

Extinctions Caused by Host-Range Expansion*

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Abstract. Nearly all emerging diseases in humans are a result of host-range expansion, in which a pathogen of one species evolves the ability to infect a new host species. To present a rigorous analysis of pathogen host-range expansion, we derive a Lotka–Volterra dynamical system with two competing host species and a single parasite species; the parasite infects only one of the host species. We provide a stability and bifurcation analysis of this model. We then ask what happens if the parasite evolves the ability to infect the alternate host, extending the model to include a parasite population with an expanded host range. We derive explicit global stability and bifurcation conditions for this four-dimensional model in terms of the system parameters. We demonstrate that only four outcomes may occur following the range expansion of a parasite or pathogen, and provide both local and global asymptotic stability conditions for these outcomes. While three of these outcomes were expected, the fourth is counterintuitive, predicting that host-range expansion can drive the original host species to extinction. For example, a native species could be driven to extinction by a longstanding native parasite if that parasite acquires the ability to infect a cultivated species. We briefly discuss the phenomena driving this unexpected prediction and its implications.

Key words. parasite, pathogen, host range, bifurcation theory, mathematical biology

MSC codes. 92D30, 37L10, 37N25

DOI. 10.1137/23M1605582

1. Introduction. The dynamic interaction between parasites and their hosts has been one of the richest and most significant topics in population modelling [2, 26], and remains of critical public health importance [4, 21, 22, 31]. While the underlying dynamical systems are often closely related to well-studied predator-prey models [5, 19, 20], host-parasite dynamics differ in a number of key aspects. In particular, with relatively short generation times and large population sizes, parasites often have immense adaptive potential, and can evolve rapidly to exploit new resources or avoid immune pressures [3, 17].

One of the most important consequences of this adaptive potential is that parasites can, and do, expand their host range [8, 9]. Nearly all emerging diseases in humans over the last

*Received by the editors September 28, 2023; accepted for publication (in revised form) by A. Layton March 2, 2024; published electronically June 25, 2024.

<https://doi.org/10.1137/23M1605582>

Funding: The work of the first author was supported by Natural Sciences and Engineering Research Council of Canada grant R2686A02. The work of the third author was supported by Australian Research Council grant DP210102463. The work of the fourth author was supported by Natural Sciences and Engineering Research Council of Canada grant RGPIN-2019-06294.

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century are zoonoses [15]; that is, they emerged when a parasite expanded its host range to humans. For this reason, public health authorities uniformly aim to minimize host-range expansion by potential pathogens [25, 37]. In contrast, the use of bacteriophages (viruses that infect bacteria) as therapeutic agents has necessitated the development of laboratory protocols that are specifically designed to increase parasite host range [32]. Recent work has highlighted an emerging view that host range is a dynamic feature of parasite species, including both rapid shifts to new hosts [1, 35] and the gain and loss of hosts over longer time scales [9].

Given the importance of host-range expansions to human health, ecosystem health, and biodiversity [1, 7, 9], realistic predictions of the long-term impacts of such expansions are essential. It has long been appreciated that when a parasite expands its range to infect a new host, the new host may be threatened by extinction. This has been discussed, for example, in the context of unintended range expansions for biocontrol agents [27] or other introduced pathogens [1], for plant pathogens [35], and for emerging infectious diseases of wildlife [7], including primates [30].

Despite this sustained interest in empirical studies of both ecological and disease dynamics, host-range expansion has been relatively understudied in rigorous mathematical models. Models that include a predator and two potential prey species have been well-studied, and these form a foundation for the host-range expansion model we develop here. For example, motivated by work demonstrating that a predator could stabilize the co-existence of two prey species [6, 28, 29], Hsu completed a global stability analysis of a system of two competing prey and a single predator [12]; a full bifurcation analysis followed [34]. This early model has been extended to include predator switching [13, 24] and spatial dimensions [14, 16], while impulsive [40] and delay [23] differential equation formulations have also been studied. The underlying model [12] has also been extended to study the stabilizing effects of predators in more generalized settings [10, 11, 33, 36]. In the absence of competition between species, global stability properties of both the two-predator one-prey and one-predator two-prey models are now known [18].

Building on this work, here we develop a model that allows for a rigorous study of host-range expansion. We begin by analyzing a system in which a parasite infects only one of two competing species. We then answer the question: what happens if a parasite evolves the ability to infect the alternate host? We delineate the range of outcomes that may occur following range expansion, providing both local and global asymptotic stability conditions for these outcomes. We demonstrate that when a parasite expands its range to infect a new host, the new host may be driven, deterministically, to extinction. While this result makes intuitive sense, our work reveals another surprising prediction: when a parasite expands its range to infect a new host, the new host may survive but the *original host may go extinct* as a result of the range expansion. The latter result is paradoxical, since the range expansion burdens the new species, a competitor of the original host.

In section 2, we present a simple Lotka–Volterra system with two competing host species and a single parasite species. In this three-dimensional (3-d) model, the parasite infects only one of the host species. We provide an analysis of the existence, stability, and bifurcations among the six equilibria of this model. In section 3, we extend this model to include a parasite population with an expanded host range, and find the equilibria of this four-dimensional model. In section 4 we examine the boundedness of solutions to these models, while in section 5 we provide global stability and bifurcation analyses of the four-dimensional model.

Section 6 uses these results to derive relevant conclusions about host-range expansion in natural settings. We conclude in section 7 with a brief discussion of the main results, focussing on the unexpected prediction described above.

2. Three-dimensional model: Before host-range expansion. We begin by deriving a simple host-parasite model that includes a focal species (species 1), and its parasite. We also include a competitor (species 2) of the focal species, which, for example, occupies a similar ecological niche. The competitor is a potential host for the parasite, but in this model we determine the dynamics when the parasite has not (yet) expanded its host range.

In this model, the density of each host population ($N_i, i \in \{1, 2\}$) has intrinsic growth rate r_i per unit time, and grows logistically with carrying capacity K_i . The parasite population, with density P , infects host N_1 with mass-action kinetics. To model obligately lethal parasites, infection occurs at rate $\alpha_1 N_1 P$ and kills the host. To model nonlethal parasites, we can take $\alpha_1 N_1 P$ to be the increased death rate (reduced lifespan) of hosts due to parasitism. The parameter β_1 is the conversion factor, at infection, between hosts and parasites. For example, if the parasite is a lytic virus infecting a bacterium, β_1 represents the burst size. We assume that the production of new parasites occurs instantaneously when hosts are infected, thus assuming that any delay in the production of parasites is negligible. In the absence of the host, the parasite population decays at per capita rate δ . In addition, species j reduces the growth rate of species i with mass action kinetics, described by competition coefficient γ_{ij} . These assumptions yield:

$$\begin{aligned}
 \text{host: } & \frac{dN_1}{dt} = r_1 N_1 \left(1 - \frac{N_1}{K_1} \right) - \alpha_1 N_1 P - \gamma_{12} N_1 N_2, \\
 \text{competitor: } & \frac{dN_2}{dt} = r_2 N_2 \left(1 - \frac{N_2}{K_2} \right) - \gamma_{21} N_1 N_2, \\
 \text{parasite: } & \frac{dP}{dt} = \beta_1 \alpha_1 N_1 P - \delta P.
 \end{aligned}
 \tag{1}$$

In the absence of the competitor, system (1) yields the standard Lotka–Volterra predator–prey model with a logistic growth term. For convenience, we provide equilibria and stability results for this reduced model in the Supplementary Material (section SM1). We also note that if the parasite could infect both hosts, system (1) would be equivalent to the two-prey-one-predator system studied in [12]. That study, however, used the predation rate on the second host (which is zero in our system) as a scaling parameter in the nondimensionalization.

In the Supplementary Material (M160558.01.pdf [local/web 1.54MB]), we demonstrate that system (1) can alternatively be nondimensionalized as

$$\begin{aligned}
 \frac{dN_1}{dt} &= r_1 N_1 \left(1 - \frac{N_1}{K_1} \right) - N_1 N_2 - N_1 P, \\
 \frac{dN_2}{dt} &= r_2 N_2 \left(1 - \frac{N_2}{K_2} \right) - N_1 N_2, \\
 \frac{dP}{dt} &= B N_1 P - P,
 \end{aligned}
 \tag{2}$$

which we will use as the basis for the analysis to follow. We will refer to system (2) as the “3-d model.”

The 3-d model has six equilibrium solutions:

$$(3) \quad E_k = (N_{1k}, N_{2k}, P_k), \quad k = 0, 1, 2, 3, 4, 5,$$

where

$$(4) \quad \begin{aligned} N_{10} = N_{20} = P_0 = 0, \quad N_{11} = K_1, \quad N_{21} = P_1 = 0, \quad N_{12} = P_2 = 0, \quad N_{22} = K_2, \\ N_{13} = \frac{K_1 r_2 (K_2 - r_1)}{g}, \quad N_{23} = \frac{K_2 r_1 (K_1 - r_2)}{g}, \quad P_3 = 0, \quad g = K_1 K_2 - r_1 r_2, \\ N_{14} = \frac{1}{B}, \quad N_{24} = 0, \quad P_4 = r_1 \left(1 - \frac{1}{BK_1} \right), \\ N_{15} = \frac{1}{B}, \quad N_{25} = K_2 \left(1 - \frac{1}{r_2 B} \right), \quad P_5 = r_1 \left(1 - \frac{1}{BK_1} \right) - N_{25} = r_1 - K_2 + \frac{g}{K_1 r_2 B}. \end{aligned}$$

We first consider the existence and stability conditions for the equilibrium solutions E_k , $k = 0, 1, 2, 3, 4$, and have the following result.

Theorem 2.1. *The equilibria E_0, E_1 and E_2 exist for positive parameter values. The equilibrium E_3 exists for $(K_2 - r_1)(K_1 - r_2) > 0$, and E_4 exists if $K_1 > \frac{1}{B}$. E_0 is always unstable; E_1 is locally asymptotically stable (LAS) for $r_2 < K_1 < \frac{1}{B}$; E_2 is LAS for $r_1 < K_2$; E_3 is LAS for $K_1 < \frac{1}{B} < r_2$, $K_2 < r_1$, or $\frac{1}{B} < K_1 < r_2$, $K_2 < r_1 < r_1^*$, where*

$$(5) \quad r_1^* = \frac{K_1 K_2 (B r_2 - 1)}{r_2 (B K_1 - 1)};$$

E_4 is LAS for $r_2 < \frac{1}{B}$ ($< K_1$). There are three transcritical bifurcations: one between E_1 and E_3 at $r_2 = K_1$; one between E_2 and E_3 at $r_1 = K_2$; and one between E_1 and E_4 at $K_1 = \frac{1}{B}$. No Hopf bifurcation or Bogdanov–Takens (B-T) bifurcation can occur from these first five equilibrium solutions.

The proof is given in section SM2.2. Next, we consider the equilibrium solution E_5 for which we have the following theorem.

