. Free nutrient levels at E^* and $E^\dagger$ are revealing. At $E^\dagger$, the (scaled) free nutrient level is given by $\lambda_n = 1/r_n$, the same as at E_n where only bacteria strain B_n is present with no virus. At E^* , the nutrient level is greater than at $E^\dagger$. It is given by $\frac{1}{1+Q_n}$, thus the ratio of the nutrient levels is precisely (2.9). Chao et al. (1977) refer to E^* as a “phage-limited” community while $E^\dagger$ is referred to as a “nutrient-limited” one when $k = 1$.

Remark 2.0.6. (2.9) implies that $E^\dagger$ is unstable to invasion by P_n since

$$\frac{s_n P_n'}{P_n}|_{E^\dagger} = (1 - \frac{1 + Q_n}{r_n}) > 0.$$

The additional nutrient level available at $E^\dagger$ facilitates the invasion of the virus P_n .

There are other equilibria. A complete list of them is given below. However, we will not have need of these details.

Lemma 2.0.7. Let E be an equilibrium with at least one $P_i > 0$. Then there exists some k with $1 \leq k \leq n$ such that E has exactly k nonzero virus components and either k or $k + 1$ nonzero bacteria components. Moreover, if we denote by $I = \{i_1, i_2, \dots, i_k\}$ the ordered indices with $P_i > 0 \Leftrightarrow i \in I$, then there exist a set $J = \{j_1, j_2, \dots, j_k\}$ uniquely determined by $B_j > 0$, $j \in J$ and by

$$j_1 \leq i_1 < j_2 \leq i_2 < j_3 \leq i_3 \cdots \leq i_{k-1} < j_k \leq i_k. \quad (2.13)$$

If there are $k + 1$ positive bacterial components, then $i_k < n$ and there exists $j_{k+1} > i_k$ such that $B_{j_{k+1}} > 0$.

Moreover, if (2.9) holds, for every such k and any such ordered set $I = \{i_1, i_2, \dots, i_k\}$ and any corresponding set $J = \{j_1, j_2, \dots, j_k\}$ as in (2.13), there exists a unique equilibrium E where $P_i > 0 \Leftrightarrow i \in I$ and $B_j > 0 \Leftrightarrow j \in J$ having exactly k nonzero virus and k nonzero bacteria.

The only equilibria without any virus present are the $E_i \equiv (1 - 1/r_i)e_i$, $1 \leq i \leq n$ with only $B_i > 0$.

Figure 2.1 provides illuminating simulations of (2.6) for the case $n = 3$. Parameter values are $r_1 = 3.2, r_2 = 3.1, r_3 = 3.0; s_1 = 0.1, s_2 = 0.15, s_3 = 0.2$. For the top row, all initial population densities are given by $B_i(0) = P_i(0) = 0.1$. Observe that free nutrient level is high in this case because P_3 , the dominant virus, keeps B_3 at low density. The bacterial community is "phage limited" in this case. In the second row, initial data are $B_i(0) = 0.1, 1 \leq i \leq 3, P_j(0) = 0.1, j = 1, 2$ and $P_3(0) = 0$. Observe that free nutrient levels are much lower than for the top row because B_3 is free to consume it. The bacterial community is "nutrient limited" in this case. In the third row has initial data are $B_i(0) = P_i(0) = 0.1, 1 \leq i \leq 2$ and $B_3(0) = P_3(0) = 0$.

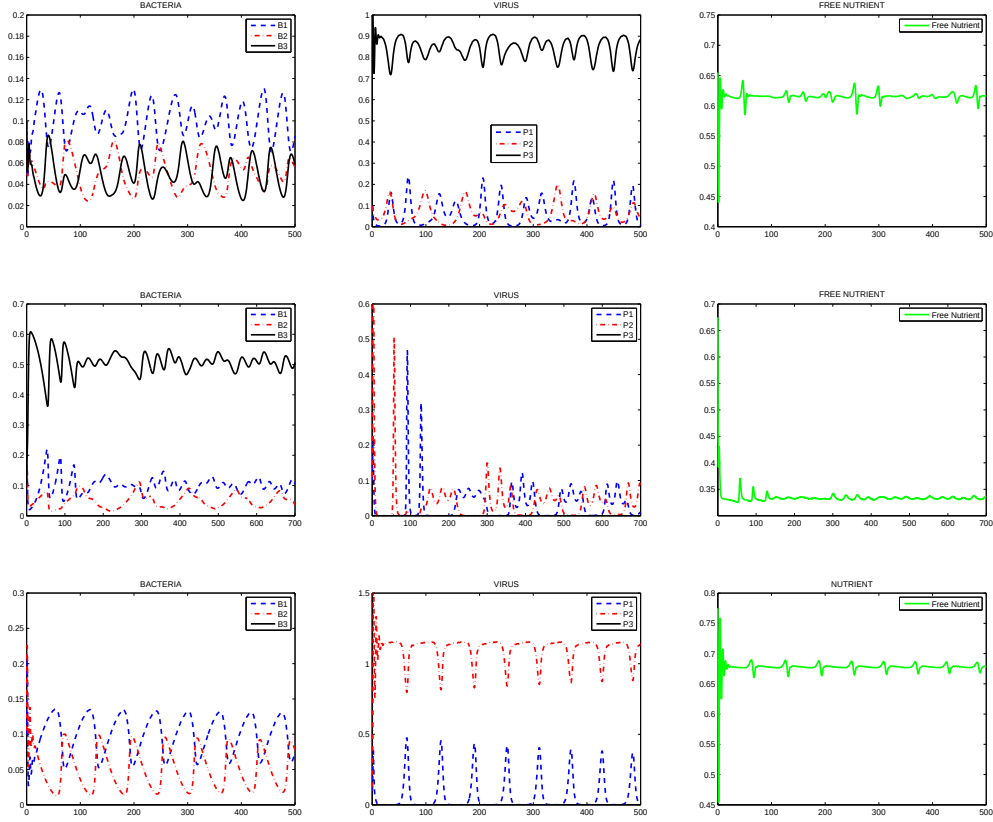


Figure 2.1: Top row: $B_i(0) = P_i(0) = 0.1, 1 \leq i \leq 3$; second row: same except $P_3 \equiv 0$; bottom row, as above except $B_3 = P_3 \equiv 0$.

Permanence

In this section we state and prove our main results, Theorem 2.0.14 and Corollary 2.0.15. We begin by establishing a competitive exclusion principle in the context of our model.

Two virus strains cannot share the same set of host bacterial strains; the weaker virus strain, the one with largest index, is doomed to extinction. This is due to our assumption that each virus strain does not distinguish among the host that it infects in terms of adsorption rate or burst size. Similarly, two bacteria strains cannot share the same set of infecting virus strains; the bacterial strain which is the least competitive for nutrient, the one with largest index, is doomed to extinction. The next result formalizes these conclusions.

Lemma 2.0.8 (Competitive Exclusion Principle). *Let $1 \leq i < j \leq n$.*

If $P_i(0) > 0$, $P_j(0) > 0$ and $B_k(0) = 0$, $i < k \leq j$, then $P_j(t) \rightarrow 0$ as $t \rightarrow \infty$.

If $B_i(0) > 0$, $B_j(0) > 0$ and $P_k(0) = 0$, $i \leq k < j$, then $B_j(t) \rightarrow 0$ as $t \rightarrow \infty$.

Proof. The first assertion follows from Lemma 3.1 Smith and Thieme (2013), applied to the equations for P_i and P_j , where $\kappa_1 = 1/s_i$, $\kappa_2 = 1/s_j$, $h_1(t) = h_2(t) \equiv -1$, and $g(t) = \sum_{k \leq i} B_k(t) = \sum_{k \leq j} B_k(t)$. Note that

$$s_j \int_0^t h_2(s) ds - s_i \int_0^t h_1(s) ds = (s_i - s_j)t \rightarrow -\infty.$$

Hence the result follows from the quoted result since $P_i(t)$ is bounded.

The second assertion also follows from Lemma 3.1, applied to the equations for B_i and B_j , where $\kappa_1 = \kappa_2 = 1$, $g(t) = \sum_{k \geq i} P_k(t) = \sum_{k \geq j} P_k(t)$, and $h_1 = r_i - 1 - r_i U$, $h_2 = r_j - 1 - r_j U$ where $U = \sum_k (B_k + s_k P_k)$. Note that

$$\int_0^t h_2(s) - h_1(s) ds = (r_j - r_i) \int_0^t (1 - U(s)) ds \rightarrow -\infty,$$

where the concluded limit is due to Lemma 2.0.10 and (2.5). □

Remark 2.0.9. *Lemma 2.0.8 strongly constrains the evolution of bacteria and virus communities, at least under our assumption that virus do not distinguish among their host in terms of adsorption rate and burst size. For example if a community consisting of a single virus strain and a single bacterial strain is invaded by a new virus strain then either the resident virus strain or the invader must be driven to extinction. However, our community can be successfully invaded by a new bacterial strain which is resistant to the virus but an inferior competitor for nutrient than the resident.*

Hereafter, we assume without further mention that (2.9) holds.

If $h : (a, \infty) \rightarrow \mathbb{R}$, we write $h_\infty = \liminf_{t \rightarrow \infty} h(t)$ and h^∞ with limit superior in place of limit inferior.

Lemma 2.0.10. *Every solution of (2.6) starting in Ω satisfies*

$$\limsup_{t \rightarrow \infty} U(t) \leq \frac{W^\infty}{1 + W^\infty} \leq \frac{r_1}{1 + r_1} \quad (2.14)$$

where $U = \sum_i (B_i + s_i P_i)$ and $W = \sum_i r_i B_i$ are defined by (2.7).

Proof. Apply the fluctuation lemma, e.g. Prop. A.14 Smith and Thieme (2011), to (2.7) and use (2.5) and the invariance of Ω to conclude that $\sum_j B_j \leq 1$. $\square$

Proposition 2.0.11. *If $P_i(0) > 0$, then $(\sum_{j \leq i} B_j)_\infty \leq s_i$.*

If $B_1(0), P_n(0) > 0$, then

$$\left(\sum_j (r_1 s_j + 1) P_j \right)^\infty \geq r_1 - 1 - r_1 s_n > 0. \quad (2.15)$$

(a) *If $(\sum_{j \leq i} B_j)^\infty < s_i$ then $P_i(t) \rightarrow 0$.*

(b) *If $i < j$, $P_i(0) > 0$, and if $(B_{i+1} + B_{i+2} + \cdots + B_j)^\infty < s_j - s_i$, then $P_j(t) \rightarrow 0$.*

(c) *If $i < j$, $B_i(0) > 0$, and if $(P_i + P_{i+1} + \cdots + P_{j-1})^\infty < \frac{r_i - r_j}{1 + r_1}$, then $B_j(t) \rightarrow 0$.*

Proof. The equation for P_i implies that

$$\frac{d}{dt} \log P_i^{s_i}(t) = \sum_{j \leq i} B_j - s_i.$$

If $(\sum_{j \leq i} B_j)_\infty \leq s_i$ is false, then $P_i(t) \rightarrow \infty$, a contradiction to boundedness of solutions.

Assertion (a) is transparent.

(2.12) implies that $r_n(1 - s_n) - 1 = r_n - 1 - r_n s_n > 0$ and, with (2.3), (2.5) together, imply that $r_1 - 1 - r_1 s_n > 0$. We have

$$\frac{B'_1}{B_1} = r_1 - 1 - r_1 \sum_j B_j - \sum_j (r_1 s_j + 1) P_j$$

and

$$\frac{s_n P'_n}{P_n} = \sum_j B_j - s_n.$$

Multiplying the second expression by r_1 and adding to the first gives

$$\begin{aligned} \frac{d}{dt} \log B_1 P_n^{r_1 s_n} &= \frac{B'_1}{B_1} + \frac{r_1 s_n P'_n}{P_n} \\ &= r_1 - 1 - r_1 s_n - \sum_j (r_1 s_j + 1) P_j \end{aligned}$$

(2.15) follows since the alternative is that $B_1 P_n$ is unbounded, a contradiction.

Proof of (b): if $i < j$, $P_i(0) > 0$, $P_j(0) > 0$, and if $(B_{i+1} + \cdots + B_j)^\infty < s_j - s_i$, then

$$\begin{aligned} \frac{d}{dt} \log \frac{P_i^{s_i}(t)}{P_j^{s_j}(t)} &= \frac{s_i P'_i}{P_i} - \frac{s_j P'_j}{P_j} \\ &= -(B_{i+1} + \cdots + B_j) + s_j - s_i \\ &\geq \epsilon, \quad t \geq T \end{aligned}$$

for some $\epsilon, T > 0$. Therefore, $\frac{P_i^{s_i}(t)}{P_j^{s_j}(t)} \rightarrow \infty$, which implies that $P_j(t) \rightarrow 0$ since $P_i(t)$ is bounded.

proof of (c): assume that $B_i(0) > 0$, $B_j(0) > 0$, and $(P_i + P_{i+1} + \cdots + P_{j-1})^\infty < \frac{r_i - r_j}{1 + r_1}$.

Then, recalling that $U = \sum_k (B_k + s_k P_k)$, we have

$$\begin{aligned} \frac{d}{dt} \log \frac{B_i(t)}{B_j(t)} &= \frac{B'_i}{B_i} - \frac{B'_j}{B_j} \\ &= (r_i - r_j)(1 - U) - (P_i + P_{i+1} + \cdots + P_{j-1}) \\ &\geq (r_i - r_j) \left(\frac{1 - \epsilon}{1 + r_1} \right) - (P_i + P_{i+1} + \cdots + P_{j-1}), \quad t \geq T \end{aligned}$$

where, by (2.14), we can choose $\epsilon > 0$ so small that $(P_i + P_{i+1} + \cdots + P_{j-1})^\infty < (r_i - r_j) \left(\frac{1 - \epsilon}{1 + r_1} \right)$. It follows that $B_i/B_j \rightarrow \infty$ which implies that $B_j(t) \rightarrow 0$.