Theorem 2.2. *The equilibrium E_5 exists if*

$$(6) \quad r_2 > \frac{1}{B}, \quad K_1 > \frac{1}{B}, \quad \text{and} \quad r_1 > r_1^*.$$

It is LAS for

$$(7) \quad \frac{1}{B} < K_1 \leq r_2, \quad r_1 > r_1^* \quad \text{or} \quad \frac{1}{B} < r_2 < K_1, \quad r_1 > r_{1H},$$

where

$$(8) \quad r_{1H} = \frac{K_1 (B r_2 - 1)}{2 r_2 [B (B K_1 - 1) + B r_2 - 1]} \left\{ (B + 1) K_2 - r_2 (B r_2 - 1) + \sqrt{[(B + 1) K_2 - r_2 (B r_2 - 1)]^2 + 4 r_2 K_2 [B (B K_1 - 1) + B r_2 - 1]} \right\}.$$

Moreover, E_5 is globally asymptotically stable (GAS) for $r_2 \geq K_1$ and $r_1 > r_1^*$. A transcritical bifurcation occurs between E_4 and E_5 at the critical point $r_2 = \frac{1}{B}$; another transcritical

bifurcation happens between E_3 and E_5 at the critical point $r_1 = r_1^*$. Hopf bifurcation occurs from E_5 at the critical point $r_1 = r_{1H}$, but B-T bifurcation cannot occur from E_5 .

Proof. The proof of existence and LAS conditions is provided in section SM2.2 of the Supplementary Material.

To prove that E_5 is GAS for $r_2 \geq K_1$ and $r_1 > r_1^*$, we construct the Lyapunov function:

$$V_{35} = N_1 - N_{15} - N_{15} \ln \frac{N_1}{N_{15}} + N_2 - N_{25} - N_{25} \ln \frac{N_2}{N_{25}} + \frac{1}{B} \left(P - P_5 - P_5 \ln \frac{P}{P_5} \right).$$

Then, computing the derivative of V_{35} with respect to time t , along the trajectory of system (2), we obtain

$$\begin{aligned} \frac{dV_{35}}{dt} \Big|_{(2)} &= \left(1 - \frac{N_{15}}{N_1} \right) \frac{dN_1}{dt} + \left(1 - \frac{N_{25}}{N_2} \right) \frac{dN_2}{dt} + \frac{1}{B} \left(1 - \frac{P_5}{P} \right) \frac{dP}{dt} \\ &= (N_1 - N_{15}) \left[r_1 \left(1 - \frac{N_1}{K_1} \right) - N_2 - P \right] + (N_2 - N_{25}) \left[r_2 \left(1 - \frac{N_2}{K_2} \right) - N_1 \right] \\ &\quad + \frac{1}{B} (P - P_5) (BN_1 - 1) \\ &= -\frac{r_1}{K_1} (N_1 - N_{15})^2 - (N_1 - N_{15})(N_2 - N_{25}) - (N_1 - N_{15})(P - P_5) \\ &\quad - \frac{r_2}{K_2} (N_2 - N_{25})^2 - (N_2 - N_{25})(N_1 - N_{15}) + (P - P_5)(N_1 - N_{15}) \\ &= -\frac{1}{K_1 r_1} [r_1(N_1 - N_{15}) + K_1(N_2 - N_{25})]^2 - \frac{r_1 r_2 - K_1 K_2}{K_2 r_1} (N_2 - N_{25})^2. \end{aligned}$$

For $r_2 \geq K_1$ and $r_1 > r_1^* = \frac{K_1 K_2 (B r_2 - 1)}{r_2 (B K_1 - 1)}$, it is easy to prove that

$$r_1 > r_1^* = K_2 \frac{B K_1 r_2 - r_2 + r_2 - K_1}{B K_1 r_2 - r_2} = K_2 \left[1 + \frac{r_2 - K_1}{r_2 (B K_1 - 1)} \right] \geq K_2,$$

yielding $r_1 r_2 > K_1 K_2$. Thus, $\frac{dV_{35}}{dt} \leq 0$, and equals zero only if $N_1 = N_{15}$ and $N_2 = N_{25}$, at which system (2) reduces to

$$\begin{aligned} 0 &= N_{15} \left[r_1 \left(1 - \frac{N_{15}}{K_1} \right) - N_{25} - P \right] = N_{15} (P_5 - P), \\ 0 &= N_{25} \left[r_2 \left(1 - \frac{N_{25}}{K_2} \right) - N_{15} \right] = 0, \\ \frac{dP}{dt} &= P (B N_{15} - 1) = 0. \end{aligned}$$

This implies that P is a constant, which is solved from the first equation as $P = P_5$, leading to the equilibrium E_5 . So, the GAS of E_5 is proved by the LaSalle's Invariance Principle.

When $r_2 < K_1$, we have $\frac{1}{B} < r_2 < K_1$ which ensures $r_1^* < r_1^{**} < r_{1H}$. Hence, E_5 is LAS when $r_1 > r_{1H}$; and unstable for $r_1 < r_{1H}$. Hopf bifurcation occurs at the critical point $r_1 = r_{1H}$. More precisely, we can use a direct calculation to prove that $\frac{K_1 K_2}{r_2} > r_{1H}$:

$$\begin{aligned} & \frac{K_1 K_2}{r_2} - r_{1H} \\ &= \frac{4K_1 K_2^2 B^2 (K_1 - r_2)}{4r_2^2 (Br_2 - 1)^2 + 4r_2 K_2 B^2 (K_1 - r_2) + 2r_2 (Br_2 - 1) \sqrt{[(B+1)K_2 - r_2 (Br_2 - 1)]^2 + 4r_2 K_2 [B(BK_1 - 1) + Br_2 - 1]}} \\ &> 0 \quad \text{due to } \frac{1}{B} < r_2 < K_1. \end{aligned}$$

Thus, E_5 is LAS but not GAS for $r_{1H} < r_1 \leq \frac{K_1 K_2}{r_2}$, and GAS for $r_1 > \frac{K_1 K_2}{r_2}$.

It seems that B-T bifurcation may occur from E_5 when $a_2 = a_3 = 0$, yielding two zero eigenvalues, by choosing $r_2 = \frac{1}{B}$ which gives $a_3 = 0$, with $r_1^* = r_1^{**} = 0$, then $a_2 = 0$ yields $K_1 = \frac{1}{B}$. If $r_2 = K_1 \neq \frac{1}{B}$ ($BK_1 > 1$), then $a_2 = a_3 = 0$ leads to $r_1 = r_1^* = r_1^{**} = K_2$. However, a careful check shows that these two zero eigenvalues form a semisimple case (i.e., the linearized system can still have two linearly independent eigenvectors corresponding to the two zero eigenvalues), not a double-zero eigenvalue (non-semi-simple case). Therefore, B-T bifurcation is not possible from the equilibrium E_5 . ■

We give an example of Hopf bifurcation from E_5 in the Supplementary Material (section SM2.3).

3. Four-dimensional model: After host-range expansion. We now expand system (1), assuming that the parasite has expanded its host range, such that some evolved parasite lineage can infect both the original host and the competitor. The expanded system has the following form:

$$(9) \quad \begin{aligned} \text{host:} & \quad \frac{dN_1}{dt} = r_1 N_1 \left(1 - \frac{N_1}{K_1}\right) - \alpha_1 N_1 P - (1-c)\alpha_1 N_1 Q - \gamma_{12} N_1 N_2, \\ \text{competitor:} & \quad \frac{dN_2}{dt} = r_2 N_2 \left(1 - \frac{N_2}{K_2}\right) - \alpha_2 N_2 Q - \gamma_{21} N_1 N_2, \\ \text{parasite:} & \quad \frac{dP}{dt} = \beta_1 \alpha_1 N_1 P - \delta P, \\ \text{evolved parasite:} & \quad \frac{dQ}{dt} = \beta_{21}(1-c)\alpha_1 N_1 Q + \beta_{22}\alpha_2 N_2 Q - \delta Q. \end{aligned}$$

Here, Q is the population density of the evolved parasite, which is able to infect the competitor species at rate α_2 . We note that α_2 could be greater than or less than α_1 , such that the evolved parasite is not necessarily well-adapted to the competitor. Similarly, the parameter $c \in (0, 1)$ is a potential cost to generalization, that is, the evolved parasite may not be able to infect the original host with full efficacy. The conversion rate (burst size) of the evolved parasite is β_{2i} after infecting host i , and we assume for simplicity that the decay rate of the evolved parasite, δ , is unchanged.

Once again, system (9) can be nondimensionalized (see Supplementary Material (M160558_01.pdf [local/web 1.54MB])) to yield

$$\begin{aligned} \frac{dN_1}{dt} &= r_1 N_1 \left(1 - \frac{N_1}{K_1}\right) - N_1 N_2 - N_1 P - \tilde{c} N_1 Q, \\ \frac{dN_2}{dt} &= r_2 N_2 \left(1 - \frac{N_2}{K_2}\right) - N_1 N_2 - A N_2 Q, \end{aligned}$$

$$(10) \quad \begin{aligned} \frac{dP}{dt} &= BN_1P - P, \\ \frac{dQ}{dt} &= \tilde{D}N_1Q + EN_2Q - Q. \end{aligned}$$

We will refer to system (10) as the “4-d model.”

The 4-d model admits 10 equilibrium solutions. For the convenience of the following analysis, denote the 10 equilibrium solutions as

$$(11) \quad E_k = (N_{1k} N_{2k}, P_k, Q_k), \quad k = 0, 1, \dots, 9,$$

where $Q_k = 0$, $k = 0, 1, \dots, 5$, while N_{1k} , N_{2k} , and P_k are given in (4), and

$$(12) \quad \begin{aligned} N_{16} &= \frac{1}{\tilde{D}}, \quad Q_6 = \frac{r_1}{\tilde{c}} \left(1 - \frac{1}{\tilde{D}K_1} \right), \quad N_{26} = P_6 = 0, \\ N_{27} &= \frac{1}{E}, \quad Q_7 = \frac{r_2}{A} \left(1 - \frac{1}{EK_2} \right), \quad N_{17} = P_7 = 0, \\ N_{18} &= \frac{N_{18n}}{E_{8d}}, \quad N_{28} = \frac{N_{28n}}{E_{8d}}, \quad Q_8 = \frac{Q_{8n}}{E_{8d}}, \quad P_8 = 0, \quad \text{in which} \\ N_{18n} &= K_1[EK_2(Ar_1 - \tilde{c}r_2) - (AK_2 - \tilde{c}r_2)], \\ N_{28n} &= K_2[(Ar_1 - \tilde{c}K_1) - K_1\tilde{D}(Ar_1 - \tilde{c}r_2)], \\ Q_{8n} &= g + \tilde{D}K_1r_2(r_1 - K_2) + EK_2r_1(r_2 - K_1), \\ E_{8d} &= \tilde{D}N_{18n} + EN_{28n}, \\ N_{19} &= \frac{1}{B}, \quad N_{29} = \frac{1}{BE}(B - \tilde{D}), \quad Q_9 = \frac{1}{ABEK_2} \{r_2[BEK_2 - B + \tilde{D}] - EK_2\}, \\ P_9 &= \left(1 - \frac{1}{BK_1} \right) \left[r_1 - \frac{K_1\{AK_2(B - \tilde{D}) + \tilde{c}[r_2(BEK_2 - B + \tilde{D}) - EK_2]\}}{AEK_2(BK_1 - 1)} \right]. \end{aligned}$$

Note that the first six equilibrium solutions, E_0 – E_5 , are those of the 3-d model with the addition of $Q = 0$.