□

Note that case (b) and (c) of Proposition 2.0.11 extend Lemma 2.0.8.

Proposition 2.0.12. *If $B_1(0) > 0$, then $B_1^\infty \geq s_1$.*

If $B_1(0) > 0$ and $P_1(0) > 0$, then

$$B_1^\infty \geq s_1, \quad P_1^\infty \geq \min\left\{\frac{r_1 - r_2}{1 + r_1}, \frac{r_1 - 1 - r_1 s_1}{r_1 s_1 + 1}\right\}.$$

Proof. Assume the conclusion is false. Then $P_1 \rightarrow 0$ by Proposition 2.0.11 (a). If $P_i(0) = 0$ for all i , then $B_1(t) \rightarrow 1 - 1/r_1 \geq s_1$ by the classical chemostat theory, e.g. Theorem 3.2 in Smith and Waltman (1995), so we suppose that $P_i(0) > 0$ for some i . Let k denote the smallest such integer i for which $P_i(0) > 0$.

If $k = 1$, then, as noted above, $P_1 \rightarrow 0$ and so $B_2 \rightarrow 0$ by Proposition 2.0.11 (c). Then $P_2 \rightarrow 0$ by Proposition 2.0.11 (a) or (b).

If $k = 2$, then $P_1 \equiv 0$ so $B_2 \rightarrow 0$ by Lemma 2.0.8 since B_1 and B_2 share the same virus. Since $(B_1 + B_2)^\infty = B_1^\infty < s_1 < s_2$, it follows that $P_2 \rightarrow 0$ by Proposition 2.0.11 (a). Now we can use Proposition 2.0.11 (c) to show $B_3 \rightarrow 0$ and then Proposition 2.0.11 (a) or (b) to show $P_3 \rightarrow 0$.

If $k > 2$, then $P_1 \equiv P_2 \equiv \dots \equiv P_{k-1} \equiv 0$ and $P_k(0) > 0$. As $B_1, \dots, B_{k-1}$ share the same virus, then $B_i \equiv 0$ or $B_i \rightarrow 0$ for $1 < i \leq k-1$ by Lemma 2.0.8. $B_k \rightarrow 0$ by Proposition 2.0.11 (c). Then, $P_k \rightarrow 0$ by Proposition 2.0.11 (a) since $(\sum_{j \leq k} B_j)^\infty = B_1^\infty < s_1 < s_k$. So $B_{k+1} \rightarrow 0$ by Proposition 2.0.11 (c). Proposition 2.0.11 (a) or (b) implies that $P_{k+1} \rightarrow 0$.

We see that for all values of k , $B_2, \dots, B_{k+1} \rightarrow 0$ and $P_1, \dots, P_{k+1} \rightarrow 0$. Successive additional applications of Proposition 2.0.11 (a) or (b) and (c) then imply that $B_2, \dots, B_n \rightarrow 0$ and $P_1, \dots, P_n \rightarrow 0$. But, then

$$B'_1/(r_1 B_1) \geq 1 - \frac{1}{r_1} - \epsilon - B_1 > s_1 + \epsilon - B_1, \quad t \geq T$$

for some $\epsilon > 0$ and $T > 0$ (recall that $s_1 < 1 - 1/r_1$). This implies that $B_1^\infty > s_1$, a contradiction. This completes the proof of the first assertion.

Now, suppose that $B_1(0) > 0$, $P_1(0) > 0$ and $P_1^\infty < \frac{r_1-r_2}{1+r_1}$. Proposition 2.0.11 (c) implies that $B_2 \rightarrow 0$. By Proposition 2.0.11 (b), $P_2 \rightarrow 0$. Applying Proposition 2.0.11 (c) with $i = 1$ and $j = 3$, as $(P_1 + P_2)^\infty = P_1^\infty < \frac{r_1-r_2}{1+r_1} < \frac{r_1-r_3}{1+r_1}$, we conclude that $B_3 \rightarrow 0$. Then, Proposition 2.0.11 (b) implies that $P_3 \rightarrow 0$. Clearly, we can continue sequential application of Proposition 2.0.11 (b) and (c) to conclude that $B_i, P_i \rightarrow 0$ for $i > 1$. Now, we may argue as in the proof of (2.15)

$$\begin{aligned} \frac{d}{dt} \log B_1 P_1^{r_1 s_1} &= \frac{B_1'}{B_1} + \frac{r_1 s_1 P_1'}{P_1} \\ &= r_1 - 1 - r_1 s_1 - (r_1 s_1 + 1) P_1 - \text{terms that go to zero} \end{aligned}$$

to conclude that $P_1^\infty \geq \frac{r_1-1-r_1 s_1}{1+s_1 r_1}$.

□

The following is a slight modification of Theorem 5.2.3 in Hofbauer and Sigmund (1998).

Lemma 2.0.13. *Let $x(t)$ be a bounded positive solution of the Lotka-Volterra system*

$$x_i' = x_i \left(r_i + \sum_{j=1}^n a_{ij} x_j \right), \quad 1 \leq i \leq n$$

and suppose there exists $k < n$ and $m, M, \delta > 0$ such that $m \leq x_i(t) \leq M$, $1 \leq i \leq k$, $t > 0$, $x_{k+1}(t) \leq \delta$, $t > 0$, and $x_j(t) \rightarrow 0$ for $j > k+1$. Suppose also that the $k \times k$ subsystem obtained by setting $x_j = 0, j > k$ has a unique positive equilibrium $p = (p_1, p_2, \dots, p_k)$. Then

$$\liminf_{T \rightarrow \infty} \frac{1}{T} \int_0^T x_i(t) dt = p_i + O(\delta), \quad 1 \leq i \leq k.$$

The same expression holds for the limit superior.

Proof. As in Hofbauer and Sigmund (1998) Thm 5.2.3, we have that $z_j(T) = \frac{1}{T} \int_0^T x_j(t) dt$ satisfies

$$\frac{\log x_i(T) - \log x_i(0)}{T} = \sum_{i=1}^k a_{ij} (z_j(T) - p_j) + a_{i(k+1)} z_{k+1}(T) + \sum_{j>k+1} a_{ij} z_j(T).$$

for $i = 1, 2, \dots, k$. As $T \rightarrow \infty$, the left hand side converges to zero and so does the final sum on the right since $x_j \rightarrow 0$ for $j > k+1$. The $k \times k$ matrix $\tilde{A} = (a_{ij})_{1 \leq i, j \leq k}$ is invertible by hypothesis so we may write the above in vector form as

$$z(T) = p + (\tilde{A})^{-1}(O(1/T) - z_{k+1}(T)A_{k+1})$$

where $O(1/T) \rightarrow 0$ and A_{k+1} is the first k entries of the $k+1$ column of $A = (a_{ij})_{1 \leq i, j \leq n}$. As $0 \leq z_{k+1} \leq \delta$, it follows that $\|z(T) - p\| \leq c\delta$ for some c and all large T . The result follows. $\square$

Our main result follows.

Theorem 2.0.14. *Let $1 \leq k \leq n$.*

(a) *There exists $\epsilon_k > 0$ such that if $B_i(0) > 0$, $1 \leq i \leq k$ and $P_j(0) > 0$, $1 \leq j \leq k-1$, then*

$$B_{i,\infty} \geq \epsilon_k, \ 1 \leq i \leq k \text{ and } P_{j,\infty} \geq \epsilon_k, \ 1 \leq j \leq k-1.$$

(b) *There exists $\epsilon_k > 0$ such that if $B_i(0) > 0$, $P_i(0) > 0$, $1 \leq i \leq k$, then*

$$B_{i,\infty} \geq \epsilon_k, \ P_{i,\infty} \geq \epsilon_k, \ 1 \leq i \leq k.$$

Proof. We use the notation $[B_i]_t \equiv \frac{1}{t} \int_0^t B_i(s) ds$. Our proof is by mathematical induction using the ordering of the $2n$ cases as follows

$$(a, 1) < (b, 1) < (a, 2) < (b, 2) < \dots < (a, n) < (b, n)$$

where (a, k) denotes case (a) with index k .

The cases $(a, 1)$ and $(b, 1)$ follow immediately from Proposition 2.0.12 and by the general result that weak uniform persistence implies strong uniform persistence under suitable compactness assumptions. See Prop. 1.2 in Thieme (1993) or Corollary 4.8 in Smith and

Thieme (2011) with persistence function $\rho = \min\{B_1, P_1\}$ in case $(b, 1)$. Note that our state space is compact.

For the induction step, assuming that (a, k) holds, we prove that (b, k) holds and assuming that (b, k) holds, we prove that $(a, k + 1)$ holds.

We begin by assuming that (a, k) holds and prove that (b, k) holds. We consider solutions satisfying $B_i(0) > 0, P_i(0) > 0$ for $1 \leq i \leq k$. Note that other components $B_j(0)$ or $P_j(0)$ for $j > k$ may be positive or zero, we make no assumptions. As (a, k) holds, there exists $\epsilon_k > 0$ such that $B_{i,\infty} \geq \epsilon_k, 1 \leq i \leq k$ and $P_{i,\infty} \geq \epsilon_k, 1 \leq i \leq k - 1$. We need only show the existence of $\delta > 0$ such that $P_{k,\infty} \geq \delta$ for every solution with initial values as described above. In fact, by the above-mentioned result that weak uniform persistence implies strong uniform persistence, it suffices to show that $P_k^\infty \geq \delta$.

If $P_k^\infty < \frac{r_k - r_{k+1}}{1 + r_1}$, then $B_{k+1} \rightarrow 0$ by Proposition 2.0.11 (c). Then, by Proposition 2.0.11 (b), $P_{k+1} \rightarrow 0$. Clearly, we may sequentially apply Proposition 2.0.11 (b) and (c) to show that $B_j \rightarrow 0, P_j \rightarrow 0$ for $j \geq k + 1$.

If there is no $\delta > 0$ such that $P_k^\infty \geq \delta$ for every solution with initial data as described above, then for every $\delta > 0$, we may find a solution with such initial data such that $P_k^\infty < \delta$. By a translation of time, we may assume that $P_k(t) \leq \delta, t \geq 0$ for $0 < \delta < \frac{r_k - r_{k+1}}{1 + r_1}$ to be determined later. Then $B_j, P_j \rightarrow 0, j \geq k + 1$. Now, as (a, k) holds, we may apply Lemma 2.0.13. The subsystem with $B_i = 0, k + 1 \leq i \leq n$ and $P_i = 0, k \leq i \leq n$ has a unique positive equilibrium by Proposition 2.0.1. See Remark 2.0.3. The equation

$$\frac{s_k P'_k}{P_k} = \sum_{j \leq k} B_j - s_k$$

implies that

$$\frac{1}{t} \log \frac{P_k^{s_k}(t)}{P_k^{s_k}(0)} = \sum_{j \leq k} [B_j]_t - s_k.$$

By (2.11) and Lemma 2.6, we have for large t

$$\sum_{j \leq k} [B_j]_t = \sum_{j \leq k} B_j^\dagger + O(\delta) = s_k + q + O(\delta)$$

where $q = (1 - \frac{1+Q_k}{r_k}) > 0$. On choosing δ small enough and an appropriate solution, then $\sum_{j \leq k} [B_j]_t - s_k > q/2$ for large t , implying that $P_k \rightarrow +\infty$, a contradiction. We have proved that (a, k) implies (b, k) .

Now, we assume that (b, k) holds and prove that $(a, k+1)$ holds. We consider solutions satisfying $B_i(0) > 0, P_i(0) > 0$ for $1 \leq i \leq k$ and $B_{k+1}(0) > 0$. As (b, k) holds by assumption, and following the same arguments as in the previous case, we only need to show that there exists $\delta > 0$ such that $B_{k+1}^\infty \geq \delta$ for all solutions with initial data as just described.

If $B_{k+1}^\infty < s_{k+1} - s_k$, then $P_{k+1} \rightarrow 0$ by Proposition 2.0.11 (b) and then $B_{k+2} \rightarrow 0$ by Proposition 2.0.11 (c). This reasoning may be iterated to yield $B_i \rightarrow 0, k+2 \leq i \leq n$ and $P_i \rightarrow 0, k+1 \leq i \leq n$.

If there is no $\delta > 0$ such that $B_{k+1}^\infty \geq \delta$ for every solution with initial data as described above, then for every $\delta > 0$, we may find a solution with such initial data such that $B_{k+1}^\infty < \delta$. By a translation of time, we may assume that $B_{k+1}(t) \leq \delta, t \geq 0$ for $0 < \delta < s_{k+1} - s_k$ to be determined later. Then $B_j, P_j \rightarrow 0, j \geq k+2$ and $P_{k+1} \rightarrow 0$. Now, using that (b, k) holds, we apply Lemma 2.0.13. The subsystem with $B_i = 0, P_i = 0, k+1 \leq i \leq n$ has a unique positive equilibrium by Proposition 2.0.1. See Remark 2.0.3. The equation for B_{k+1} is

$$\frac{B'_{k+1}}{B_{k+1}} = r_{k+1} - 1 - r_{k+1} \sum_{j=1}^k (B_j + s_j P_j) - r_{k+1} \sum_{j=k+1}^n (B_j + s_j P_j) - \sum_{j=k+1}^n P_j$$

Integrating, we have

$$\frac{1}{t} \log \frac{B_{k+1}(t)}{B_{k+1}(0)} = r_{k+1} - 1 - r_{k+1} \sum_{j=1}^k ([B_j]_t + s_j [P_j]_t) - r_{k+1} [B_{k+1}]_t + O(1/t)$$

By (2.11) and Lemma 2.0.13, we have that for all large t

$$\sum_{j=1}^k ([B_j]_t + s_j [P_j]_t) = \sum_{j=1}^k (B_j^* + s_j P_j^*) + O(\delta) = \frac{Q_k}{1 + Q_k} + O(\delta).$$

Since $B_{k+1}(t) \leq \delta$, $[B_{k+1}]_t = O(\delta)$. Hence, for large t

$$\frac{1}{t} \log \frac{B_{k+1}(t)}{B_{k+1}(0)} = \frac{r_{k+1}}{1 + Q_k} - 1 + O(\delta) + O(1/t).$$

Now, $\frac{r_{k+1}}{1+Q_k} > \frac{r_{k+1}}{1+Q_{k+1}} > 1$ so by choosing δ sufficiently small and an appropriate solution, we can ensure that the right hand side is bounded below by a positive constant for all large t , implying that $B_{k+1}(t)$ is unbounded. This contradiction completes our proof that (b, k) implies $(a, k+1)$. Thus, our proof is complete by mathematical induction. $\square$

Corollary 2.0.15. *For every solution of (2.6) starting with all components positive, we have that*

$$\frac{1}{t} \int_0^t B_i(s) ds \rightarrow B_i^*, \quad \frac{1}{t} \int_0^t P_i(s) ds \rightarrow P_i^* \quad (2.16)$$

where B_i^*, P_i^* are as in (2.11).

For every solution of (2.6) starting with all components positive except $P_n(0) = 0$, we have that

$$\frac{1}{t} \int_0^t B_i(s) ds \rightarrow B_i^\dagger, \quad \frac{1}{t} \int_0^t P_i(s) ds \rightarrow P_i^\dagger \quad (2.17)$$

where $B_i^\dagger, P_i^\dagger$ are as in (2.11).

Proof. This follows from the previous theorem together with Theorem 5.2.3 in Hofbauer and Sigmund (1998). $\square$

Chapter 3

PERSISTENCE IN PHAGE-BACTERIA COMMUNITIES WITH NESTED AND ONE-TO-ONE INFECTION NETWORKS

Introduction

We show that a bacteria and bacteriophage system with either a perfectly nested or a one-to-one infection network is permanent, a.k.a uniformly persistent, provided that bacteria that are superior competitors for nutrient devote the least to defence against infection and the virus that are the most efficient at infecting host have the smallest host range. By ensuring that the density-dependent reduction in bacterial growth rates are independent of bacterial strain, we are able to arrive at the permanence conclusion sought by Jover *et al.* (2013). The same permanence results hold for the one-to-one infection network considered by Thingstad and Lignell (1997) but without virus efficiency ordering. Additionally we show the global stability for the nested infection network, and the global dynamics for the one-to-one network.

Jover *et al.* (2013) observe that some bipartite infection networks in bacteria and virus communities tend to have a nested structure, characterized by a hierarchy among both host and virus strains, which determines which virus may infect which host. They argue that trade-offs between competitive ability of the bacteria hosts and defence against infection and, on the part of virus, between virulence and transmissibility versus host range can sustain a nested infection network (NIN). Specifically, they find that: “bacterial growth rate should decrease with increasing defence against infection” and “the efficiency of viral infection should decrease with host range”. Their findings are based on the analysis of a Lotka-Volterra model incorporating the above-mentioned trade-offs which strongly sug-

gests that the perfectly nested community structure of n -host bacteria and n -virus is permanent, or uniformly persistent Hofbauer and Sigmund (1998); Smith and Thieme (2011).

Inspired by their work, in Korytowski and Smith (2015a) we replace the Lotka-Volterra model by a chemostat based model in which bacteria compete for a growth-limiting nutrient. In a chemostat model, each bacterial strain is endowed with a break-even concentration, R^* , of nutrient below which it cannot grow such that, in the absence of virus, only the strain with smallest R^* survives. Thus, within a community of bacteria competing for a single limiting nutrient, the competitiveness of the various strains are naturally ordered by their R^* values. In Korytowski and Smith (2015a), we show that a community of n bacteria and n virus strains with a nested infection network, where n is restricted by the amount of supplied nutrient, is permanent provided that R^* values increase with increasing defence against infection and that the efficiency of viral infection should decrease with host range. We also show how a bacteria-virus community with NIN can be assembled by the successive addition of one new species at a time, answering the question of “How do NIN come to be?”.

We show that the Lotka-Volterra based model of Jover *et al.* (2013) can be modified in such a way that the permanence conclusions which they sought can be attained. The key is to ensure that density-dependent reduction in bacterial growth rates be independent of bacterial strain. Following Jover *et al.* (2013), we assume that virus strain V_i is characterized by its adsorption rate ϕ_i and its burst size β_i , both of which are assumed to be independent of which host strain it infects, and its specific death rate n_i . The density of bacteria strain i is denoted by B_i , and its specific growth rate is r_i . The “mean field”, density-dependent depression of growth due to inter and intra-specific competition term $\sum_j a_j B_j$ is common to all strains. The equations of our model are the following.

$$\begin{aligned}
B'_i &= B_i \left(r_i - \sum_{j=1}^n a_j B_j \right) - B_i \sum_{j=1}^n M_{ij} \phi_j V_j \\
V'_i &= \beta_i \phi_i V_i \sum_{j=1}^n M_{ji} B_j - n_i V_i, \quad 1 \leq i \leq n.
\end{aligned} \tag{3.1}$$

where matrix M captures the infection network structure:

$$M_{ij} = \begin{cases} 1, & V_j \text{ infects } H_i \\ 0, & V_j \text{ does not infect } H_i \end{cases}$$

In the system considered in Jover *et al.* (2013), the bacterial host dynamics in the absence of virus is modeled as $B'_i = r_i B_i (1 - K^{-1} \sum_j B_j)$; a consequence of this is the simplex of equilibria $\sum_j B_j = K$ if no virus are present. We avoid this degeneracy.

We assume hereafter that the B_i are ordered according to decreasing specific growth rate:

$$r_1 > r_2 > \cdots > r_n. \tag{3.2}$$

Motivated by the work of Jover *et al.* (2013) and the work of Thingstad and Lignell (1997), we consider two special network structures: nested infection networks (NIN) with upper triangular matrix M , and one-to-one infection networks (OIN) with $M = I$, the identity matrix.

The scaling of variables

$$P_i = \phi_i V_i, \quad H_i = B_i, \quad e_i = \frac{\beta_i \phi_i}{n_i},$$

exposes a virus infection efficiency parameter e_i for each virus. Hereafter, we consider the resulting scaled system:

$$\begin{aligned}
H'_i &= H_i \left(r_i - \sum_{j=1}^n a_j H_j \right) - H_i \sum_{j=1}^n M_{ij} P_j \\
P'_i &= e_i n_i P_i \left(\sum_{j=1}^n M_{ji} H_j - \frac{1}{e_i} \right), \quad 1 \leq i \leq n.
\end{aligned} \tag{3.3}$$

Proposition 3.0.1. *Solutions of (3.3) with nonnegative (positive) initial data are well-defined for all $t \geq 0$ and remain nonnegative (positive). In addition, the system has a compact global attractor. Indeed, if $F(t) = \sum_{i=1}^n H_i(t) + \sum_{i=1}^n \frac{P_i(t)}{e_i n_i}$ then*

$$F(t) \leq \frac{Q}{W} + (F(0) - \frac{Q}{W})e^{-Wt} \leq \max\{F(0), \frac{Q}{W}\},$$

and

$$\limsup_{t \rightarrow \infty} F(t) \leq \sum_{i=1}^n (1 + \frac{r_i}{W}) \frac{r_i}{a_i},$$

where $K = \max_{i=1}^n \{H_i(0), \frac{r_i}{a_i}\}$, $W = \min_{i=1}^n \{n_i\}$ and $Q = \sum_{i=1}^n (W + r_i)K$.

Proof. Existence and positivity of solutions follow from the form of the right hand side.

Therefore, $H'_i(t) \leq H_i(t)(r_i - a_i H_i(t))$. Hence $H_i(t) \leq K$ and $\limsup_{t \rightarrow \infty} H_i(t) \leq r_i/a_i$.

$$\begin{aligned} \frac{dF}{dt} &= \sum_{i=1}^n r_i H_i - \left(\sum_{i=1}^n H_i \right) \left(\sum_{j=1}^n a_j H_j \right) - \sum_{i=1}^n \frac{P_i}{e_i} \leq \sum_{i=1}^n r_i H_i - W \sum_{i=1}^n \frac{P_i}{e_i n_i} \\ &= \sum_{i=1}^n (W + r_i) H_i - W F. \end{aligned}$$

The estimate on $F(t)$ follows by bounding the first summation by Q and integrating; the estimate on the limit superior follows from the estimate of the limit superior of the H_i above and by integration. $\square$

As a necessary condition for permanence of a dissipative system is the existence of a positive equilibrium (see e.g. Theorem 13.5.1 in Hofbauer and Sigmund (1998)), we begin by finding sharp conditions for their existence and uniqueness. Following this, we state our main results on permanence. Then we consider some special parameter regions where we are able to say more about the global dynamics of the systems.

Nested Infection Networks

If M is upper triangular, then our system becomes:

$$\begin{aligned} H'_i &= H_i \left(r_i - \sum_{j=1}^n a_j H_j - \sum_{j \geq i} P_j \right) \\ P'_i &= e_i n_i P_i \left(\sum_{j \leq i} H_j - \frac{1}{e_i} \right), \quad 1 \leq i \leq n. \end{aligned} \quad (3.4)$$

Our system has many equilibria. Only those equilibria which play a role in our results will be mentioned.

Proposition 3.0.2. *There exists an equilibrium, E^* , with $H_i > 0$ and $P_i > 0$ for all i if and only if*

$$e_1 > e_2 > e_3 > \cdots > e_n \quad (3.5)$$

and

$$r_n > Q_n, \quad (3.6)$$

where

$$Q_n = \frac{a_1}{e_1} + \left(\frac{a_2}{e_2} - \frac{a_2}{e_1} \right) + \left(\frac{a_3}{e_3} - \frac{a_3}{e_2} \right) + \cdots + \left(\frac{a_n}{e_n} - \frac{a_n}{e_{n-1}} \right) \quad (3.7)$$

In fact,

$$\begin{aligned} H_1^* &= \frac{1}{e_1}, \quad H_j^* = \frac{1}{e_j} - \frac{1}{e_{j-1}}, \quad j > 1, \\ P_j^* &= r_j - r_{j+1}, \quad j < n, \quad P_n^* = r_n - Q_n. \end{aligned} \quad (3.8)$$

Furthermore, inequalities (3.5) and (3.6) also imply the existence of a unique equilibrium $E^\dagger$ with all components positive except for $P_n = 0$. In fact,

$$\begin{aligned} H_n^\dagger &= H_n^* + \frac{P_n^*}{a_n}, \quad H_j^\dagger = H_j^*, \quad 1 \leq j < n, \\ P_j^\dagger &= P_j^*, \quad j < n, \quad P_n^\dagger = 0. \end{aligned} \quad (3.9)$$

Remark 3.0.3. (3.5) and (3.6) imply the existence of a unique family of equilibria E_k^* with $H_j, P_j = 0, j > k$ described by (3.8), but with Q_k replacing Q_n . Another family of equilibria, $E_k^\dagger$, exists with $H_j = 0, j > k$ and $P_j = 0, j \geq k$ described by (3.9), but with Q_k replacing Q_n . There are many other equilibria, but we have no need to enumerate all of them.

In view of (3.8), (3.6) is equivalent to $Q_n = \sum_j a_j H_j^* < r_n$, obviously a necessary condition for the weakest competitor H_n to survive.

One-to-One Infection Network

$M = I$ in the one-to-one infection network so the equations then becomes:

$$\begin{aligned} H'_i &= H_i \left(r_i - \sum_{j=1}^n a_j H_j \right) - H_i P_i \\ P'_i &= e_i n_i P_i \left(H_i - \frac{1}{e_i} \right), \quad 1 \leq i \leq n. \end{aligned} \quad (3.10)$$

The principle equilibria for the one-to-one infection network are now described.

Proposition 3.0.4. *There exists an equilibrium E^* with H_i and P_i positive for all i if and only if the following inequality holds:*

$$\tilde{Q}_n < r_j, 1 \leq j \leq n, \quad \tilde{Q}_n = \sum_{i=1}^n \frac{a_i}{e_i}. \quad (3.11)$$

In fact,

$$\begin{aligned} H_j^* &= \frac{1}{e_j}, \quad j \geq 1, \\ P_j^* &= r_j - \tilde{Q}_n, \quad j \geq 1. \end{aligned} \quad (3.12)$$

We also note the existence of a unique equilibrium $E^\dagger$, with all components positive except for $P_n = 0$, given by

$$\begin{aligned} H_j^\dagger &= H_j^*, \quad 1 \leq j < n, \\ H_n^\dagger &= H_n^* + \frac{P_n^*}{a_n}, \\ P_j^\dagger &= P_j^* - P_n^* = r_j - r_n, \quad j \leq n, \end{aligned} \tag{3.13}$$

provided that $r_n < r_j, j \neq n$.

Remark 3.0.5. We also note the existence of a family of equilibria $E_k^*, E_k^\dagger, 1 \leq k \leq n$, characterized as follows. E_k^* with $H_j, P_j = 0, j > k$ is described by (3.12) but with $\tilde{Q}_k$ replacing $\tilde{Q}_n$. $E_k^\dagger$ satisfies $H_j = 0, j > k$ and $P_j = 0, j \geq k$ described by (3.13) but with $\tilde{Q}_k$ replacing $\tilde{Q}_n$.