4. Boundedness of solutions. In order to consider the global behavior of the models, we need to study the behavior of solutions and their boundedness. Positivity of solutions is easy to prove. Thus we only discuss the boundedness of the solutions for the 3-d and 4-d models in this section.

Unlike the *two-dimensional* (2-d) model which naturally has bounded solutions for all positive parameter values (see Supplementary Material (section SM1.2)), the 3-d and 4-d models need a condition on the parameters to guarantee boundedness. This condition certainly does not mean that the system cannot have solutions without this condition, but simply means that the solutions are not guaranteed to be bounded without this condition. In fact, we will see that if the LAS condition for an equilibrium satisfies (or includes) the boundedness condition, then it is GAS; while if the LAS condition does not satisfy the boundedness condition, then adding the condition to the LAS condition guarantees GAS of the equilibrium.

For the 3-d and 4-d models, we have the following result.

Theorem 4.1. *The trapping region for the solutions of the 3-d model (2) is defined as an elliptic paraboloid:*

$$(13) \quad \Omega_{3d} = \left\{ (N_1, N_2, P) \mid 0 \leq P \leq B \left[r_1 N_1 + r_2 N_2 - \frac{r_1}{K_1} N_1^2 - \frac{r_2}{K_2} N_2^2 - 2N_1 N_2 \right] \right\}$$

if the following condition is satisfied:

$$(14) \quad C_{bd}^{3d} \triangleq \frac{r_1 r_2}{K_1 K_2} - 1 > 0.$$

For the 4-d model (10), the trapping region is defined as an hyperelliptic paraboloid:

$$(15) \quad \Omega_{4d} = \left\{ (N_1, N_2, P, Q) \mid 0 \leq P + \frac{\tilde{c}B}{\tilde{D}} Q \leq B \left[\frac{r_1}{K_1} N_1^2 + \frac{\tilde{c}E}{\tilde{D}A} \frac{r_2}{K_2} N_2^2 + \left(1 + \frac{\tilde{c}E}{\tilde{D}A} \right) N_1 N_2 - \left(r_1 N_1 + \frac{\tilde{c}E}{\tilde{D}A} r_2 N_2 \right) \right] \right\}$$

if the following condition holds:

$$(16) \quad C_{bd}^{4d} \triangleq \frac{r_1 r_2}{K_1 K_2} - \frac{(\tilde{D}A + \tilde{c}E)^2}{4\tilde{c}\tilde{D}AE} > 0.$$

Proof. For the 3-d model (2), we construct the Lyapunov function:

$$(17) \quad V_{3d} = N_1 + N_2 + \frac{1}{B} P,$$

which is a positive definite and radially unbounded function of the system state variables. By a direct calculation, we obtain

$$(18) \quad \begin{aligned} \left. \frac{dV_{3d}}{dt} \right|_{(2)} &= \frac{dN_1}{dt} + \frac{dN_2}{dt} + \frac{1}{B} \frac{dP}{dt} \\ &= r_1 N_1 \left(1 - \frac{N_1}{K_1} \right) - N_1 N_2 - N_1 P + r_2 N_2 \left(1 - \frac{N_2}{K_2} \right) - N_1 N_2 + \frac{1}{B} P (BN_1 - 1) \\ &= - \left[\frac{r_1}{K_1} N_1^2 + \frac{r_2}{K_2} N_2^2 + 2N_1 N_2 - (r_1 N_1 + r_2 N_2) + \frac{1}{B} P \right]. \end{aligned}$$

Then, $\left. \frac{dV_{3d}}{dt} \right|_{(2)} = 0$ defines a boundary, as given in (13), and $\left. \frac{dV_{3d}}{dt} \right|_{(2)} < 0$ if trajectories are outside this boundary, implying that all trajectories are attracted to Ω_{3d} . To guarantee that the base of the elliptic paraboloid is an ellipse, rather than a hyperbola (unbounded), we will show that the condition (14) is needed.

Similarly, for the 4-d model (10), we construct the following Lyapunov function:

$$(19) \quad V_{4d} = N_1 + \frac{\tilde{c}E}{\tilde{D}A} N_2 + \frac{1}{B} P + \frac{\tilde{c}}{\tilde{D}} Q$$

to obtain

$$(20) \quad \left. \frac{dV_{4d}}{dt} \right|_{(10)} = - \left[\frac{r_1}{K_1} N_1^2 + \frac{\tilde{c}E}{\tilde{D}A} \frac{r_2}{K_2} N_2^2 + \left(1 + \frac{\tilde{c}E}{\tilde{D}A} \right) N_1 N_2 - \left(r_1 N_1 + \frac{\tilde{c}E}{\tilde{D}A} r_2 N_2 \right) + \frac{1}{B} P + \frac{\tilde{c}}{\tilde{D}} Q \right].$$

Then, $\left. \frac{dV_{4d}}{dt} \right|_{(10)} = 0$ defines the boundary given in (15).

To derive the conditions (14) and (16), we need only consider the quadratic form in the square bracket of (18) and (20) involving N_1 and N_2 , and write them in the general form of

$$(21) \quad \tilde{Q} = C_1 N_1^2 + C_2 N_2^2 + C_3 N_1 N_2 - C_4 N_1 - C_5 N_2, \quad C_k > 0, \quad k = 1, 2, \dots, 5,$$

where C_k denote, respectively, the coefficients of N_1^2 , N_2^2 , $N_1 N_2$, N_1 , and N_2 in the quadratic form. Next, introducing the following rotation transformation,

$$N_1 = X \cos \theta - Y \sin \theta, \quad N_2 = X \sin \theta + Y \cos \theta$$

into (21) yields

$$(22) \quad \begin{aligned} \tilde{Q} = & \frac{1}{2} [C_1 + C_2 + (C_1 - C_2) \cos(2\theta) + C_3 \sin(2\theta)] X^2 \\ & + \frac{1}{2} [C_1 + C_2 - (C_1 - C_2) \cos(2\theta) - C_3 \sin(2\theta)] Y^2 \\ & + [(C_1 - C_2) - C_3 \cos(2\theta)] XY \\ & - (C_4 \sin \theta + C_5 \cos \theta) X - (C_5 \sin \theta - C_4 \cos \theta) Y. \end{aligned}$$

Setting the term of XY in \tilde{Q} equal to zero we have two cases: $C_2 = C_1$ or $C_2 \neq C_1$. For $C_2 = C_1$, we obtain $\theta = \frac{\pi}{4}$, and

$$\begin{aligned} \tilde{Q} &= \left(C_1 + \frac{C_3}{2} \right) X^2 + \left(C_1 - \frac{C_3}{2} \right) Y^2 - \frac{1}{\sqrt{2}} (C_5 + C_4) X - \frac{1}{\sqrt{2}} (C_5 - C_4) Y \\ &= \frac{1}{2} (2C_1 + C_3) \left[X - \frac{C_5 + C_4}{\sqrt{2}(2C_1 + C_3)} \right]^2 + \frac{1}{2} (2C_1 - C_3) \left[Y - \frac{C_5 - C_4}{\sqrt{2}(2C_1 - C_3)} \right]^2 \\ &\quad - \frac{C_1(C_5 - C_4)^2 + C_4 C_5 (2C_1 - C_3)}{(2C_1 + C_3)(2C_1 - C_3)} \end{aligned}$$

which is an ellipse if $2C_1 > C_3$.

Next, consider $C_2 \neq C_1$. Vanishing the term XY in \tilde{Q} yields

$$(23) \quad \tan 2\theta = \frac{C_3}{C_1 - C_2} \implies \cos 2\theta = \frac{|C_1 - C_2|}{\sqrt{(C_1 - C_2)^2 + C_3^2}}, \quad \theta \in \left(-\frac{\pi}{4}, \frac{\pi}{4} \right).$$

Then, (22) is simplified to

$$\begin{aligned} \tilde{Q} = & \frac{1}{2} \left(C_1 + C_2 \pm \sqrt{(C_1 - C_2)^2 + C_3^2} \right) \left[X - \frac{C_5 \sin \theta + C_4 \cos \theta}{C_1 + C_2 \pm \sqrt{(C_1 - C_2)^2 + C_3^2}} \right]^2 \\ & + \frac{1}{2} \left(C_1 + C_2 \mp \sqrt{(C_1 - C_2)^2 + C_3^2} \right) \left[Y - \frac{C_5 \cos \theta - C_4 \sin \theta}{C_1 + C_2 \mp \sqrt{(C_1 - C_2)^2 + C_3^2}} \right]^2 \\ & - \frac{1}{2} \left[\left(\frac{C_5 \sin \theta + C_4 \cos \theta}{C_1 + C_2 \pm \sqrt{(C_1 - C_2)^2 + C_3^2}} \right)^2 + \left(\frac{C_5 \cos \theta - C_4 \sin \theta}{C_1 + C_2 \mp \sqrt{(C_1 - C_2)^2 + C_3^2}} \right)^2 \right], \end{aligned}$$

where the positive and negative signs correspond to the cases $C_1 > C_2$ and $C_1 < C_2$, respectively. It is easy to see that \tilde{Q} represents an ellipse if

$$C_1 + C_2 - \sqrt{(C_1 - C_2)^2 + C_3^2} > 0 \iff 4C_1C_2 - C_3^2 > 0.$$

Note that the case $C_2 = C_1$ is a special case included in $4C_1C_2 - C_3^2 > 0$.

Now, for the 3-d model, we have

$$C_1 = \frac{r_1}{K_1}, \quad C_2 = \frac{r_2}{K_2}, \quad C_3 = 2 \implies 4C_1C_2 - C_3^2 = 4C_{bd}^{3d} > 0,$$

and for the 4-d model, we obtain

$$C_1 = \frac{r_1}{K_1}, \quad C_2 = \frac{\tilde{c}E}{\tilde{D}A} \frac{r_2}{K_2}, \quad C_3 = 1 + \frac{\tilde{c}E}{\tilde{D}A} \implies 4C_1C_2 - C_3^2 = 4C_{bd}^{4d} > 0. \quad \blacksquare$$

Note in the proof of Theorem 2.2 that the stability condition of E_5 for the 3-d model does satisfy $r_1r_2 > K_1K_2$, leading to the conclusion that E_5 is GAS.

5. Stability of equilibria in the 4-d model. In the following subsections, we first summarize the stability results for the equilibrium solutions of E_0 - E_7 , and then present a detailed analysis for the equilibrium solutions E_8 and E_9 .