In view of (3.12), (3.11) is equivalent to $\tilde{Q}_n = \sum_j a_j H_j^* < r_n$, obviously a necessary condition for the weakest competitor H_n to survive. Unlike the NIN case, no ordering of virus infection efficiencies is required for existence of E^* .

Permanence

Our permanence result applies to both types of networks. We use the notion $(H, P) = (H_1, H_2, \dots, H_n, P_1, \dots, P_n)$ for a solution of (3.4), or of (3.10). We write $H_{i,\infty} = \liminf_{t \rightarrow \infty} H_i(t)$ and H_i^∞ with limit superior in place of limit inferior.

Theorem 3.0.6. Let $1 \leq k \leq n$. For NIN assume (3.5), (3.6), and (3.2) and for (OIN) assume (3.11).

(a) There exists $\epsilon_k > 0$ such that if (H, P) is a solution satisfying

$H_i(0) > 0, 1 \leq i \leq k$, and $P_j(0) > 0, 1 \leq j \leq k - 1$, then

$$H_{i,\infty} \geq \epsilon_k, \quad 1 \leq i \leq k \text{ and } P_{j,\infty} \geq \epsilon_k, \quad 1 \leq j \leq k - 1.$$

(b) *There exists $\epsilon_k > 0$ such that if (H, P) is a solution satisfying*

$$H_i(0) > 0, P_i(0) > 0, 1 \leq i \leq k, \text{ then}$$

$$H_{i,\infty} \geq \epsilon_k, P_{i,\infty} \geq \epsilon_k, 1 \leq i \leq k.$$

Observe that in both cases (a) and (b), we require only certain prescribed components of the initial data to be positive, but we make no restrictions on the other components except, of course, that they are nonnegative. In particular, a community consisting of only virus V_1 and bacteria H_1 is permanent. Furthermore, the addition of bacteria H_2 , say through a mutation or a colonization event, results in a permanent community. And the subsequent addition of new virus V_2 results in a permanent community, and so on. Note that the order of the alternating sequence of additions of new bacteria and new virus types is important. Bacteria types are added in descending order of specific growth rate. Virus are added in descending order of infection efficiency (ascending order of host range) in the NIN case but in the OIN case, virus are added that specialize on infection of the most recently added bacteria type.

As a consequence of permanence, time averages of positive solutions are asymptotic to equilibrium values by the well-known Theorem 5.2.3 in Hofbauer and Sigmund (1998).

Corollary 3.0.7. *For every solution of (3.4) or of (3.10) starting with all components positive, we have that*

$$\frac{1}{t} \int_0^t H_i(s) ds \rightarrow H_i^*, \frac{1}{t} \int_0^t P_i(s) ds \rightarrow P_i^* \quad (3.14)$$

where H_i^*, P_i^* are as in (3.8) or (3.12).

For every solution of (3.4) or of (3.10) starting with all components positive except $P_n(0) = 0$, we have that

$$\frac{1}{t} \int_0^t H_i(s) ds \rightarrow H_i^\dagger, \frac{1}{t} \int_0^t P_i(s) ds \rightarrow P_i^\dagger \quad (3.15)$$

where $H_i^\dagger, P_i^\dagger$ are as in (3.9) or (3.13).

Theorem 3.0.6 is proved separately in the two cases in the following subsections.

Permanence for Nested Infection Networks

Hereafter, we assume without further comment that (3.6), and (3.2) hold.

If there are no virus present, then host H_1 drives the other hosts to extinction.

Proposition 3.0.8. (a) If $(\sum_{j \leq i} H_j(t))^\infty < \frac{1}{e_i}$ then $P_i(t) \rightarrow 0$.

(b) If $i < j$, $P_i(0) > 0$, and if $(H_{i+1} + H_{i+2} + \cdots + H_j)^\infty < \frac{1}{e_j} - \frac{1}{e_i}$ then $P_j(t) \rightarrow 0$.

(c) If $i < j$, $H_i(0) > 0$, and if $(P_i + P_{i+1} + \cdots + P_{j-1})^\infty < (r_i - r_j)$ then $H_j(t) \rightarrow 0$.

Proof. of (a): The equation for P_i implies that

$$\frac{d}{dt} \log P_i^{\frac{1}{n_i e_i}} = \sum_{j \leq i} H_j(t) - \frac{1}{e_i}$$

If $(\sum_{j \leq i}^n H_j(t))^\infty < \frac{1}{e_i}$ is false, then $P_i \rightarrow \infty$, a contradiction to P_i being bounded. Assertion (a) is transparent.

Proof of (b): If $i < j$, $P_i(0) > 0$, and if $(H_{i+1} + H_{i+2} + \cdots + H_j)^\infty < \frac{1}{e_j} - \frac{1}{e_i}$ then

$$\begin{aligned} \frac{d}{dt} \log \frac{P_i^{\frac{1}{n_i e_i}}}{P_j^{\frac{1}{n_j e_j}}} &= \frac{P'_i}{e_i n_i P_i} - \frac{P'_j}{n_j e_j P_j} \\ &= \frac{-1}{e_i} + \frac{1}{e_j} - (H_{i+1} + H_{i+2} + \cdots + H_j) \geq \epsilon, t \geq T \end{aligned}$$

for some $\epsilon, T > 0$. Therefore, $\frac{P_i^{\frac{1}{n_i e_i}}}{P_j^{\frac{1}{n_j e_j}}} \rightarrow \infty$, and since P_i, P_j are bounded, $P_j(t) \rightarrow 0$.

Proof of (c): assume that $H_i(0) > 0$ and $(P_i + P_{i+1} + \cdots + P_{j-1})^\infty < (r_i - r_j)$, then

$$\begin{aligned} \frac{d}{dt} \log \frac{H_i(t)}{H_j(t)} &= \frac{H'_i}{H_i} - \frac{H'_j}{H_j} \\ &= (r_i - r_j) - (P_i(t) + P_{i+1}(t) + \cdots + P_{j-1}(t)) \end{aligned}$$

It follows that $\frac{H_i}{H_j} \rightarrow \infty$, and since H_i, H_j are bounded, $H_j(t) \rightarrow 0$. □

Lemma 3.0.9. *If $P_i \equiv 0$, $1 \leq i \leq n$, $H_1(0) > 0$ then $H_1 \rightarrow \frac{r_1}{a_1}$.*

Proof. Since $P_i \equiv 0$, $H_{i+1} \rightarrow 0$ by Proposition 3.0.8 (c) for $1 \leq i < n$. Therefore $\forall \epsilon > 0$, $\exists T > 0$ such that $\forall t \geq T$, $\sum_{j=2}^n a_j H_j(t) < \epsilon$. Then for $t > T$, $H_1' > H_1(r_1 - a_1 H_1 - 2\epsilon)$. Therefore $H_{1,\infty} \geq \frac{r_1 - 2\epsilon}{a_1}$ and since $\epsilon > 0$ is arbitrary, $H_{1,\infty} \geq \frac{r_1}{a_1}$. On the other hand, $H_1' \leq H_1(r_1 - a_1 H_1)$, so $H_1^\infty \leq \frac{r_1}{a_1}$. Therefore $H_1 \rightarrow \frac{r_1}{a_1}$. $\square$

Now we show that H_1 persists if initially present regardless of who else is around; similarly, H_1 and V_1 persist if initially present regardless of which other host and virus are present.

Proposition 3.0.10. (a) *If $H_1(0) > 0$, then $H_1^\infty \geq \frac{1}{e_1}$.*

(b) *If $H_1(0) > 0$ and $P_1(0) > 0$, then*

$$H_1^\infty \geq \frac{1}{e_1}, \quad P_1^\infty \geq \min\{r_1 - r_2, \frac{r_1 e_1 - a_1}{e_1}\}.$$

Proof. of (a). Assume the conclusion is false. Then $P_1 \rightarrow 0$ by Proposition 3.0.8 (a).

If $P_i(0) = 0$ for all i , then $H_1(t) \rightarrow \frac{r_1}{a_1} \geq \frac{1}{e_1}$ by Lemma 3.0.9 and (3.2) and (3.7), so we suppose that $P_i(0) > 0$ for some i . Let k denote the smallest such integer i for which $P_i(0) > 0$.

If $k = 1$, then, as noted above, $P_1 \rightarrow 0$ and so $H_2 \rightarrow 0$ by Proposition 3.0.8 (c). Then $P_2 \rightarrow 0$ by Proposition 3.0.8 (a) or (b).

If $k = 2$, then $P_1 \equiv 0$ so $H_2 \rightarrow 0$ by Lemma 3.0.8 (c) since H_1 and H_2 share the same virus. Since $(H_1 + H_2)^\infty = H_1^\infty < \frac{1}{e_1} < \frac{1}{e_2}$, it follows that $P_2 \rightarrow 0$ by Proposition 3.0.8 (a). Now we can use Proposition 3.0.8 (c) to show $H_3 \rightarrow 0$ and then Proposition 3.0.8 (a) or (b) to show $P_3 \rightarrow 0$.

If $k > 2$, then $P_1 \equiv P_2 \equiv \dots \equiv P_{k-1} \equiv 0$ and $P_k(0) > 0$. As $H_1, \dots, H_{k-1}$ share the same virus, then $H_i \equiv 0$ or $H_i \rightarrow 0$ for $1 < i \leq k-1$ by Proposition 3.0.8 (c). $H_k \rightarrow 0$ by Proposition 3.0.8 (c). Then, $P_k \rightarrow 0$ by Proposition 3.0.8 (a) since

$(\sum_{j \leq k} H_j)^\infty = H_1^\infty < \frac{1}{e_1} < \frac{1}{e_k}$. So $H_{k+1} \rightarrow 0$ by Proposition 3.0.8 (c). Proposition 3.0.8 (a) or (b) implies that $P_{k+1} \rightarrow 0$.

We see that for all values of k , $H_2, \dots, H_{k+1} \rightarrow 0$ and $P_1, \dots, P_{k+1} \rightarrow 0$. Successive additional applications of Proposition 3.0.8 (a) or (b) and (c) then imply that $H_2, \dots, H_n \rightarrow 0$ and $P_1, \dots, P_n \rightarrow 0$. But, then for all $\epsilon > 0$, there exists $T > 0$ such that

$$H_1'(t)/(H_1) \geq r_1 - \epsilon - a_1 H_1, \quad t \geq T.$$

This implies that $H_1^\infty > \frac{r_1}{a_1} > \frac{1}{e_1}$, by (3.6), a contradiction. This completes the proof of the first assertion.

Proof of (b): Now, suppose that $H_1(0) > 0$, $P_1(0) > 0$ and $P_1^\infty < r_1 - r_2$.

Proposition 3.0.8 (c) implies that $H_2 \rightarrow 0$. By Proposition 3.0.8 (b), $P_2 \rightarrow 0$. Applying Proposition 3.0.8 (c) with $i = 1$ and $j = 3$, as $(P_1 + P_2)^\infty = P_1^\infty < r_1 - r_2 < r_1 - r_3$, we conclude that $H_3 \rightarrow 0$. Then, Proposition 3.0.8 (b) implies that $P_3 \rightarrow 0$. Clearly, we can continue sequential application of Proposition 3.0.8 (b) and (c) to conclude that $H_i, P_i \rightarrow 0$ for $i > 1$. Then we use that

$$\begin{aligned} \frac{d}{dt} \log H_1 P_1^{\frac{a_1}{e_1 n_1}} &= \frac{H_1'}{H_1} + \frac{a_1 P_1'}{P_1 e_1 n_1} \\ &= r_1 - \frac{a_1}{e_1} - P_1 - \text{terms that go to zero} \end{aligned}$$

to conclude that $P_1^\infty \geq \frac{r_1 e_1 - a_1}{e_1}$. □

Lemma 3.0.11 (Lemma 1.2 Korytowski and Smith (2015a)). *Let $x(t)$ be a bounded positive solution of the Lotka-Volterra system*

$$x_i' = x_i \left(r_i + \sum_{j=1}^n a_{ij} x_j \right), \quad 1 \leq i \leq n$$

and suppose there exists $k < n$ and $m, M, \delta > 0$ such that $m \leq x_i(t) \leq M$, $1 \leq i \leq k$, $t > 0$, $x_{k+1}(t) \leq \delta$, $t > 0$, and $x_j(t) \rightarrow 0$ for $j > k + 1$. Suppose also that the

$k \times k$ subsystem obtained by setting $x_j = 0, j > k$ has a unique positive equilibrium $p = (p_1, p_2, \dots, p_k)$. Then

$$\liminf_{T \rightarrow \infty} \frac{1}{T} \int_0^T x_i(t) dt = p_i + O(\delta), \quad 1 \leq i \leq k.$$

The same expression holds for the limit superior.

Proof. Proof of Theorem 3.0.6 for NIN case. We use the notation $[H_i]_t \equiv \frac{1}{t} \int_0^t H_i(s) ds$.

Our proof is by mathematical induction using the ordering of the $2n$ cases as follows

$$(a, 1) < (b, 1) < (a, 2) < (b, 2) < \dots < (a, n) < (b, n)$$

where (a, k) denotes case (a) with index k .

The cases $(a, 1)$ and $(b, 1)$ follow immediately from Proposition 3.0.10 and Corollary 4.8 in Smith and Thieme (2011) with persistence function $\rho = \min\{H_1, P_1\}$ in case $(b, 1)$. The latter result says that weak (limsup) uniform persistence implies strong (liminf) uniform persistence when the dynamical system is dissipative.

For the induction step, assuming that (a, k) holds, we prove that (b, k) holds and assuming that (b, k) holds, we prove that $(a, k + 1)$ holds.

We begin by assuming that (a, k) holds and prove that (b, k) holds. We consider solutions satisfying $H_i(0) > 0, P_i(0) > 0$ for $1 \leq i \leq k$. Note that other components $H_j(0)$ or $P_j(0)$ for $j > k$ may be positive or zero, we make no assumptions. As (a, k) holds, there exists $\epsilon_k > 0$ such that $H_{i,\infty} \geq \epsilon_k, 1 \leq i \leq k$ and $P_{i,\infty} \geq \epsilon_k, 1 \leq i \leq k - 1$. We need only show the existence of $\delta > 0$ such that $P_{k,\infty} \geq \delta$ for every solution with initial values as described above. In fact, by Corollary 4.8 in Smith and Thieme (2011), weak uniform persistence implies strong uniform persistence, it suffices to show that $P_k^\infty \geq \delta$.

If $P_k^\infty < r_k - r_{k+1}$, then $H_{k+1} \rightarrow 0$ by Proposition 3.0.8 (c). Then, by Proposition 3.0.8 (b), $P_{k+1} \rightarrow 0$. Clearly, we may sequentially apply Proposition 3.0.8 (b) and (c) to show that $H_j \rightarrow 0, P_j \rightarrow 0$ for $j \geq k + 1$.

If there is no $\delta > 0$ such that $P_k^\infty \geq \delta$ for every solution with initial data as described above, then for every $\delta > 0$, we may find a solution with such initial data such that $P_k^\infty < \delta$. By a translation of time, we may assume that $P_k(t) \leq \delta$, $t \geq 0$ for $0 < \delta < r_k - r_{k+1}$ to be determined later. Then $H_j, P_j \rightarrow 0, j \geq k+1$. Now, as (a, k) holds, we may apply Lemma 3.0.11. The subsystem with $H_i = 0, k+1 \leq i \leq n$ and $P_i = 0, k \leq i \leq n$ has a unique positive equilibrium by Proposition 3.0.2. See Remark 3.0.3. The equation

$$\frac{P'_k}{P_k e_k n_k} = \sum_{j \leq k} H_j - \frac{1}{e_k}$$

implies that

$$\frac{1}{t} \log \frac{P_k^{\frac{1}{e_k n_k}}(t)}{P_k^{\frac{1}{e_k n_k}}(0)} = \sum_{j \leq k} [H_j]_t - \frac{1}{e_k}.$$

By (3.9) and Lemma 3.0.11, we have for large t

$$\sum_{j \leq k} [H_j]_t - \frac{1}{e_k} = \sum_{j \leq k} H_j^\dagger - \frac{1}{e_k} + O(\delta) = \frac{1}{e_{k-1}} + q - \frac{1}{e_k} + O(\delta)$$

where $q = \frac{1}{a_k}(r_k - Q_{k-1}) + \frac{1}{e_{k-1}} - \frac{1}{e_k} > 0$. On choosing δ small enough and an appropriate solution, then $\sum_{j \leq k} [H_j]_t - \frac{1}{e_k} > q/2$ for large t , implying that $P_k \rightarrow +\infty$, a contradiction. We have proved that (a, k) implies (b, k) .

Now, we assume that (b, k) holds and prove that $(a, k+1)$ holds. We consider solutions satisfying

$H_i(0) > 0, P_i(0) > 0$ for $1 \leq i \leq k$ and $H_{k+1}(0) > 0$. As (b, k) holds by assumption, and following the same arguments as in the previous case, we only need to show that there exists $\delta > 0$ such that $H_{k+1}^\infty \geq \delta$ for all solutions with initial data as just described.

If $H_{k+1}^\infty < \frac{1}{e_{k+1}} - \frac{1}{e_k}$, then $P_{k+1} \rightarrow 0$ by Proposition 3.0.8 (b) and then $H_{k+2} \rightarrow 0$ by Proposition 3.0.8 (c). This reasoning may be iterated to yield $H_i \rightarrow 0, k+2 \leq i \leq n$ and $P_i \rightarrow 0, k+1 \leq i \leq n$.

If there is no $\delta > 0$ such that $H_{k+1}^\infty \geq \delta$ for every solution with initial data as described above, then for every $\delta > 0$, we may find a solution with such initial data such that $H_{k+1}^\infty <$

δ . By a translation of time, we may assume that $H_{k+1}(t) \leq \delta$, $t \geq 0$ for $0 < \delta < \frac{1}{e_{k+1}} - \frac{1}{e_k}$ to be determined later. Then $H_j, P_j \rightarrow 0, j \geq k+2$ and $P_{k+1} \rightarrow 0$. Now, using that (b, k) holds, we apply Lemma 3.0.11. The subsystem with $H_i = 0, P_i = 0, k+1 \leq i \leq n$ has a unique positive equilibrium by Proposition 3.0.2. See Remark 3.0.3. The equation for H_{k+1} is

$$\frac{H'_{k+1}}{H_{k+1}} = r_{k+1} - \sum_{j=1}^k a_j H_j - \sum_{j=k+1}^n a_j H_j - \sum_{j=k+1}^n P_j$$

Integrating, we have

$$\frac{1}{t} \log \frac{H_{k+1}(t)}{H_{k+1}(0)} = \sum_{j=1}^{k+1} a_j [H_j]_t + O(1/t)$$

By Remark 3.0.3 and Lemma 3.0.11, we have that for all large t

By (3.8) and Lemma 3.0.11, we have that for all large t

$$\sum_{j=1}^k a_j [H_j]_t = \sum_{j=1}^k a_j H_j^* + O(\delta) = Q_n + O(\delta)$$

since $H_{k+1}(t) \leq \delta$, $[H_{k+1}]_t = O(\delta)$. Now, $Q_n > 0$ so by choosing δ sufficiently small and an appropriate solution, we can ensure that the right hand side is bounded below by a positive constant for all large t , implying that $H_{k+1}(t)$ is unbounded. This contradiction completes our proof that (b, k) implies $(a, k+1)$. Thus, our proof is complete by mathematical induction. $\square$

Permanence for One-to-One Infection Networks

$$\begin{aligned} H'_i &= H_i \left(r_i - \sum_{j=1}^n a_j H_j \right) - H_i P_i \\ P'_i &= e_i n_i P_i \left(H_i - \frac{1}{e_i} \right), \quad 1 \leq i \leq n. \end{aligned} \tag{3.16}$$

Proposition 3.0.12. (a) If $H_i(t)^\infty < \frac{1}{e_i}$ then $P_i(t) \rightarrow 0$.

(b) If $i < j$, $H_i(0) > 0$, and $(P_i - P_j)^\infty < r_i - r_j$, then $H_j(t) \rightarrow 0$.

Proof. of (a). The equation for P_i implies that

$$\frac{d}{dt} \log P_i^{\frac{1}{n_i e_i}} = H_i(t) - \frac{1}{e_i}$$

If $H_i(t)^\infty < \frac{1}{e_i}$ then $P_i \rightarrow 0$.

Proof of (b). Assume that $i < j$, $H_i(0), H_j(0) > 0$ and $(P_i - P_j)^\infty < r_i - r_j$. As

$$\frac{d}{dt} \log \frac{H_i(t)}{H_j(t)} = \frac{H'_i}{H_i} - \frac{H'_j}{H_j} = (r_i - r_j) - (P_i(t) - P_j(t)),$$

it follows that $\frac{H_i}{H_j} \rightarrow \infty$, which by the boundedness of H_i, H_j , implies that $H_j(t) \rightarrow 0$. $\square$

Lemma 3.0.13. If $P_1 \equiv 0$, $H_1(0) > 0$ then $H_1 \rightarrow \frac{r_1}{a_1}$.

Proof. Since $P_1 \equiv 0$, $H_i \rightarrow 0$ by Proposition 3.0.12 (b) for $1 < i \leq n$. Therefore, $\forall \epsilon > 0, \exists T > 0$ such that $\forall t \geq T, \sum_{j=2}^n a_j H_j(t) < \epsilon$. Then for $t > T$, $H'_1 > H_1(r_1 - a_1 H_1 - 2\epsilon)$. Therefore $H_{1,\infty} \geq \frac{r_1 - 2\epsilon}{a_1}$ and since $\epsilon > 0$ is arbitrary, $H_{1,\infty} \geq \frac{r_1}{a_1}$. On the other hand, $H'_1 \leq H_1(r_1 - a_1 H_1)$, so $H_1^\infty \leq \frac{r_1}{a_1}$. Therefore $H_1 \rightarrow \frac{a_1}{r_1}$. $\square$

Proposition 3.0.14. (a) If $H_1(0) > 0$, then $H_1^\infty \geq \frac{1}{e_1}$.

(b) If $H_1(0) > 0$ and $P_1(0) > 0$, then

$$H_1^\infty \geq \frac{1}{e_1}, \quad P_1^\infty \geq \min\{r_1 - r_2, \frac{r_1 e_1 - a_1}{e_1}\}.$$

Proof. of (a): Assume the conclusion is false. Then $P_1 \rightarrow 0$ by Proposition 3.0.12 (a). Then $H_2 \rightarrow 0$ by Proposition 3.0.12 (b). Therefore by sequential applications of Proposition 3.0.12 (a) and (b), we can conclude that $H_i, P_i \rightarrow 0$, for $i > 1$. But, then

$$H'_1 / (H_1) \geq r_1 - \epsilon - a_1 H_1 > r_n - \epsilon - a_1 H_1 > \frac{a_1}{e_1} - \epsilon - a_1 H_1, \quad t \geq T$$

for some $\epsilon > 0$ and $T > 0$ (recall that $r_i > r_n$ from (3.2) and $\frac{a_1}{e_1} < r_1$ from (3.11)). This implies that $H_1^\infty > \frac{1}{e_1}$, a contradiction. This completes the proof of the first assertion.

Proof of (b): Now, suppose that $H_1(0) > 0, P_1(0) > 0$ and $P_1^\infty < r_1 - r_2$. Then $(P_1 - P_2)^\infty \leq P_1^\infty < r_1 - r_2$, therefore Proposition 3.0.12 (b) implies that $H_2 \rightarrow 0$. Then $P_2 \rightarrow 0$ by Proposition 3.0.12 (a). Then $(P_2 - P_3)^\infty \leq P_2^\infty < r_2 - r_3$ therefore Proposition 3.0.12 (b) implies that $H_3 \rightarrow 0$. Clearly, we can continue sequential applications of Proposition 3.0.12 (a) and (b) to conclude that $H_i, P_i \rightarrow 0$ for $i > 1$.

$$\begin{aligned} \frac{d}{dt} \log H_1 P_1^{\frac{a_1}{e_1 n_1}} &= \frac{H_1'}{H_1} + \frac{a_1 P_1'}{P_1 e_1 n_1} \\ &= r_1 - \frac{a_1}{e_1} - P_1 - \text{terms that go to zero} \end{aligned}$$

to conclude that $P_1^\infty \geq \frac{r_1 e_1 - a_1}{e_1}$. □

Proof. Proof of Theorem 3.0.6 in OIN case. We use the notation $[H_i]_t \equiv \frac{1}{t} \int_0^t H_i(s) ds$.

Our proof is by mathematical induction using the ordering of the $2n$ cases as follows

$$(a, 1) < (b, 1) < (a, 2) < (b, 2) < \cdots < (a, n) < (b, n)$$

where (a, k) denotes case (a) with index k .

The cases $(a, 1)$ and $(b, 1)$ follow immediately from Proposition 3.0.14 and Corollary 4.8 in Smith and Thieme (2011) with persistence function $\rho = \min\{H_1, P_1\}$ in case $(b, 1)$.

For the induction step, assuming that (a, k) holds, we prove that (b, k) holds and assuming that (b, k) holds, we prove that $(a, k + 1)$ holds.

We begin by assuming that (a, k) holds and prove that (b, k) holds. We consider solutions satisfying $H_i(0) > 0, P_i(0) > 0$ for $1 \leq i \leq k$. Note that other components $H_j(0)$ or $P_j(0)$ for $j > k$ may be positive or zero, we make no assumptions. As (a, k) holds, there exists $\epsilon_k > 0$ such that $H_{i,\infty} \geq \epsilon_k, 1 \leq i \leq k$ and $P_{i,\infty} \geq \epsilon_k, 1 \leq i \leq k - 1$. We need only show the existence of $\delta > 0$ such that $P_{k,\infty} \geq \delta$ for every solution with initial values

as described above. In fact, by the above-mentioned result that weak uniform persistence implies strong uniform persistence, it suffices to show that $P_k^\infty \geq \delta$.

If $P_k^\infty < r_k - r_{k+1}$, then $H_{k+1} \rightarrow 0$ by Proposition 3.0.12 (b). Then, by Proposition 3.0.12 (a), $P_{k+1} \rightarrow 0$. Clearly, we may sequentially apply Proposition 3.0.12 (b) and (a) to show that $H_j \rightarrow 0, P_j \rightarrow 0$ for $j \geq k + 1$.

If there is no $\delta > 0$ such that $P_k^\infty \geq \delta$ for every solution with initial data as described above, then for every $\delta > 0$, we may find a solution with initial data such that $P_k^\infty < \delta$. By a translation of time, we may assume that $P_k(t) \leq \delta, t \geq 0$ for $0 < \delta < r_k - r_{k+1}$ to be determined later. Then $H_j, P_j \rightarrow 0, j \geq k + 1$. Now, as (a, k) holds, we may apply Lemma 3.0.11. The subsystem with $H_i = 0, k + 1 \leq i \leq n$ and $P_i = 0, k \leq i \leq n$ has a unique positive equilibrium by Proposition 3.0.4. See Remark 3.0.5. The equation

$$\frac{P'_k}{P_k e_k n_k} = H_k - \frac{1}{e_k}$$

implies that

$$\frac{1}{t} \log \frac{P_k^{\frac{1}{e_k n_k}}(t)}{P_k^{\frac{1}{e_k n_k}}(0)} = [H_k]_t - \frac{1}{e_k}.$$

By (3.13) and Lemma 3.0.11, we have for large t

$$[H_k]_t - \frac{1}{e_k} = H_k^\dagger - \frac{1}{e_k} + O(\delta) = H_k^* + \frac{P_k^*}{a_k} - \frac{1}{e_k} + O(\delta) = \frac{P_k^*}{a_k} + O(\delta) > 0$$

Implying that $P_k \rightarrow +\infty$, a contradiction. We have proved that (a, k) implies (b, k) .