5.1. Stability of E_0 - E_7 .

Theorem 5.1. *The equilibria E_0 , E_1 , and E_2 exist for positive parameter values. The equilibrium E_3 exists for $(K_2 - r_1)(K_1 - r_2) > 0$, E_4 exists if $K_1 > \frac{1}{B}$, E_5 exists if $r_2 > \frac{1}{B}$, $K_1 > \frac{1}{B}$, $r_1 > r_1^*$, E_6 exists for $K_1 > \frac{1}{D}$, and E_7 exists for $E > \frac{1}{K_2}$. E_0 is always unstable; E_1 is LAS for $r_2 < K_1 < \min\{\frac{1}{B}, \frac{1}{D}\}$; E_2 is LAS for $r_1 < K_2 < \frac{1}{E}$; E_3 is LAS if the following conditions hold:*

$$(24) \quad \begin{aligned} & K_1 < \frac{1}{B} < r_2, \quad K_2 < r_1 \quad \text{or} \quad \frac{1}{B} < K_1 < r_2, \quad K_2 < r_1 < r_1^* \\ & \text{together with} \quad B < \frac{g}{r_2 K_1 (K_2 - r_1)} \quad \text{and} \quad E < \frac{g - \tilde{D}r_2 K_1 (K_2 - r_1)}{K_2 r_1 (K_1 - r_2)}, \end{aligned}$$

where r_1^* is given in (5); E_4 is LAS for $r_2 < \frac{1}{B} < \min\{K_1, \frac{1}{D}\}$; E_5 is LAS for

$$(25) \quad \begin{aligned} & \frac{1}{B} < K_1 < r_2, \quad r_1 > r_1^* \quad \text{or} \quad \frac{1}{B} < r_2 < K_1, \quad r_1 > r_{1H}, \\ & \text{together with} \quad E < \frac{Br_2}{K_2(Br_2 - 1)} \quad \text{and} \quad \tilde{D} < \frac{Br_2 - EK_2(Br_2 - 1)}{r_2}, \end{aligned}$$

where r_{1H} is given in (9); E_6 is LAS for

$$(26) \quad B < \tilde{D} \quad \text{and} \quad r_2 < \frac{1}{\tilde{D}} + \frac{Ar_1}{\tilde{c}} \left(1 - \frac{1}{\tilde{D}K_1}\right);$$

and E_7 is LAS for

$$(27) \quad r_1 < \frac{1}{E} + \frac{\tilde{c}r_2}{A} \left(1 - \frac{1}{EK_2}\right).$$

There exist seven transcritical bifurcations shown in the following table:

Equilibria :	(E_1, E_3)	(E_1, E_4)	(E_1, E_6)	(E_2, E_3)	(E_2, E_7)	(E_3, E_5)	(E_4, E_5) ,
Critical Point :	$r_2=K_1$	$BK_1=1$	$\tilde{D}=1$	$r_1=K_2$	$EK_2=1$	$r_1=r_1^*$	$Br_2=1$.

A Hopf bifurcation can only occur from E_5 at the critical point $r_1 = r_{1H}$. But B-T bifurcations cannot happen from any of the seven equilibria.

The proof is given in the Supplementary Material (section SM4.2). We provide a numerical example of the Hopf bifurcation from E_5 in the Supplementary Material (section SM4.3).

We now demonstrate that all equilibrium solutions E_1 – E_7 are GAS when they are LAS with the additional boundedness condition (16). We note that the conclusions in the following theorem about the GAS of the equilibria E_1 – E_5 are also true for the 3-d model (2), with the proof using the boundedness condition C_{bd}^{3d} instead of C_{bd}^{4d} , setting $\frac{\tilde{c}E}{\tilde{D}A} = 1$, and neglecting the term Q in the Lyapunov function.

Theorem 5.2. *The seven equilibria E_1 – E_7 of the 4-d model (10) are GAS if, in addition, to their LAS conditions, the boundedness condition (16) is also satisfied.*

Proof. The following seven Lyapunov functions are used to prove the GAS of the seven equilibria E_1 – E_7 (V_k for E_k). Since the proofs are similar, we only outline the proofs for E_1 , E_3 , and E_5 .

$$(28) \quad \begin{aligned} V_1 &= N_1 - N_{11} - N_{11} \ln \left(\frac{N_1}{N_{11}} \right) + \frac{\tilde{c}E}{\tilde{D}A} N_2 + \frac{1}{B} P + \frac{\tilde{c}}{\tilde{D}} Q, \\ V_2 &= N_1 + \frac{\tilde{c}E}{\tilde{D}A} \left[N_2 - N_{22} - N_{22} \ln \left(\frac{N_2}{N_{22}} \right) \right] + \frac{1}{B} P + \frac{\tilde{c}}{\tilde{D}} Q, \\ V_3 &= N_3 - N_{13} - N_{13} \ln \left(\frac{N_1}{N_{13}} \right) + \frac{\tilde{c}E}{\tilde{D}A} \left[N_2 - N_{23} - N_{23} \ln \left(\frac{N_2}{N_{23}} \right) \right] + \frac{1}{B} P + \frac{\tilde{c}}{\tilde{D}} Q, \\ V_4 &= N_4 - N_{14} - N_{14} \ln \left(\frac{N_1}{N_{14}} \right) + \frac{\tilde{c}E}{\tilde{D}A} N_2 + \frac{1}{B} \left[P - P_4 - P_4 \ln \left(\frac{P}{P_4} \right) \right] + \frac{\tilde{c}}{\tilde{D}} Q, \\ V_5 &= N_5 - N_{15} - N_{15} \ln \left(\frac{N_1}{N_{15}} \right) + \frac{\tilde{c}E}{\tilde{D}A} \left[N_2 - N_{25} - N_{25} \ln \left(\frac{N_2}{N_{25}} \right) \right] \\ &\quad + \frac{1}{B} \left[P - P_4 - P_4 \ln \left(\frac{P}{P_4} \right) \right] + \frac{\tilde{c}}{\tilde{D}} Q, \\ V_6 &= N_1 - N_{16} - N_{16} \ln \left(\frac{N_1}{N_{16}} \right) + \frac{\tilde{c}E}{\tilde{D}A} N_2 + \frac{1}{B} P + \frac{\tilde{c}}{\tilde{D}} \left[Q - Q_6 - Q_6 \ln \left(\frac{Q}{Q_6} \right) \right], \\ V_7 &= N_1 + \frac{\tilde{c}E}{\tilde{D}A} \left[N_2 - N_{27} - N_{27} \ln \left(\frac{N_2}{N_{27}} \right) \right] + \frac{1}{B} P + \frac{\tilde{c}}{\tilde{D}} \left[Q - Q_7 - Q_7 \ln \left(\frac{Q}{Q_7} \right) \right]. \end{aligned}$$

Define

$$(29) \quad \frac{d\bar{V}_k}{dt} = \frac{r_1}{K_1} \left[N_1 - N_{1k} + \frac{K_1}{2r_1} \left(1 + \frac{\tilde{c}E}{\tilde{D}A} \right) (N_2 - N_{2k}) \right]^2 + \frac{\tilde{c}E}{\tilde{D}AK_2r_1} C_{bd}^{4d} (N_2 - N_{2k})^2.$$

It is seen that $\frac{d\bar{V}_k}{dt} \geq 0$ if $C_{bd}^{4d} > 0$.

Differentiating V_1 with respect to time t and computing it along the trajectory of (10) we obtain

$$(30) \quad \begin{aligned} \left. \frac{dV_1}{dt} \right|_{(10)} &= \left(1 - \frac{N_{11}}{N_1} \right) \frac{dN_1}{dt} + \frac{\tilde{c}E}{\tilde{D}A} \frac{dN_2}{dt} + \frac{1}{B} \frac{dP}{dt} + \frac{\tilde{c}}{\tilde{D}} \frac{dQ}{dt} \\ &= -\frac{d\bar{V}_1}{dt} - \frac{\tilde{c}E}{\tilde{D}A} (K_1 - r_2) N_2 - \left(\frac{1}{B} - K_1 \right) P - \tilde{c} \left(\frac{1}{\tilde{D}} - K_1 \right) Q, \end{aligned}$$

which shows that $\left. \frac{dV_1}{dt} \right|_{(10)} \leq 0$ for $(N_1, N_2, P, Q) \neq E_1$ if the LAS condition $r_1 < K_1 < \min\{\frac{1}{B}, \frac{1}{\tilde{D}}\}$ and the boundedness condition $C_{bd}^{4d} > 0$ are satisfied, and $\left. \frac{dV_1}{dt} \right|_{(10)} = 0$ only if $(N_1, N_2, P, Q) = E_1$. This implies that E_1 is GAS under these conditions by the Lyapunov function theory.

Using the function V_3 gives

$$\begin{aligned} \left. \frac{dV_3}{dt} \right|_{(10)} &= \left(1 - \frac{N_{13}}{N_1} \right) \frac{dN_1}{dt} + \frac{\tilde{c}E}{\tilde{D}A} \left(1 - \frac{N_{23}}{N_2} \right) \frac{dN_2}{dt} + \frac{1}{B} \frac{dP}{dt} + \frac{\tilde{c}}{\tilde{D}} \frac{dQ}{dt} \\ &= -\frac{d\bar{V}_3}{dt} - \frac{1}{B} (1 - BN_{13}) P - \frac{\tilde{c}}{\tilde{D}} (1 - \tilde{D}N_{13} - EN_{23}) Q, \end{aligned}$$

which leads to $\left. \frac{dV_3}{dt} \right|_{(10)} \leq 0$ for $(N_1, N_2, P, Q) \neq E_3$ if $C_{bd}^{4d} > 0$, as well as $BN_{13} < 1$ and $\tilde{D}N_{13} + EN_{23} < 1$. The latter two conditions are the LAS conditions for E_3 given in (24) expressed in B and E . $\left. \frac{dV_3}{dt} \right|_{(10)} = 0$ only if $(N_1, N_2, P, Q) = E_3$. Thus, E_3 is GAS under these conditions.

For E_5 , we obtain

$$\begin{aligned} \left. \frac{dV_5}{dt} \right|_{(10)} &= \left(1 - \frac{N_{15}}{N_1} \right) \frac{dN_1}{dt} + \frac{\tilde{c}E}{\tilde{D}A} \left(1 - \frac{N_{25}}{N_2} \right) \frac{dN_2}{dt} + \frac{1}{B} \left(1 - \frac{P_5}{P} \right) \frac{dP}{dt} + \frac{\tilde{c}}{\tilde{D}} \frac{dQ}{dt} \\ &= -\frac{d\bar{V}_5}{dt} - \frac{\tilde{c}}{\tilde{D}} (1 - \tilde{D}N_{15} - EN_{25}) Q, \end{aligned}$$

from which we have that $\left. \frac{dV_5}{dt} \right|_{(10)} \leq 0$ for $(N_1, N_2, Q) \neq (N_{15}, N_{25}, P_5)$ if $C_{bd}^{4d} > 0$, and $\tilde{D}N_{15} + EN_{25} < 1$, which is equivalent to the LAS condition for E_5 given in (25) expressed in \tilde{D} . $\left. \frac{dV_5}{dt} \right|_{(10)} = 0$ if $(N_1, N_2, Q) = (N_{15}, N_{25}, P_5)$ under which the first three equations of system (10) are reduced to

$$0 = \frac{1}{B} \left[r_1 \left(1 - \frac{1}{BK_1} \right) - N_{25} - P \right], \quad 0 = N_{25} \left[r_1 \left(1 - \frac{N_{25}}{K_2} \right) - \frac{1}{B} \right], \quad \frac{dP}{dt} = P(BN_{15} - 1) = 0,$$

yielding $N_2 = N_{25}$ and $P = P_5$. Hence, E_5 is GAS by the LaSalle's Invariance Principle.