Now, we assume that (b, k) holds and prove that $(a, k + 1)$ holds. We consider solutions satisfying

$H_i(0) > 0, P_i(0) > 0$ for $1 \leq i \leq k$ and $H_{k+1}(0) > 0$. As (b, k) holds by assumption, and following the same arguments as in the previous case, we only need to show that there exists $\delta > 0$ such that $H_{k+1}^\infty \geq \delta$ for all solutions with initial data as just described.

If $H_{k+1}^\infty < \frac{1}{e_{k+1}}$, then $P_{k+1} \rightarrow 0$ by Proposition 3.0.12 (a) and then $H_{k+2} \rightarrow 0$ by Proposition 3.0.12 (b). This reasoning may be iterated to yield $H_i \rightarrow 0$, $k+2 \leq i \leq n$ and $P_i \rightarrow 0$, $k+1 \leq i \leq n$.

If there is no $\delta > 0$ such that $H_{k+1}^\infty \geq \delta$ for every solution with initial data as described above, then for every $\delta > 0$, we may find a solution with such initial data such that $H_{k+1}^\infty < \delta$. By a translation of time, we may assume that $H_{k+1}(t) \leq \delta$, $t \geq 0$ for $0 < \delta < \frac{1}{e_{k+1}}$ to be determined later. Then $H_j, P_j \rightarrow 0$, $j \geq k+2$ and $P_{k+1} \rightarrow 0$. Now, using that (b, k) holds, we apply Lemma 3.0.11. The subsystem with $H_i = 0$, $P_i = 0$, $k+1 \leq i \leq n$ has a unique positive equilibrium by Proposition 3.0.4. See Remark 3.0.5. The equation for H_{k+1} is

$$\frac{H'_{k+1}}{H_{k+1}} = r_{k+1} - \sum_{j=1}^k a_j H_j - \sum_{j=k+1}^n a_j H_j - P_{k+1}$$

Integrating, we have

$$\frac{1}{t} \log \frac{H_{k+1}(t)}{H_{k+1}(0)} = \sum_{j=1}^{k+1} a_j [H_j]_t + O(1/t)$$

By (3.12) and Lemma 3.0.11, we have that for all large t

$$\sum_{j=1}^k a_j [H_j] = \sum_{j=1}^k a_j H_j^* + O(\delta) = \tilde{Q}_n + O(\delta).$$

Since $H_{k+1}(t) \leq \delta$, $[H_{k+1}]_t = O(\delta)$. Now, $\tilde{Q}_n > 0$ so by choosing δ sufficiently small and an appropriate solution, we can ensure that the right hand side is bounded below by a positive constant for all large t , implying that $H_{k+1}(t)$ is unbounded. This contradiction completes our proof that (b, k) implies $(a, k+1)$. Thus, our proof is complete by mathematical induction. $\square$

Global Dynamics

In this section we employ a standard Lyapunov function to our systems to obtain some results on global behavior of solutions. Let $U(x, x^*) = x - x^* - x^* \log x/x^*$, $x, x^* > 0$,

be the familiar Volterra function and let

$$V = \sum_i c_i U(H_i, H_i^*) + \sum_i d_i U(P_i, P_i^*)$$

where positive numbers $c_1, \dots, c_n$ and $d_1, \dots, d_n$ are to be determined and

$E^* = (H_1^*, \dots, H_n^*, P_1^*, \dots, P_N^*)$ is the positive equilibrium of either the NIN or OIN system. For suitable choices of the c_i and d_i , we get

$$\dot{V} = \begin{pmatrix} -a^2 \left(\sum_i H_i - \sum_i H_i^* \right)^2, & \text{for NIN if } a_i = a, 1 \leq i \leq n \\ - \left(\sum_i a_i H_i - \sum_i a_i H_i^* \right)^2, & \text{for OIN} \end{pmatrix}$$

From the nonnegativity of $\dot{V}$, we conclude that E^* is locally stable (see Theorem X.1.1 in Hale (1980)) but more can be deduced from an application of the LaSalle invariance principle (see e.g. Theorem 2.6.1 in Hofbauer and Sigmund (1998)). Our result for the NIN system is the following.

Theorem 3.0.15. *Assume that (3.6) and (3.5) hold for the (NIN) system, and $a_j = a > 0$, $1 \leq j \leq n$. Then E^* is globally asymptotically stable relative to the open positive orthant of $\mathbb{R}_+^{2n}$.*

With the same assumptions, but $H_i^\dagger, V_i^\dagger$ replacing H_i^*, V_i^* and additionally $P_n \equiv 0$, $E^\dagger$ is globally asymptotically stable relative to the open positive orthant of $\mathbb{R}_+^{2n-1}$.

The simulation depicted in Figure 3.1 suggests that if the a_i are not identical, the conclusions of Theorem 3.0.15 may not hold.

Our result for the OIN system is weaker but does not require identical a_i .

Theorem 3.0.16. *The ω -limit set of a positive solution of (3.10) is either E^* or it consists of non-constant entire orbits, $(H(t), P(t))$, satisfying all of the following:*

$$(a) \sum_{i=1}^n a_i H_i(t) = \sum_{i=1}^n a_i H_i^*, \quad t \in \mathbb{R}.$$

(b) $\prod_{i=1}^n P_i(t)^{a_i/e_i n_i}$ is independent of t .

(c) $\forall i, (H_i(t), P_i(t))$ is a positive solution of the conservative planar system

$$H'_i = H_i (P_i^* - P_i) \quad (3.17)$$

$$P'_i = e_i n_i P_i (H_i - H_i^*).$$

In the special case that $n = 2$, since $H_1(P_1)$ can be expressed in terms of $H_2(P_2)$, on $\{(H, V) : \dot{V} = 0\}$, every solution in an omega limit set is periodic (possibly constant).

All simulations of the OIN system that we have attempted suggest that solutions converge to E^* .

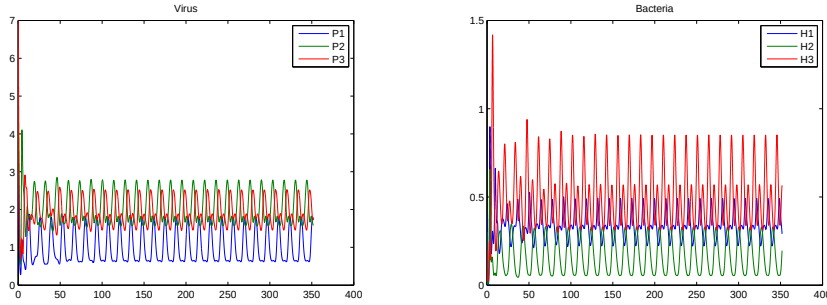


Figure 3.1: NIN Simulation with $n = 3$ and Parameters: $r_1 = 6, r_2 = 5, r_3 = 3, e_1 = 3, e_2 = 2, e_3 = 1, n_1 = n_2 = n_3 = 1, a_1 = 1, a_2 = 3, a_3 = 0.5$.

First, consider the NIN system. Since positive equilibrium E^* exists we can write the system as

$$H'_i = H_i \left(\sum_{j=1}^n a_j (H_j^* - H_j) + \sum_{j \geq i} (P_j^* - P_j) \right) \quad (3.18)$$

$$P'_i = e_i n_i P_i \left(\sum_{j \leq i} (H_j - H_j^*) \right), \quad 1 \leq i \leq n.$$

Then the derivative of V along solutions of (3.18), $\dot{V}$, is given by

$$\begin{aligned}\dot{V} = & - \left(\sum_i c_i (H_i - H_i^*) \right) \left(\sum_j a_j (H_j - H_j^*) \right) - \sum_i c_i (H_i - H_i^*) \sum_{j \geq i} (P_j - P_j^*) \\ & + \sum_i d_i e_i n_i (P_i - P_i^*) \sum_{j \leq i} (H_j - H_j^*)\end{aligned}$$

We aim to choose parameters so that the last two terms cancel each other. The second summation may be rewritten as $\sum_i (P_i - P_i^*) \sum_{j \leq i} c_j (H_j - H_j^*)$ so that the last two sums may be combined as $\sum_i (P_i - P_i^*) \sum_{j \leq i} (d_i e_i n_i - c_j) (H_j - H_j^*)$. It vanishes if $\forall i, d_i e_i n_i - c_j = 0, j \leq i$. Taking $i = n$, we see that the c_j must be identical so $c_j = a$ for all j for some $a > 0$ and $d_i = a/e_i n_i$. Therefore, in this case, we have

$$\dot{V} = - \left(\sum_i a (H_i - H_i^*) \right) \left(\sum_j a_j (H_j - H_j^*) \right)$$

If, in addition, $a_j = a$ for all j , then we have

$$\dot{V} = -a^2 \left(\sum_i H_i - \sum_i H_i^* \right)^2 \quad (3.19)$$

Similarly for the (OIN) system. Using the positive equilibrium E^* , we can write the system as

$$\begin{aligned}H_i' &= H_i \left(\sum_{j=1}^n a_j (H_j^* - H_j) + P_i^* - P_i \right) \\ P_i' &= e_i n_i P_i (H_i - H_i^*), \quad 1 \leq i \leq n.\end{aligned} \quad (3.20)$$

Then the derivative of V along solutions of (3.20), $\dot{V}$, is given by

$$\begin{aligned}\dot{V} = & - \left(\sum_i c_i (H_i - H_i^*) \right) \left(\sum_j a_j (H_j - H_j^*) \right) - \sum_i c_i (H_i - H_i^*) (P_i - P_i^*) \\ & + \sum_i d_i e_i n_i (P_i - P_i^*) (H_i - H_i^*)\end{aligned}$$

Letting $c_i = a_i$ and $d_i = \frac{a_i}{e_i n_i}$ causes the last two summations to cancel each other out.

Therefore in this case we have

$$\dot{V} = - \left(\sum_i a_i H_i - \sum_i a_i H_i^* \right)^2 \quad (3.21)$$

Proof. Proof of Theorem 3.0.15. We first note that since

$$V(H(t), P(t)) \leq V(H(0), P(0)), t \geq 0,$$

for every positive solution of (3.18), each component is bounded above and below: $0 < p \leq x(t) \leq P, t \geq 0$, where $x = H_i, P_j$ and p, P may depend on the solution.

Consider a positive solution of (3.18). By LaSalle's invariance principle, every point in its (invariant) limit set L must satisfy $\sum_i H_i = \sum_i H_i^*$ since $L \subset \{(H, V) : \dot{V} = 0\}$. Since $V(x) \leq V(H(0), P(0))$ for all $x \in L$, L belongs to the interior of the positive orthant and it is bounded away (but maybe not uniformly) from the boundary of the orthant. We now consider a trajectory belonging to L ; until further notice, all considerations involve this solution. Notice that this solution satisfies

$$H'_i = H_i \left(\sum_{j \geq i} (P_j^* - P_j) \right) \quad (3.22)$$

$$P'_i = e_i n_i P_i \left(\sum_{j \leq i} (H_j - H_j^*) \right) \quad (3.23)$$

From (3.23), we see that $P'_n \equiv 0$ so $P_n(t)$ is constant. Then, $H'_n = H_n(P_n^* - P_n)$ so $H_n(t)$ is either converging exponentially fast to zero, blowing up to infinity, or identically constant depending on the value of P_n . The only alternative that is consistent with L being invariant, bounded, and bounded away from the boundary of the orthant is that $H_n(t)$ is constant and that $P_n = P_n^*$. As we use a similar argument repeatedly below, we refer to it as our standard argument.

Since H_n is constant and $\sum_i H_i$ is constant, equal to $\sum_i H_i^*$, then so is $\sum_{i \leq n-1} H_i$ a constant. But now we face the same dilemma as above with the equation (3.23) with

$i = n - 1$ since the sum in parentheses is constant. By our standard argument, the only alternative is that this constant is zero, i.e., that $\sum_{i \leq n-1} H_i = \sum_{i \leq n-1} H_i^*$ and $P_{n-1}(t)$ is constant. The former implies that

$$H_n = \sum_i H_i - \sum_{i \leq n-1} H_i = H_n^*.$$

Suppose that $1 < k \leq n$ and that $H_i(t) \equiv H_i^*$, $P_i(t) \equiv P_i^*$, $i \geq k$, hold. We claim that $H_{k-1}(t) \equiv H_{k-1}^*$, $P_{k-1}(t) \equiv P_{k-1}^*$. As $P_k(t)$ is constant, (3.23) implies that $\sum_{j \leq k} H_j(t) = \sum_{j \leq k} H_j^*$ and since $H_k = H_k^*$, it follows that $\sum_{j \leq k-1} H_j(t) = \sum_{j \leq k-1} H_j^*$. Notice that if $k = 2$, then the latter gives that $H_1 = H_1^*$. Now from (3.23), $P'_{k-1}(t) = 0$ so $P_{k-1}(t)$ is constant. This implies, by (3.22) and our standard argument, that $H'_{k-1} = 0$ and $P_{k-1}(t) = P_{k-1}^*$. If $k = 2$, we are done: $H_1 = H_1^*$, $P_1 = P_1^*$. If $k > 2$, then $\sum_{j \leq k-2} H_j(t) = \sum_{j \leq k-1} H_j(t) - H_{k-1}(t)$ is constant so from (3.23) and our standard argument we conclude that $P'_{k-2} = 0$ and that $\sum_{j \leq k-2} H_j(t) = \sum_{j \leq k-2} H_j^*$. The latter implies that

$$H_{k-1} = \sum_{j \leq k-1} H_j - \sum_{j \leq k-2} H_j = \sum_{j \leq k-1} H_j^* - \sum_{j \leq k-2} H_j^* = H_{k-1}^*.$$

This completes our proof of the claim. By induction, we conclude that $H_i(t) \equiv H_i^*$, $P_i(t) \equiv P_i^*$, $1 \leq i \leq n$, i.e., our solution is identical to E^* . Since we considered an arbitrary solution starting at a point of L , it follows that $L = \{E^*\}$. As our chosen solution was an arbitrary positive solution, we have established the result.