The above results show that all equilibrium solutions E_1 - E_7 are GAS when the LAS conditions and the boundedness condition (16) are satisfied. ■

Remark 1. A natural question arises: Does the LAS condition for an equilibrium always satisfy the GAS condition (16)? The answer is no, since LAS equilibria are sometimes GAS, but not always. For example, the equilibrium E_5 of the 3-d model is LAS and also GAS under the same stability conditions, $\frac{1}{B} < K_1 \leq r_2$ and $r_1 > r_1^*$. In contrast, consider equilibria E_2 and E_4 of the 3-d model. The equilibrium $E_2 = (0, K_2, 0)$ exists for any positive parameter values, and is LAS for $r_2 < K_1$; while the equilibrium $E_4 = (\frac{1}{B}, 0, r_2(1 - \frac{1}{BK_1}))$ exists for $K_1 > \frac{1}{B}$, and is LAS for $r_2 < \frac{1}{B}$. Thus, these two equilibria can co-exist for certain parameter values. With the addition of the boundedness condition $C_{bd}^{3d} > 0$; however, it can be seen that there exists a wide range of parameter values such that either E_2 or E_4 is GAS, but not both. This is certainly true because a system cannot have more than one GAS equilibrium. We describe this result further and provide numerical examples in section SM3 of the Supplementary Material.

5.2. Stability and bifurcation analysis of equilibrium E_8 . Turning our attention to equilibrium E_8 , we have the following result.

Theorem 5.3. *The equilibrium E_8 exists if one of the following two conditions holds:*

$$(31) \quad \begin{aligned} (C_1) \quad & N_{18n} > 0, \quad N_{28n} > 0, \quad Q_{8n} > 0; \\ (C_2) \quad & N_{18n} < 0, \quad N_{28n} < 0, \quad Q_{8n} < 0. \end{aligned}$$

Further, equilibrium E_8 under the condition (C_2) is unstable; E_8 under the condition (C_1) is LAS if the following conditions are satisfied:

$$(32) \quad BN_{18} < 1, \quad a_{18} > 0, \quad a_{28} > 0, \quad a_{38} > 0, \quad \Delta_{28} = a_{18}a_{28} - a_{38} > 0,$$

where

$$(33) \quad \begin{aligned} a_{18} &= \frac{1}{K_1 K_2 E_{8d}} (r_1 K_2 N_{18n} + r_2 K_1 N_{28n}), \\ a_{28} &= \frac{1}{E_{8d}^2} \left[\left(\frac{r_1 r_2}{K_1 K_2} - 1 \right) N_{18n} N_{28n} + (\tilde{c} \tilde{D} N_{18n} + A E N_{28n}) Q_{8n} \right] \equiv \frac{1}{E_{8d}^2} a_{28n}, \\ a_{38} &= \frac{N_{18n} N_{28n} Q_{8n}}{K_1 K_2 E_{8d}^2}. \end{aligned}$$

Moreover, E_8 is GAS under the conditions (C_1) , $BN_{18} < 1$, and $C_{bd}^{4d} > 0$. Three transcritical bifurcations can occur: one between E_8 and E_7 at the critical point determined by $N_{18n} = 0$; the second one between E_8 and E_6 at the critical point determined by $N_{28n} = 0$; and the third one between E_8 and E_3 at the critical point determined by $Q_{8n} = 0$. Hopf bifurcation occurs at the critical point defined by $\Delta_{28} = 0$. No B-T bifurcation can occur from E_8 .

Proof. The proof of the existence and LAS conditions are given in the Supplementary Material (section SM4.2). Before discussing Hopf bifurcation from E_8 , we find the condition under which E_8 is GAS. In other words, the LAS condition (32) does not guarantee GAS of E_8 . GAS requires the boundedness condition C_{bd}^{4d} to be added. To prove this, we construct the Lyapunov function:

$$(34) \quad \begin{aligned} V_8 = & N_1 - N_{18} - N_{18} \ln \frac{N_1}{N_{18}} + \frac{\tilde{c}E}{\tilde{D}A} \left(N_2 - N_{28} - N_{28} \ln \frac{N_2}{N_{28}} \right) \\ & + \frac{1}{B}P + \frac{\tilde{c}}{\tilde{D}} \left(Q - Q_8 - Q_8 \ln \frac{Q}{Q_8} \right). \end{aligned}$$

Then, differentiating V_8 and using (10) we obtain

$$\begin{aligned} \frac{dV_8}{dt} \Big|_{(10)} &= \left(1 - \frac{N_{18}}{N_1} \right) \frac{dN_1}{dt} + \frac{\tilde{c}E}{\tilde{D}A} \left(1 - \frac{N_{28}}{N_2} \right) \frac{dN_2}{dt} + \frac{1}{B} \frac{dP}{dt} + \frac{\tilde{c}}{\tilde{D}} \left(1 - \frac{Q_8}{Q} \right) \frac{dQ}{dt} \\ &= (N_1 - N_{18}) \left\{ r_1 \left(1 - \frac{N_1}{K_1} \right) - N_2 - P - \tilde{c}Q - \left[r_1 \left(1 - \frac{N_{18}}{K_1} \right) - N_{18} - \tilde{c}Q_8 \right] \right\} \\ &\quad + \frac{\tilde{c}E}{\tilde{D}A} (N_2 - N_{28}) \left\{ r_2 \left(1 - \frac{N_2}{K_2} \right) - N_1 - AQ - \left[r_2 \left(1 - \frac{N_{28}}{K_2} \right) - N_{28} - AQ_8 \right] \right\} \\ &\quad + N_1 P - \frac{1}{B}P + \frac{\tilde{c}}{\tilde{D}}(Q - Q_8)[\tilde{D}N_1 + EN_2 - 1 - (\tilde{D}N_{18} + EN_{28} - 1)] \\ &= -\frac{d\bar{V}_8}{dt} - \left(\frac{1}{B} - N_{18} \right) P, \end{aligned}$$

where $\frac{d\bar{V}_8}{dt}$ is given in (29), which clearly shows that under the conditions (C_1) and (16), $\frac{dV_8}{dt} \leq 0$, and equals zero only if $N_1 = N_{18}$, $N_2 = N_{28}$, and $P = 0$. When $N_1 = N_{18}$, $N_2 = N_{28}$, and $P = 0$, the first and the last equations in system (10) are reduced to

$$0 = N_{18} \left[r_1 \left(1 - \frac{N_{18}}{K_1} \right) - N_{28} - \tilde{c}Q \right] = \tilde{c}N_{18}(Q_8 - Q), \quad \frac{dQ}{dt} = Q(\tilde{D}N_{18} + EN_{28} - 1) = 0,$$

which shows that Q is a constant, and it can be derived from the first equation as $Q = Q_8$. Therefore, by the LaSalle’s Invariance Principle, we know that E_8 is GAS under the given conditions. Note that the existence condition (C_1) and the boundedness condition $C_{bd}^{4d} > 0$ imply the LAS condition of E_8 since

$$C_{bd}^{4d} > 0 \implies \frac{r_1 r_2}{K_1 K_2} > \frac{(\tilde{D}A + \tilde{c}E)^2}{4\tilde{c}\tilde{D}AE} \geq 1.$$

Now, we consider possible Hopf bifurcation from E_8 , which requires the condition $\Delta_{28} = 0$. Since $a_{18} > 0$ and $a_{38} > 0$ under the existence condition (C_1) , we know that E_8 is LAS if $BN_{18} < 1$, $a_{28} > 0$, and $\Delta_{28} > 0$. Take $B < \frac{1}{N_{18}}$. Then, it is not difficult to see that $\Delta_{28} = a_{18}a_{28} - a_{38}$ crosses zero before a_{28} does. Therefore, besides the transcritical bifurcation discussed above, when $a_{k8} > 0$ ($k = 1, 2, 3$), the only possible bifurcation is Hopf bifurcation. To prove that Hopf bifurcation can occur from E_8 , it suffices to show that Δ_{28} can reach zero under the conditions $N_{k8n} > 0$, $k = 1, 2, 3$, and $a_{28n} > 0$. A direct computation yields

$$(35) \quad \begin{aligned} \Delta_{28} &= \frac{1}{K_1 K_2 E_{8d}^3} \left[(K_2 r_1 N_{18n} + K_1 r_2 N_{28n}) a_{28n} - N_{18n} N_{28n} Q_{8n} (\tilde{D}N_{18n} + EN_{28n}) \right] \\ &= \frac{1}{K_1 K_2 E_{8d}^3} \left\{ \left(\frac{r_1 r_2}{K_1 K_2} - 1 \right) (K_2 r_1 N_{18n} + K_1 r_2 N_{28n}) N_{18n} N_{28n} \right. \end{aligned}$$

$$\begin{aligned}
 & + [\tilde{c}\tilde{D}K_2r_1N_{18n}^2 + K_1AEr_2N_{28n}^2 + K_1K_2(\tilde{D}A + \tilde{c}E)N_{18n}N_{28n}]Q_{8n} \Big\} \\
 & \equiv \frac{1}{K_1K_2E_{8d}^3} \Delta_{28n}.
 \end{aligned}$$

It is easy to see that the existing E_8 is LAS for $r_1r_2 \geq K_1K_2$ under which $a_{28} > 0$ and $\Delta_{28} > 0$. Therefore, Hopf bifurcation is possible only if $r_1r_2 < K_1K_2$. Also, it can be seen from the first line of (35) that Δ_{28} crosses zero before a_{28} does. To identify possible Hopf bifurcation, we consider the boundary conditions $N_{18n} = N_{28n} = Q_{8n} = a_{28n} = \Delta_{28n} = 0$ as lines/curves in the r_1 - r_2 plane (see Figure 1a). We choose specific parameter values (see the figure caption) to generate the bifurcation diagram with r_1 and r_2 as the perturbation parameters, where the purple dotted, green solid, blue dotted, red solid, and black dotted curves denote the graphs, $N_{28n} = 0$, $Q_{8n} = 0$, $a_{28n} = 0$, $\Delta_{28n} = 0$, and $r_1r_2 = K_1K_2$, respectively (Figure 1a). N_{18n} does not appear in the diagram since $N_{18n} > 0$ in the first quadrant of the r_1 - r_2 plane.

Note that the four curves $Q_{8n} = a_{28n} = \Delta_{28n} = r_1r_2 - K_1K_2 = 0$ intersect at the same point $(r_1, r_2) = (K_2, K_1)$, and another four curves $Q_{8n} = a_{28n} = \Delta_{28n} = N_{28n} = 0$ intersect at the same point $(r_1, r_2) = (0, \frac{1}{\tilde{D}})$, while the two curves $N_{28n} = r_1r_2 - K_1K_2 = 0$ intersect at the point $(r_1, r_2) = (r_{1s}, r_{2s})$, where

$$r_{1s} = \frac{2\tilde{c}\tilde{D}K_1K_2}{\sqrt{\tilde{c}^2 + 4\tilde{c}\tilde{D}AK_2(\tilde{D}K_1 - 1) + \tilde{c}}}, \quad r_{2s} = \frac{K_1K_2}{r_{1s}}.$$

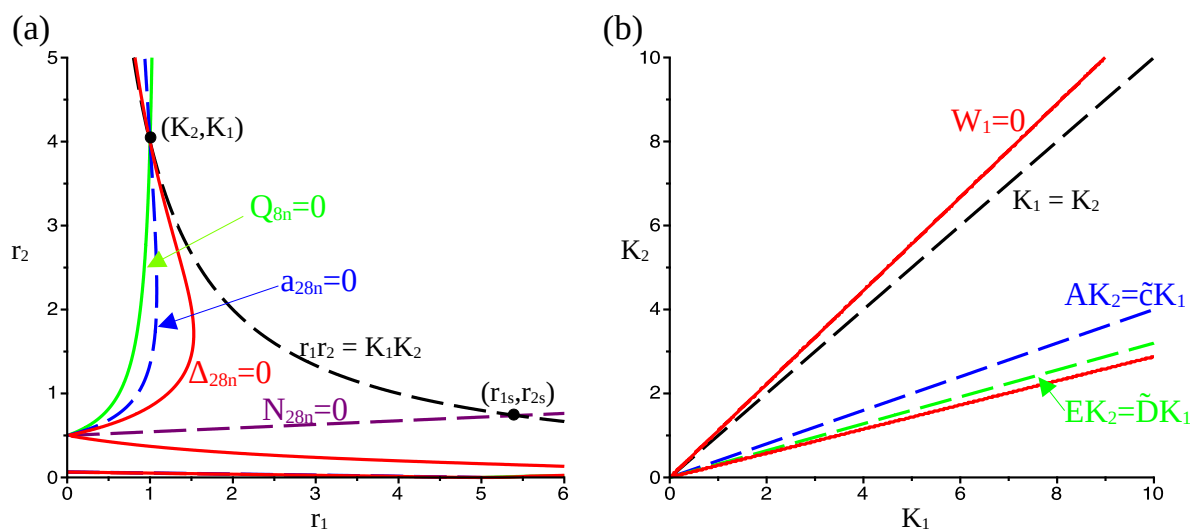


Figure 1. Bifurcation diagrams for the equilibria of the 4-d model (10). (a) Equilibrium E_8 with $\tilde{c} = \frac{2}{5}$, $E = \frac{1}{5}$, $K_2 = 1$, $\tilde{D} = 2$, $K_1 = 4$, $A = \frac{1}{50}$. The purple dashed, green, blue dashed, red, and black dashed curves denote $N_{28n} = 0$, $Q_{8n} = 0$, $a_{28n} = 0$, $\Delta_{28n} = 0$, and $r_1r_2 = K_1K_2$, respectively; and $N_{18n} > 0$ in the first quadrant. (b) Equilibrium E_9 with $\tilde{c} = \frac{2}{5}$, $\tilde{D} = \frac{4}{5}$, $A = 1$, $E = \frac{5}{2}$. The dashed black, blue, and green lines represent the equations, $K_2 = K_1$, $AK_2 = \tilde{c}K_1$, and $EK_2 = \tilde{D}K_1$, respectively; and the solid red curve plots the function $W_1 = 0$.

In the triangular region bounded by the purple, blue, and black dotted curves, we have $N_{18n} > 0$, $N_{28n} > 0$, $Q_{8n} > 0$, $a_{28n} > 0$. Inside this triangle, $\Delta_{28n} > 0$ on the right side of the red curve, and $\Delta_{28n} < 0$ on the left side of the red curve, implying that E_8 is LAS on the right side of the red curve, and loses its stability when r_1 and r_2 are varied to cross the red curve, and limit cycles bifurcate from E_8 when the (r_1, r_2) takes values in the triangle bounded by the blue and red curves. We present a numerical example, including the use of normal form theory [38] to find the first focus value, in section SM4.4 of the Supplementary Material.

We also assess whether B-T bifurcation from E_8 can occur at the critical point, determined by $a_{28} = a_{38} = 0$, which yields two zero eigenvalues. There are only two possibilities: $N_{18} = Q_8 = 0$ and $N_{28} = Q_8 = 0$. $N_{18} = N_{28} = 0$ is not allowed since it causes $E_{8d} = 0$. However, solving these two cases results in no solution, leading to a zero divisor. Hence, B-T bifurcation is not possible from E_8 . ■

5.3. Stability and bifurcation analysis of equilibrium E_9 . We have the following theorem.

Theorem 5.4. *The equilibrium E_9 exists for*

$$(36) \quad \begin{aligned} B > \tilde{D}, \quad K_1 > \frac{1}{B}, \quad E > \frac{B - \tilde{D}}{BK_2}, \quad r_2 > \frac{EK_2}{BEK_2 - B + \tilde{D}}, \\ r_1 > \frac{K_1 \{AK_2(B - \tilde{D}) + \tilde{c}[r_2(BEK_2 - B + \tilde{D}) - EK_2]\}}{AEK_2(BK_1 - 1)}, \end{aligned}$$

and is LAS under the following conditions:

$$(37) \quad a_{k9} > 0, \quad k = 1, 2, 3, 4, \quad \Delta_{29} = a_{19}a_{29} - a_{39} > 0, \quad \Delta_{39} = a_{39}\Delta_{29} - a_{19}^3a_{49} > 0,$$

where

$$(38) \quad \begin{aligned} a_{19} &= \frac{r_1}{BK_1} + \frac{r_2N_{29}}{K_2}, \\ a_{29} &= \frac{1}{B} \left(\frac{r_1r_2}{K_1K_2} - 1 \right) N_{29} + AEN_{29}Q_9 + \frac{\tilde{c}\tilde{D}}{B}Q_9 + P_9, \\ a_{39} &= N_{29} \left\{ \frac{r_2}{K_2}P_9 + \frac{1}{B} \left[\tilde{c} \left(\frac{\tilde{D}r_2}{K_2} - E \right) + A \left(\frac{Er_1}{K_1} - \tilde{D} \right) \right] Q_9 \right\}, \\ a_{49} &= AEN_{29}P_9Q_9. \end{aligned}$$

Two transcritical bifurcations can occur: one is between E_9 and E_5 at the critical point determined by $Q_9 = 0$; and the other is between E_9 and E_8 at the critical point determined by $P_9 = 0$. Hopf bifurcation occurs at the critical point, determined by $\Delta_{39} = 0$, together with $a_{k9} > 0$, $k = 1, 2, 3, 4$ and $\Delta_{29} > 0$. No B-T bifurcation can happen from E_9 .

Proof. For a proof of existence and LAS conditions, see the Supplementary Material (section SM4.2). Now, we consider Hopf bifurcation from E_9 . It is known [39] that Hopf bifurcation occurs at the critical point determined by $\Delta_{39} = 0$, with the other stability conditions $a_{k9} > 0$, $k = 1, 2, 3, 4$, and $\Delta_{29} > 0$ still hold. It is easy to see that $a_{19} > 0$, $a_{29} > 0$ when E_9 exists, and that there are many parameter values satisfying $a_{29} > 0$ and $a_{39} > 0$. If $a_{39} > 0$, then we know that Δ_{29} crosses zero before a_{29} does (see (37)). Moreover, it can be

seen from (37) that Δ_{39} crosses zero before Δ_{29} does. Therefore, when E_9 exists, besides the transcritical bifurcations, the only possible bifurcation is Hopf bifurcation.

To find the Hopf critical point, we need to identify feasible parameter values such that the above mentioned Hopf conditions are satisfied. We may follow the approach used in the analysis of E_8 , treating r_1 and r_2 as perturbation parameters. However, this is very difficult due to the complex expressions involved. We instead use the parameter B as the bifurcation parameter, and take additional restrictions on the parameters to simplify the computation. It can be seen from (38) that there exist many parameter values such that $a_{29} > 0$ and $a_{39} > 0$. However, it is not easy to find the conditions such that $\Delta_{29} > 0$ and $\Delta_{39} = 0$. To simplify the analysis, we take

$$(39) \quad r_1 = K_2, \quad r_2 = K_1,$$

which does not impose much restriction in satisfying the Hopf condition. We can see that $a_{29} > 0$ under this condition, and there still exists a range of parameter values such that $a_{39} > 0$. With (39), we have

$$N_{29} = \frac{B - \tilde{D}}{BE}, \quad Q_9 = \frac{BK_1(EK_2 - 1) + \tilde{D}K_1 - EK_2}{ABEK_2}, \quad P_9 = \frac{1}{K_1} (AK_2 - \tilde{c}K_2) Q_9.$$

Then, $a_{k9} > 0$, $k = 1, 2, 3, 4$, as long as $N_{29} > 0$, $Q_9 > 0$, and $P_9 > 0$. With the condition (39), a direct computation yields

$$\begin{aligned} \Delta_{29} &= \frac{BK_1(EK_2 - 1) + \tilde{D}K_1 - EK_2}{AB^3E^2K_1^2K_2^2} \\ &\quad \times \{AK_1^3(B - \tilde{D})^2 + K_2[A(\tilde{D}K_1^2 + EK_2^2) + \tilde{c}K_1(K_1 - K_2)](B - \tilde{D}) + \tilde{D}AEK_2^3\}, \\ \Delta_{39} &= \frac{(B - \tilde{D})^2(AK_2 - \tilde{c}K_1)[BK_1(EK_2 - 1) + \tilde{D}K_1 - EK_2]^2}{A^2B^6E^4K_1^2K_2^4} \\ &\quad \times (K_2 - K_1)\{B[AK_1(\tilde{D}K_1 - EK_2) + EK_2(AK_2 - \tilde{c}K_1)] \\ &\quad - (\tilde{D}K_1 - EK_2)(A\tilde{D}K_1 - EK_2\tilde{c})\}. \end{aligned}$$

Solving $\Delta_{39} = 0$ we obtain the Hopf critical point,

$$(40) \quad B_H = \frac{(\tilde{D}K_1 - EK_2)(A\tilde{D}K_1 - EK_2\tilde{c})}{AK_1(\tilde{D}K_1 - EK_2) + EK_2(AK_2 - \tilde{c}K_1)},$$

under which

$$\Delta_{29}|_{B=B_H} = \frac{E^2K_2^2(AK_2 - \tilde{c}K_1)^2(K_1 - K_2)[A\tilde{D}K_1^2 - EK_1K_2\tilde{c} + A(K_2 - K_1)]}{AK_1^2(\tilde{D}K_1 - EK_2)^2(\tilde{D}K_1 - EK_2)^2}.$$