The arguments are nearly identical for the $E^\dagger$ case. From (3.22), $H'_n = 0$ since $P_n \equiv 0$, therefore the standard argument starts at $n - 1$ instead. $\square$

Proof. **Proof of Theorem 3.0.16.** We first note that since

$$V(H(t), P(t)) \leq V(H(0), P(0)), t \geq 0,$$

for every positive solution of (3.20), each component is bounded above and below: $0 < p \leq x(t) \leq P, t \geq 0$, where $x = H_i, P_j$ and p, P may depend on the solution.

Consider a positive solution of (3.20). By LaSalle's invariance principle, every point in its (invariant) limit set L must satisfy $\sum_i a_i H_i = \sum_i a_i H_i^*$ since $L \subset \{(H, V) : \dot{V} = 0\}$. As in the *NIN* case, L belongs to the interior of the positive orthant and it is bounded away from the boundary of the orthant. We now consider a trajectory belonging to L ; until further notice, all considerations involve this solution. Notice that this solution satisfies (3.17). Thus on L , the system decouples into n independent planar conservative systems, the positive solution of which is either periodic or is the positive equilibrium. See e.g. section 2.3 of Hofbauer and Sigmund (1998). Notice that $\sum_i \frac{a_i P_i'}{e_i n_i P_i} = \sum_i a_i (H_i - H_i^*) = 0$, consequently $\prod_{i=1}^n P_i(t)^{a_i/e_i n_i}$ is independent of t .

If $E^* \in L$, then $E^* = L$ since E^* is stable. Consequently, if $E^* \notin L$, then at least one of the (H_i, P_i) must be a non-trivial periodic orbit.

The arguments are nearly identical for the case that the solution satisfies $P_n \equiv 0$ and other coordinates positive. Lyapunov function V differs from the previous one only in that the sum goes from one to $n - 1$ in the second summation and $H_i^\dagger, V_i^\dagger$ replace H_i^*, V_i^* ; the choice of the c_i and d_i are as before. (3.21) is changed only in that superscript $\dagger$ replaces $*$.

We only note that the counterpart to (3.17) for $i = n$ reads $H_n' = 0$. As $\sum_i a_i (H_i - H_i^\dagger) = 0$ on the limit set and since any positive periodic limiting solution must satisfy $\int_0^T H_i dt = H_i^\dagger$, it follows that $H_n \equiv H_n^\dagger$.

□

Discussion

Jover *et al.* (2013) construct a Lotka-Volterra model of a balanced community consisting of bacterial host strains and virus strains in which the infection network relating each virus strain to the bacteria strains that it infects has a perfectly nested structure. They provide substantial evidence, but do not prove, that their model community is permanent (uniformly persistent) provided that (1) bacteria strains with greater specific growth rate

devote less effort to defence against infection and (2) virus strains that are more efficient at infecting host have smaller host range. Their model has the degenerate feature that in the absence of virus, there is a continuum (a simplex) of coexistence equilibria for the competing bacteria strains. We have modified their model to remove this degeneracy in such a way that competitive interactions among bacteria are identical for each strain. We succeed in showing permanence for the modified model assuming the trade-offs (1) and (2). Permanence is also established for a one-to-one infection network in which each virus specializes on infecting a single host strain and where we do not require the tradeoffs. In both cases, time averages of positive solutions are shown to converge to a unique coexistence equilibrium.

Using a standard Lyapunov function and the LaSalle invariance principle, we have additionally shown that for the special case when our perfectly nested Lotka-Volterra model has identical inter- and intra-specific bacterial competition coefficients, and satisfies (1) and (2), then the coexistence equilibrium is globally asymptotically stable. However, when the inter- and intra-specific competition coefficients between bacteria are not identical, the coexistence equilibrium may not be attracting, as seen in Figure 3.1. In the case of the one-to-one infection network model, we show that the dynamics restricted to the omega limit set of every positive solution is governed by a conservative system consisting of uncoupled planar Lotka-Volterra host-virus equations.

Chapter 4

PERMANENCE AND STABILITIES OF A KILL THE WINNER MODEL IN MARINE ECOLOGY

Introduction

We focus on the long term dynamics of “kill the winner” Lotka-Volterra models of marine communities consisting of bacteria, virus, and zooplankton. Under suitable conditions, it is shown that there is a unique equilibrium with all populations present which is stable, the system is permanent, and the limiting behavior of its solutions is strongly constrained.

It is now known that the microbial and viral communities in marine environments are remarkably diverse but are supported by relatively few nutrients in very limited concentrations Suttle (2007); Weitz (2016). What can explain the observed diversity? What prevents the most competitive bacterial strains from achieving large densities at the expense of less competitive strains? Thingstad and Lignell (1997); Thingstad (2000); Winter *et al.* (2010); Thingstad *et al.* (2014) has suggested that virus impose top down control of bacterial densities. Together with various coauthors, Thingstad has described an idealized food web consisting of bacteria, virus and zooplankton to illustrate mechanisms of population control, referred to as “killing the winner” since any proliferation of a “winning” bacterial strain results in increased predation by some virus. The kill the winner (KtW) mathematical model of this scenario, in the form of a system of Lotka-Volterra equations for bacterial, virus, and zooplankton densities is, as noted by Weitz (2016), based on the assumptions that (1) all microbes compete for a common resource, (2) all microbes, except for one population, are susceptible to virus infection, (3) all microbes are subjected to zooplankton grazing, (4) viruses infect only a single type of bacteria.

Various forms of the KtW model have appeared in the work of Thingstad and Lignell (1997); Thingstad (2000); Winter *et al.* (2010); Thingstad *et al.* (2014) and recently in the monograph of Weitz (2016). As the nutrient level can be assumed to be in quasi-steady state with consumer densities, the models typically involve only the n bacteria types, $n - 1$ virus types, and a single zooplankton. While the literature contains many numerical simulations of KtW solutions, very little is known about the long term behavior of these solutions. It is the aim of this chapter to initiate a mathematical analysis of this important model system. We will show that the equilibrium with all populations present is unique and stable to small perturbations, that the system is permanent in the sense that all population densities are ultimately bounded away from extinction by an initial condition independent positive quantity, and that the long-term average of each population's density is precisely equal to its corresponding positive equilibrium value. In addition, we are able to provide some qualitative information about the long term dynamics. It is shown that the zooplankton density and the density of the bacterial strain resistant to virus infection converge to their equilibrium value. Furthermore, if a solution does not converge to the positive equilibrium, then its long-term dynamics can be described by an uncoupled system consisting of $n - 1$ conservative two-species systems involving each virus-susceptible bacteria and its associated virus. This implies that non-convergent solutions are, at worst, quasi-periodic.

Thingstad notes in Thingstad (2000) that a weakness of the killing the winner hypothesis is the assumption (4) that each virus infects only a single type of bacteria. Indeed, recent data Flores *et al.* (2013); Jover *et al.* (2013); Weitz (2016) suggests that some viruses have large host range. We will also show that most of our conclusions stated above hold without the restriction (4). For example, they hold for a nested infection network.

The results described above allow one to determine a plausible route by which a KtW community (satisfying (1) – (4)) consisting of n bacterial strains, $n - 1$ virus strains, and a single non-specific zooplankton grazer might be assembled starting with a community

consisting of a single bacteria and its associated virus and subsequently adding one new population at a time until the final community is achieved. By a plausible route, we require that each intermediate community be permanent Hofbauer and Sigmund (1998), also called uniformly persistent Smith and Zhao (2001); Thieme (1993); Smith and Thieme (2011), since a significant time period may be required to make the transition from one community to the next in the succession and therefore each community must be resistant to extinctions of its members, as noted in Law and Morton (1996). In Korytowski and Smith (2015a, 2017b), considering only bacteria and virus communities, we established a plausible route to the assembly of a community consisting of n bacterial strains and either n or $n - 1$ virus strains in which the infection network is one to one under suitable conditions. See also Haerter *et al.* (2014) although they did not infer permanence. Therefore, since we merely need to add zooplankton to community consisting of n bacteria and $n - 1$ virus, the main result of this chapter ensures that there is a plausible assembly path to the KtW community.

In the next section, we formulate our KtW model and state our main results. Technical details are include in a final section.

The KtW Model

Our KtW model, consisting of $n \geq 2$ bacterial types, $n - 1$ virus types and one zooplankton, is patterned after equations (7.28) in Weitz (2016) with slight changes. Densities of bacteria strains are denoted by B_i , virus strains by V_i , and zooplankton by Y . The difference in our model and (7.28) is in the way that inter and intra-specific competition among bacteria is modeled. We assume that the density dependent reduction in growth rate due to competition is identical for all bacterial strains as in Korytowski and Smith (2015a,b, 2017b). Virus strain V_i infects bacterial strain B_i for $i \neq n$ but B_n is resistant to virus infection. Zooplankton graze on bacteria at a strain independent rate. Virus adsorption rate is ϕ_i and burst size is β_i ; w represents a common loss rate. The equations follow.

$$\begin{aligned}
B'_i &= B_i(r_i - w - aB) - B_i\phi_i V_i - \alpha B_i Y, \\
V'_i &= V_i(\beta_i \phi_i B_i - k_i - w), \quad 1 \leq i \leq n-1 \\
B'_n &= B_n(r_n - w - aB) - \alpha B_n Y \\
Y' &= Y(\alpha \rho B - w - m),
\end{aligned} \tag{4.1}$$

where $B = \sum_j B_j$ is the sum of all bacterial densities.

It is convenient to scale variables as:

$$P_i = \phi_i V_i, \quad H_i = a B_i, \quad Z = \alpha Y,$$

and parameters as

$$n_i = \beta_i \phi_i / a, \quad \lambda = \alpha \rho / a, \quad e_i = \frac{k_i + w}{n_i}, \quad q = \frac{w + m}{\lambda}.$$

This results in the following scaled system where $H = \sum_j H_j$:

$$\begin{aligned}
H'_i &= H_i(r_i - w - H) - H_i P_i - H_i Z, \\
P'_i &= n_i P_i (H_i - e_i), \quad 1 \leq i \leq n-1 \\
H'_n &= H_n(r_n - w - H) - H_n Z \\
Z' &= \lambda Z (H - q).
\end{aligned} \tag{4.2}$$

Only positive solutions of (4.2) with $H_i(0) > 0, P_j(0) > 0, Z(0) > 0$ for all i, j are of interest. It is then evident that $H_i(t) > 0, P_j(t) > 0, Z(t) > 0$ for all t and i, j .

There is a unique positive equilibrium E^* if and only if the virus-resistant microbe H_n has the lowest growth rate among the bacteria

$$w < r_n < r_j, \quad 1 \leq j \leq n-1, \tag{4.3}$$

and if

$$\sum_{i=1}^{n-1} e_i < q < r_n - w. \quad (4.4)$$

Then E^* is given by

$$H_j^* = e_j, P_j^* = r_j - r_n, j \neq n, H_n^* = q - \sum_{i=1}^{n-1} e_i, Z^* = r_n - w - q.$$

Evidently, (4.4) requires that each virus strain controls the population density of its targeted bacterial strain such that the zooplankton cannot be maintained without the presence of the resistant strain, which cannot grow too slowly.

Our main result follows. We assume that (4.3) and (4.4) hold.

Theorem 4.0.1. *E^* is a stable equilibrium and the system is permanent in the sense that there exists $\epsilon > 0$ such that every positive solution satisfies:*

$$H_i(t) > \epsilon, P_j(t) > \epsilon, Z(t) > \epsilon, t > T \quad (4.5)$$

for all i, j where $T > 0$, but not ϵ , depends on initial conditions.

The long term time average of each population is its equilibrium value:

$$\lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t X(s) ds = X^*, X = H_i, P_j, Z, \quad (4.6)$$

and $H_n(t)$ and $Z(t)$ converge to their equilibrium values H_n^* and Z^* .

Moreover, a positive solution either converges to E^* or its omega limit set consists of non-constant positive entire trajectories satisfying $\sum_{i=1}^n H_i(t) = \sum_{i=1}^n H_i^*$, $H_n(t) = H_n^*$, $Z(t) = Z^*$, and where $(H_i(t), P_i(t))$ is a positive solution of the classical Volterra system

$$H_i' = H_i(P_i^* - P_i) \quad (4.7)$$

$$P_i' = n_i P_i (H_i - H_i^*), 1 \leq i \leq n-1.$$

As advertised in the introduction, Theorem 4.0.1 says that the KtW equilibrium is unique and stable to perturbations. More importantly, the system is permanent in the sense

that all population densities are ultimately bounded away from extinction by an initial condition independent positive quantity. The zooplankton density and the density of the bacterial strain resistant to virus infection converge to their equilibrium values and if a solution does not converge to the positive equilibrium, then its long-term dynamics is described by the system consisting of $n - 1$ conservative two-species systems (4.7). The latter would imply that H_i, P_i are periodic with period depending on parameters and its amplitude. However, the restriction $\sum_{i=1}^n H_i(t) = \sum_{i=1}^n H_i^*$ requires a very special resonance among the periods, suggesting that this alternative is unlikely.