Now, summarizing the conditions $B > 0$, $B > \tilde{D}$, $Q_9 > 0$, $P_9 > 0$, and $\Delta_{29}|_{B=B_H} > 0$, we have the following conditions which need to be satisfied:

$$(41) \quad \begin{aligned} &AK_2 - \tilde{c}K_2 > 0, \\ &(\tilde{c}E - \tilde{D}A)W_1 > 0, \\ &(\tilde{D}K_1 - EK_2)(A\tilde{D}K_1 - \tilde{c}EK_2)W_1 > 0, \\ &(\tilde{D}K_1 - EK_2)W_1W_2 > 0, \\ &(K_1 - K_2)W_2 > 0, \end{aligned}$$

where

$$\begin{aligned} W_1 &= AK_1(\tilde{D}K_1 - EK_2) + EK_2(AK_2 - \tilde{c}K_1), \\ W_2 &= A\tilde{D}K_1^2 - EK_1K_2\tilde{c} + A(K_2 - K_1). \end{aligned}$$

There are two cases: $\tilde{c}E - \tilde{D}A > 0$, $W_1 > 0$ and $\tilde{c}E - \tilde{D}A < 0$, $W_1 < 0$. It can be shown that the second case does not have solutions. For the first case, $\tilde{c}E > \tilde{D}A$ and $AK_2 > \tilde{c}K_1$ yields $EK_2 > \tilde{D}K_1$, which leads to $W_2 < 0$ using the 4th condition, and so $K_2 > K_1$ by the 5th condition. Then it is easy to verify that $A\tilde{D}K_1 < \tilde{c}EK_2$. Finally, checking $W_1 > 0$ we have

$$A\left(\tilde{D}K_1^2 - EK_1K_2 + EK_2^2\right) > \tilde{c}EK_1K_2,$$

which needs $\tilde{D}K_1^2 - EK_1K_2 + EK_2^2 > 0$, yielding a sufficient condition $E \leq 4\tilde{D}$. Then, it follows from $\tilde{D}A < \tilde{c}E \leq 4\tilde{c}\tilde{D}$ that $A < 4\tilde{c}$. Summarizing the above analysis we obtain the following solutions:

$$(42) \quad E \leq 4\tilde{D}, \quad A < 4\tilde{c}, \quad K_2 > K_1, \quad AK_2 > \tilde{c}K_1, \quad EK_2 > \tilde{D}K_1, \quad W_1 > 0. \quad \blacksquare$$

As an example, in Figure 1b we plot the three lines and a curve:

$$K_2 = K_1, \quad AK_2 = \tilde{c}K_1, \quad EK_2 = \tilde{D}K_1, \quad W_1 = 0,$$

on the K_1 - K_2 plane. As long as we choose the values (K_1, K_2) above the top red curve ($W_1 = 0$), all the required conditions are satisfied.

It is clear in Figure 1b that even with the restrictions $r_1 = K_2$ and $r_2 = K_1$, a wide range of parameter values still satisfies the conditions for the Hopf critical point, as long as (K_1, K_2) takes values from the region above the top red curve. (Without this restriction, even more parameter values should satisfy the Hopf bifurcation conditions, but the computation is unwieldy.) We provide an illustrative example, including the use of normal form theory to further analyse the existence and stability of limit cycles, in the Supplementary Material (section SM4.5).

5.4. GAS of E_9 . We end this section with the following theorem.

Theorem 5.5. *The equilibrium E_9 is GAS when the conditions for existence (36) and LAS (37) are satisfied, along with the additional boundedness condition (16).*

Proof. Following our previous approach, we construct the Lyapunov function:

$$(43) \quad \begin{aligned} V_9 &= N_1 - N_{19} - N_{19} \ln \frac{N_1}{N_{19}} + \frac{\tilde{c}E}{\tilde{D}A} \left(N_2 - N_{29} - N_{29} \ln \frac{N_2}{N_{29}} \right) \\ &\quad + \frac{1}{B} \left(P - P_9 - P_9 \ln \frac{P}{P_9} \right) + \frac{\tilde{c}}{\tilde{D}} \left(Q - Q_9 - Q_9 \ln \frac{Q}{Q_9} \right). \end{aligned}$$

Then, differentiating V_9 and using (10) we obtain

$$\begin{aligned} \frac{dV_9}{dt} \Big|_{(10)} &= \left(1 - \frac{N_{19}}{N_1}\right) \frac{dN_1}{dt} + \frac{\tilde{c}E}{\tilde{D}A} \left(1 - \frac{N_{29}}{N_2}\right) \frac{dN_2}{dt} + \frac{1}{B} \left(1 - \frac{P_9}{P}\right) \frac{dP}{dt} + \frac{\tilde{c}}{\tilde{D}} \left(1 - \frac{Q_9}{Q}\right) \frac{dQ}{dt} \\ &= (N_1 - N_{18}) \left\{ r_1 \left(1 - \frac{N_1}{K_1}\right) - N_2 - P - \tilde{c}Q - \left[r_1 \left(1 - \frac{N_{18}}{K_1}\right) - N_{18} - \tilde{c}Q_8 \right] \right\} \\ &\quad + \frac{\tilde{c}E}{\tilde{D}A} (N_2 - N_{28}) \left\{ r_2 \left(1 - \frac{N_2}{K_2}\right) - N_1 - AQ - \left[r_2 \left(1 - \frac{N_{28}}{K_2}\right) - N_{28} - AQ_8 \right] \right\} \\ &\quad + \frac{1}{B} (P - P_9) [BN_1 - 1 - (BN_{19} - 1)] \\ &\quad + \frac{\tilde{c}}{\tilde{D}} (Q - Q_9) [\tilde{D}N_1 + EN_2 - 1 - (\tilde{D}N_{19} + EN_{29} - 1)] \\ &= -\frac{d\bar{V}_9}{dt}, \end{aligned}$$

where $\frac{d\bar{V}_9}{dt}$ is given in (29). This indicates that $\frac{dV_9}{dt} \Big|_{(10)} \leq 0$ for $N_1 \neq N_{19}$, $N_2 \neq N_{29}$, and equals zero only if $N_1 = N_{19}$ and $N_2 = N_{29}$. When $N_1 = N_{19}$, $N_2 = N_{29}$, system (10) is reduced to

$$\begin{aligned} 0 &= N_{19} \left[r_1 \left(1 - \frac{N_{19}}{K_1}\right) - N_{29} - P - \tilde{c}Q \right] = N_{19} [(P_9 - P) + \tilde{c}(Q_9 - Q)], \\ 0 &= N_{29} \left[r_2 \left(1 - \frac{N_{29}}{K_2}\right) - N_{19} - AQ \right] = AN_{29}(Q_9 - Q), \\ \frac{dP}{dt} &= P(BN_{19} - 1) = 0, \\ \frac{dQ}{dt} &= \tilde{D}Q(N_{19} + EN_{29} - 1) = 0, \end{aligned}$$

which shows that P and Q are constants, and can be derived from the first and second equations to get $P = P_9$ and $Q = Q_9$. Therefore, by the LaSalle's Invariance Principle, we know that E_9 is GAS under the given conditions. ■

6. Host-range expansion. We are now able to address a number of important biological questions regarding host-range expansion. We are interested in situations in which the host, competitor, and parasite stably co-exist before the range expansion. We ask the following: what outcomes are possible if the parasite successfully expands its host range? We therefore restrict our interest to parameter regions for which the following conditions hold: (A) E_5 is GAS in the 3-d model but unstable in the 4-d model; and (B) at least one of E_6 – E_9 is LAS in the 4-d model. Condition (B) requires that for the range expansion to be considered successful, there must be at least one LAS equilibrium in which Q is nonzero.

In the Supplementary Material (section SM5), we demonstrate that the only states that can be bistable, among E_6 – E_9 , is the pair (E_6, E_7) . However, we are also able to show that it is not possible for condition (A) to hold together with *both* E_6 and E_7 LAS Supplementary Material (section SM4.6). Thus, if condition (A) holds, there are no bistable pairs among equilibria that include the evolved parasite. We can then ask: which of E_6 – E_9 can be either LAS or GAS under these conditions?

We first demonstrate that there is a range of parameter values such that condition (A) holds, together with either LAS E_6 (E_7 unstable) or LAS E_7 (E_6 unstable). This implies that host-range expansion can result in either the deterministic extinction of the original host, or the deterministic extinction of the novel host (competitor). We give the following examples to illustrate these two cases.

Example 1. For the case that E_5 is GAS for the 3-d model but unstable for the 4-d model, with LAS E_6 (E_7 unstable), we choose the parameter values:

$$\tilde{c} = \frac{2}{5}, \quad B = \frac{1}{2}, \quad \tilde{D} = \frac{3}{5}, \quad K_1 = \frac{5}{2}, \quad A = \frac{1}{2}, \quad K_2 = 2, \quad r_1 = 8, \quad r_2 = 3, \quad E = \frac{1}{2},$$

under which the four characteristic polynomials are

$$\begin{aligned} P_{3d}(E_5) &= \lambda^3 + \frac{37}{5}\lambda^2 + 6\lambda + \frac{14}{15}, \\ P_{4d}(E_5) &= \frac{1}{225}(15\lambda - 8)(15\lambda^3 + 111\lambda^2 + 90\lambda + 14), \\ P_{4d}(E_6) &= \frac{1}{18}(\lambda + 1)(6\lambda + 1)(3\lambda^2 + 16\lambda + 8), \\ P_{4d}(E_7) &= \lambda(\lambda - 6)(\lambda + 3)(\lambda + 1). \end{aligned}$$

For the case that E_5 is GAS for the 3-d model but unstable for the 4-d model, with LAS E_7 (E_6 unstable), we take the parameter values from Example 1, except that $K_2 = 1$, $r_1 = 101/60$, and $E = 2$. In this case the four characteristic polynomials are

$$\begin{aligned} P_{3d}(E_5) &= \lambda^3 + \frac{176}{75}\lambda^2 + \frac{41}{60}\lambda + \frac{1}{300}, \\ P_{4d}(E_5) &= \frac{1}{4500}(15\lambda - 13)(300\lambda^3 + 704\lambda^2 + 205\lambda + 1), \\ P_{4d}(E_6) &= \frac{1}{155520}(144\lambda - 91)(6\lambda + 1)(180\lambda^2 + 202\lambda + 101), \\ P_{4d}(E_7) &= \frac{1}{120}(60\lambda + 1)(\lambda + 1)(2\lambda^2 + 3\lambda + 3). \end{aligned}$$

We can similarly show that there is a range of parameter values for which condition (A) holds, together with either the LAS of E_8 (E_9 unstable) or E_9 (E_8 unstable). The former case can be confirmed by considering parameter values as in Example 1, but with $r_2 = 6$; the latter case can be confirmed by taking the same parameter values but substituting $r_2 = 6$ and $B = 4/5$. Finally, we note that in each of the four numerical examples above, the boundedness condition (16) is satisfied. Thus by Theorem 5.2, each of the four equilibria is, in fact, GAS under the parameter values in the four examples.

Although these examples demonstrate that GAS equilibria of all four types (E_6 through E_9) are possible under condition (A), we would like to demonstrate, in particular, that there is a wide range of parameter values under which E_7 , corresponding to the extinction of the original host, is LAS after a host-range expansion. To do this, we further consider the stability conditions of E_6 and E_7 under condition (A).