Of course, our KtW model (4.1) is very special. Our aim was not to offer a general KtW model. Rather, it was to say as much as we could about the long term dynamics of a KtW model and for that, we made simplifying assumptions. Most of these assumptions are also made in the system (7.28) in Weitz (2016) and in similar models in the literature Flores *et al.* (2013); Jover *et al.* (2013). It should be noted that our main result, that the KtW model is permanent, continues to hold for sufficiently small changes in system parameters Smith and Zhao (2001).

Finally, we note that the main results of our earlier work Korytowski and Smith (2015b), in which we were concerned only with bacteria-virus infection networks, can be applied to obtain results similar to Theorem 4.0.1 for KtW models with more general infection networks than the one to one network. For example, our scaled model for the nested infection network consisting of n bacteria strains and n virus strains in Korytowski and Smith (2015b) is the following:

$$\begin{aligned} H'_i &= H_i \left(r_i - \sum_{j=1}^n H_j - \sum_{j \geq i} P_j \right) \\ P'_i &= e_i n_i P_i \left(\sum_{j \leq i} H_j - \frac{1}{e_i} \right), \quad 1 \leq i \leq n. \end{aligned} \tag{4.8}$$

To compare with (4.2), set $Z = P_n$ and regard it as a zooplankton grazer. Also, we must view the r_i as $r_i - w$, $n_i = k_i + w$, and $e_i = \beta_i \phi_i / n_i$, viewed as the efficiency of virus

infection of bacteria, is comparable to the reciprocal of its value in (4.2). The existence of a positive equilibrium for (4.8) requires life history trade-offs of bacteria and virus strains. Bacteria that are more susceptible to virus infection must grow faster

$$r_1 > r_2 > \cdots > r_n > Q_n, \quad (4.9)$$

and the efficiency of virus infection should decline as its host range increases:

$$e_1 > e_2 > e_3 > \cdots > e_n. \quad (4.10)$$

Here, $Q_n = \frac{1}{e_1} + \left(\frac{1}{e_2} - \frac{1}{e_1}\right) + \left(\frac{1}{e_3} - \frac{1}{e_2}\right) + \cdots + \left(\frac{1}{e_n} - \frac{1}{e_{n-1}}\right)$. If (4.9) and (4.10) hold, there is a unique positive equilibrium E^* and all positive solutions converge to it Korytowski and Smith (2015b). By simply renaming $Z = P_n$ and regarding it is a zooplankton, we obtain an even stronger result than Theorem 4.0.1 for the KtW model with nested infection network provided these tradeoffs hold. Quite arbitrary infection networks among bacteria and phage might be treated using the approach in Korytowski and Smith (2017a).

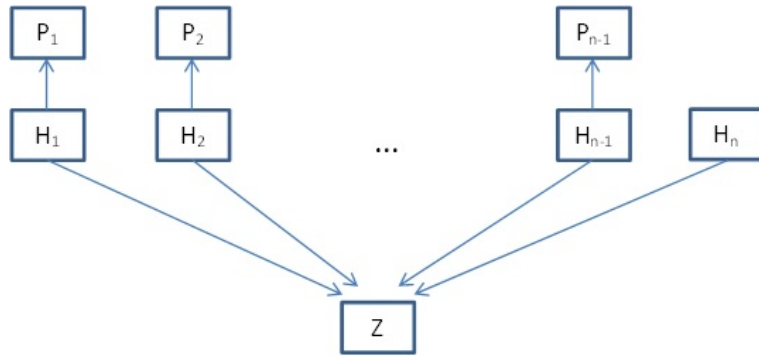


Figure 4.1: Interactions between the $n-1$ virus strains, n host strains, and the zooplankton.

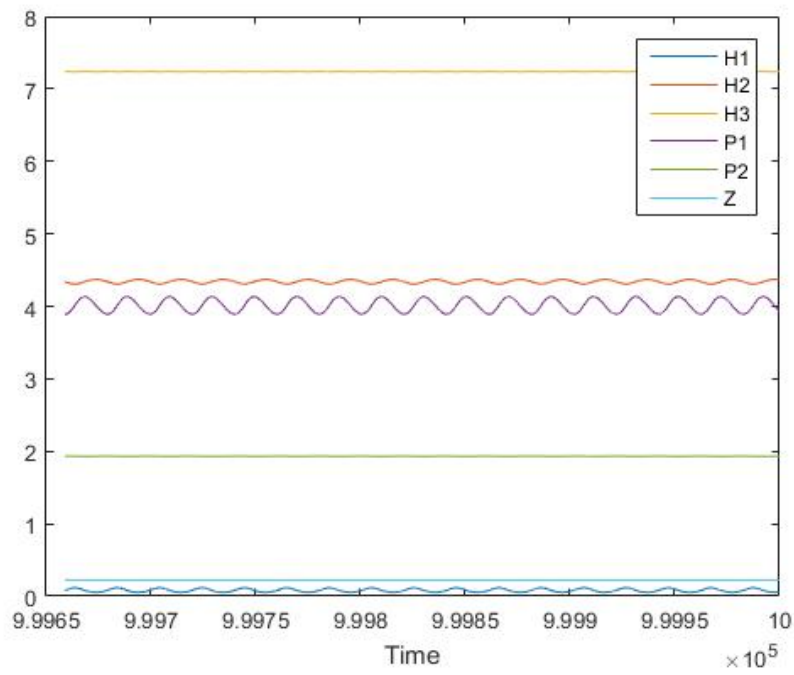


Figure 4.2: Last 1000 time units of a 1 million run on a population of 3 bacteria, 2 virus, and one zooplankton using ode45. Parameters specified in the figure are chosen to satisfy conditions (4.3), and (4.4), and are not intended to be biologically realistic. Solutions are highly oscillatory, and seem to be periodic.

Proof of Main Result

Proposition 4.0.2. *Solutions of (4.2) with nonnegative (positive) initial data are well-defined for all $t \geq 0$ and remain nonnegative (positive). In addition, the system has a compact global attractor. Indeed, if $F(t) = \sum_{i=1}^n H_i(t) + \sum_{i=1}^{n-1} \frac{P_i(t)}{n_i} + \frac{Z}{\lambda}$ then*

$$F(t) \leq \frac{Q}{W} + (F(0) - \frac{Q}{W})e^{-Wt} \leq \max\{F(0), \frac{Q}{W}\},$$

and

$$\limsup_{t \rightarrow \infty} F(t) \leq \sum_{i=1}^n (1 + \frac{r_i}{W})r_i,$$

where $K = \max_{i=1}^n \{H_i(0), r_i\}$, $W = \min_{i=1}^n \{e_i, w, q\}$ and $Q = \sum_{i=1}^n (W + r_i)K$.

Proof. Existence and positivity of solutions follow from the form of the right hand side.

Therefore, $H'_i(t) \leq H_i(t)(r_i - H_i(t))$. Hence $H_i(t) \leq K$ and $\limsup_{t \rightarrow \infty} H_i(t) \leq r_i$.

$$\begin{aligned} \frac{dF}{dt} &= \sum_{i=1}^n (r_i - w)H_i - (\sum_{i=1}^n H_i)(\sum_{j=1}^n H_j) - \sum_{i=1}^n P_i e_i - Zq \\ &\leq \sum_{i=1}^n r_i H_i - W \sum_{i=1}^n (H_i + \frac{P_i}{e_i n_i} + Z) \\ &= \sum_{i=1}^n (W + r_i)H_i - WF. \end{aligned}$$

The estimate on $F(t)$ follows by bounding the first summation by Q and integrating; the estimate on the limit superior follows from the estimate of the limit superior of the H_i above and by integration. □

Proof. **Proof of Theorem 4.0.1.** Since positive equilibrium E^* exists, we can write (4.2) as

$$\begin{aligned}
H'_i &= H_i \left(\sum_{j=1}^n (H_j^* - H_j) + P_i^* - P_i + Z^* - Z \right) \\
H'_n &= H_n \left(\sum_{j=1}^n (H_j^* - H_j) + (Z^* - Z) \right) \\
P'_i &= n_i P_i (H_i - H_i^*), \quad 1 \leq i < n \\
Z' &= Z \lambda \sum_{i=1}^n (H_i - H_i^*)
\end{aligned} \tag{4.11}$$

Then the derivative of V along solutions of (4.11), $\dot{V}$, is given by

$$\begin{aligned}
\dot{V} &= - \left(\sum_i^n c_i (H_i - H_i^*) \right) \left(\sum_j^n (H_j - H_j^*) \right) \\
&\quad - \sum_i^{n-1} c_i (H_i - H_i^*) (P_i - P_i^*) \\
&\quad - \sum_i^n c_i (H_i - H_i^*) (Z - Z^*) + \sum_i^{n-1} d_i n_i (P_i - P_i^*) (H_i - H_i^*) \\
&\quad + \sum_i^n g \lambda (Z - Z^*) (H_i - H_i^*)
\end{aligned}$$

If $c_i = 1$, $g = \frac{1}{\lambda}$, and $d_i = \frac{1}{n_i}$ then the last four summations cancel out and we have

$$\dot{V} = - \left(\sum_i H_i - \sum_i H_i^* \right)^2 \tag{4.12}$$

As $\dot{V} \leq 0$, E^* is locally stable Hale (1980) and for each positive solution there exists $p, P > 0$ such that $p \leq x(t) \leq P, t \geq 0$, where $x = H_i, P_j, Z$. Then (4.6) follows immediately from Theorem 5.2.3 in Hofbauer and Sigmund (1998).

Consider a positive solution of (4.11). By LaSalle's invariance principle Hale (1980); Hofbauer and Sigmund (1998), every point in its omega limit set L must satisfy $\sum_i H_i(t) = \sum_i H_i^*$ since $L \subset \{(H, V) : \dot{V} = 0\}$. Since $V(x) \leq V(H(0), P(0))$ for all $x \in L$,

L is a compact subset of the interior of the positive orthant. We now consider a trajectory belonging to L ; until further notice, all considerations involve this solution. Since $\sum_i H_i(t) = \sum_i H_i^*$, the solution satisfies

$$H'_i = H_i(P_i^* - P_i + Z^* - Z) \quad (4.13)$$

$$P'_i = n_i P_i(H_i - H_i^*), \quad 1 \leq i \leq n-1$$

$$H'_n = H_n(Z^* - Z)$$

$$Z' = 0$$

We see that $Z' \equiv 0$, therefore $Z(t)$ is a constant. Then, $H'_n = H_n(Z^* - Z)$ so $H_n(t)$ either converges to zero, blows up to infinity, or is identically constant, depending on the value of Z . The only alternative consistent with L being invariant, bounded, and bounded away from the boundary of the orthant is that $H_n(t)$ is constant and that $Z = Z^*$. By (4.6), it follows that $H_n = H_n^*$. Therefore (4.13) becomes:

$$H'_i = H_i(P_i^* - P_i) \quad (4.14)$$

$$P'_i = n_i P_i(H_i - H_i^*), \quad 1 \leq i \leq n-1$$

$$H_n = H_n^*$$

$$Z = Z^*$$

This establishes the assertions regarding (4.7). Note that as (4.14) holds on the limit set L of our positive solution, it follows that $H_n(t) \rightarrow H_n^*$, $Z(t) \rightarrow Z^*$ for our positive solution.

Finally, we prove (4.5). It follows from (4.6) that $\limsup_{t \rightarrow \infty} x(t) = x^*$, for each component $x = H_i, P_j, Z$ of an arbitrary positive solution of (4.11). This means that (4.11) is uniformly weakly persistent. Proposition 4.0.2 implies that the key hypotheses of Theorem 4.5 from Thieme (1993); Smith and Thieme (2011) are satisfied, and therefore weak uniform persistence implies strong uniform persistence. This is precisely (4.5). $\square$

Parameter	value
r_1	17.089453152634810
r_2	15.009830525061846
r_3	13.077955412892173
n_1	0.299362132425990
n_2	0.011514418415303
e_1	0.081255501212170
e_2	4.340892914457329
q	10.465564663600418
w	1.194565710732100
λ	4.474468552537804

Figure 4.3: Parameter Values Used in Figure 4.2

Chapter 5

CONCLUSION

In chapter 2, it was shown that a chemostat community of bacteria and bacteriophage in which bacteria compete for a single nutrient and for which the bipartite infection network is perfectly nested is permanent, a.k.a uniformly persistent, provided that bacteria that are superior competitors for nutrient devote the least to defence against infection and the virus that are the most efficient at infecting host have the smallest host range. This confirms earlier work of Jover *et al.* (2013) who raised the issue of whether nested infection networks are permanent. In addition, we provide sufficient conditions that a bacteria-phage community of arbitrary size with nested infection network can arise through a succession of permanent subcommunities each with a nested infection network by the successive addition of one new population.

In chapter 3, it was shown that a bacteria and bacteriophage system with either a perfectly nested or a one-to-one infection network is permanent, a.k.a uniformly persistent, provided that bacteria that are superior competitors for nutrient devote the least to defence against infection and the virus that are the most efficient at infecting host have the smallest host range. By ensuring that the density-dependent reduction in bacterial growth rates are independent of bacterial strain, the permanence conclusion sought by Jover *et al.* (2013) is shown. The same permanence results hold for the one-to-one infection network considered by Thingstad and Lignell (1997) but without virus efficiency ordering. Additionally global stability for the nested infection network, and the global dynamics for the one-to-one network are also shown.

In chapter 4. the long term dynamics of “kill the winner” Lotka-Volterra models of marine communities consisting of bacteria, virus, and zooplankton are analyzed. Under

suitable conditions, it is shown that there is a unique equilibrium with all populations present which is stable, the system is permanent, and the limiting behavior of its solutions is strongly constrained.

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APPENDIX A

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