Summarizing the conditions for the co-existence of the four equilibria E_5 (3-d), E_5 (4-d), E_6 (4-d), and E_7 (4-d) gives

$$r_2 > \frac{1}{B}, \quad K_1 > \frac{1}{B}, \quad \tilde{D}K_1 > 1, \quad EK_2 > 1, \quad r_1 > r_1^* = \frac{K_1K_2}{BK_1 - 1} \left(B - \frac{1}{r_2} \right).$$

The stability conditions for the four equilibria are given below:

$$\begin{aligned}
 E_5 \text{ (3-d): } & \frac{1}{B} < K_1 \leq r_2, \quad r_1 > r_1^*, \\
 E_5 \text{ (4-d): } & \frac{1}{B} < K_1 \leq r_2, \quad r_1 > r_1^*, \\
 & E < \frac{Br_2}{K_2(Br_2 - 1)}, \quad \tilde{D} < B - EK_2 \left(B - \frac{1}{r_2} \right), \\
 E_6 \text{ (4-d): } & B < \tilde{D}, \quad r_2 < \frac{1}{\tilde{D}} + \frac{A}{\tilde{c}} \left(1 - \frac{1}{\tilde{D}K_1} \right) r_1, \\
 E_7 \text{ (4-d): } & r_1 < \frac{1}{E} + \frac{\tilde{c}}{A} \left(1 - \frac{1}{EK_2} \right) r_2.
 \end{aligned}$$

Now, suppose E_5 (3-d) is stable but E_5 (4-d) is unstable (condition (A)). Then, combining the co-existence condition and the stability of E_5 (3-d), E_6 and E_7 yields

$$\begin{aligned}
 \frac{1}{B} < K_1 \leq r_2, \quad \tilde{D}K_1 > 1, \quad EK_2 > 1, \quad r_1 > \frac{K_1K_2}{BK_1 - 1} \left(B - \frac{1}{r_2} \right), \\
 r_2 < \frac{1}{\tilde{D}} + \frac{A}{\tilde{c}} \left(1 - \frac{1}{\tilde{D}K_1} \right) r_1, \quad r_1 < \frac{1}{E} + \frac{\tilde{c}}{A} \left(1 - \frac{1}{EK_2} \right) r_2.
 \end{aligned}$$

The bifurcation diagram showing the above conditions is given in Figure 2. It is shown that E_5 (3-d) is GAS for the parameter values located in the purple shaded region, bounded by $r_2 > K_1$ and $r_1 > \frac{K_1K_2}{BK_1 - 1} \left(B - \frac{1}{r_2} \right)$. Note that there exists a vertical asymptote at $r_1 = \frac{K_1K_2}{K_1 - \frac{1}{B}}$

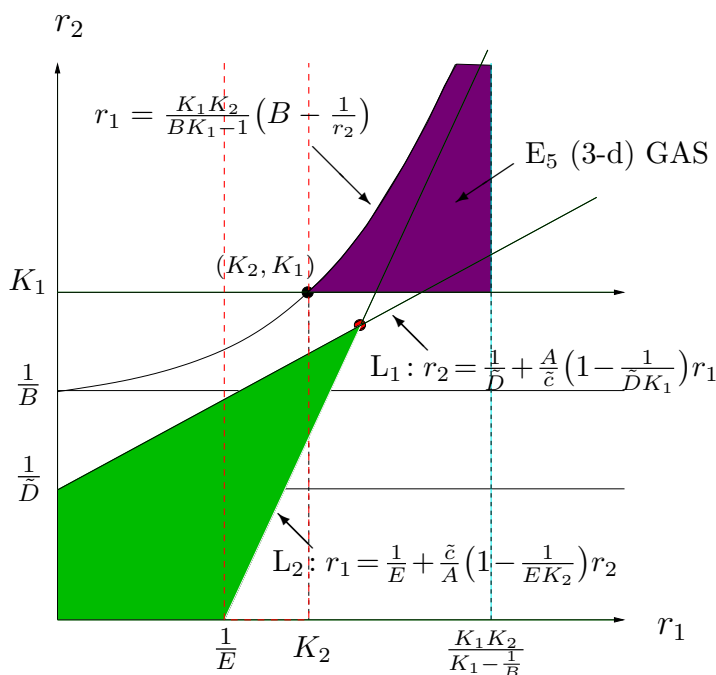


Figure 2. Bifurcation diagram projected on the r_1 - r_2 parameter plane, showing the possibility for bistability between E_5 (3-d) and E_6 (4-d), or E_5 (3-d) and E_7 (4-d), but not both.

and the region on the right side of this asymptote satisfying $r_1 > \frac{K_1 K_2}{B K_1 - 1} (B - \frac{1}{r_2})$ must be below the r_1 axis since $r_2 < 0$, and therefore, this region does not contain biologically meaningful parameter values. E_6 is LAS in the region on the right of the line L_1 and E_7 is LAS in the region on the left of the line L_2 .

As shown in the Supplementary Material (section SM4.6), it is impossible to have co-stable equilibria E_5 (3-d), E_6 and E_7 , which can also be seen on geometric grounds from this bifurcation diagram (not shown). Thus, depending upon on the position of the intersection point of the two lines L_1 and L_2 (the red circle in the figure), i.e., depending on the parameter values, E_5 (3-d) is co-stable with E_6 or E_7 or neither.

The most interesting prediction of our analysis is that host-range expansion can drive the original host to extinction. This situation occurs in the bifurcation diagram Figure 2 when the purple region overlaps with the region to the left of line L_2 . To maximize this parameter regime, we may let L_2 pass through the lower-right corner of the red square: $(r_1, r_2) = (\frac{K_1 K_2}{K_1 - \frac{1}{B}}, K_1)$, which yields

$$\frac{\tilde{c}}{A} = \frac{K_1 K_2 \left(1 - \frac{1}{E K_2}\right) + \frac{1}{B E}}{K_1^2 \left(1 - \frac{1}{B K_1}\right) \left(1 - \frac{1}{E K_2}\right)}.$$

Figure 3 demonstrates that the purple region may be entirely contained within the green region, showing a large region of r_1 - r_2 space in which host-range expansion would lead to the extinction of the original host.

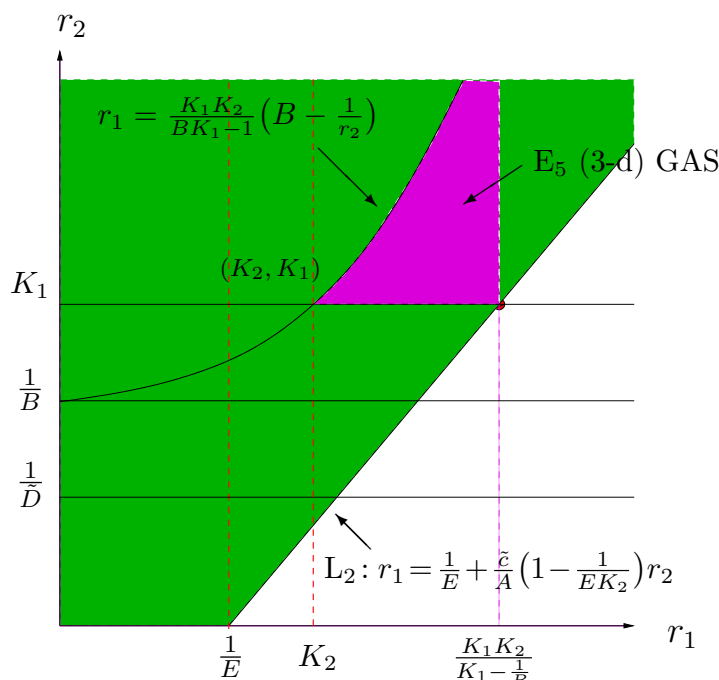


Figure 3. Bifurcation diagram projected on the r_1 - r_2 parameter plane, showing a large region (purple) in which E_5 is stable in the 3-d model but unstable in the 4-d model, while E_7 is LAS in the 4-d model.

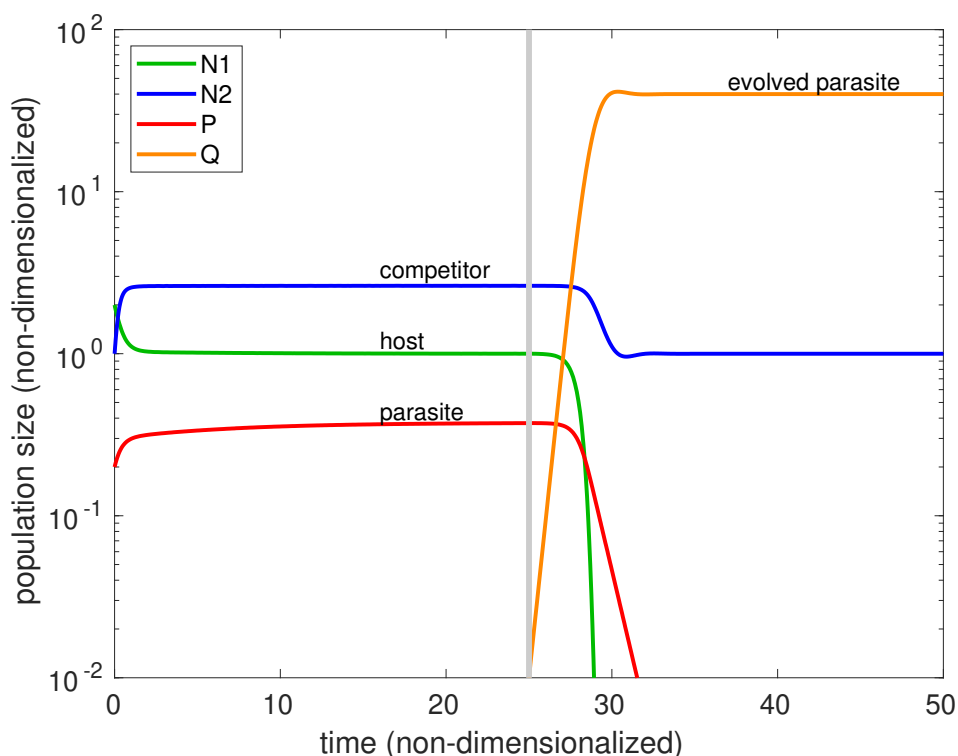


Figure 4. Simulated time history of a host-range expansion that drives the original host to extinction. The 3-d model (2.2) is integrated numerically up until the vertical grey line. The final conditions of the 3-d model are then taken as initial conditions of the 4-d model (3.2), along with a small population of the evolved parasite, Q . In the absence of Q , we observe the GAS of E_5 (3-d), while in the 4-d model the solution approaches the LAS E_7 . We see that the novel host sustains the evolved parasite at high densities, driving the original host to extinction. Parameters are $B = 1$, $K_1 = 2$, $K_2 = 3$, $r_1 = 6$, and $r_2 = 8$ in both models with $\tilde{c} = \frac{1}{2}$, $\tilde{D} = \frac{3}{5}$, $E = 1$, $A = \frac{2}{15}$ in the 4-d model.

Choosing parameter values within the purple region, we simulate the timecourse of the 3-d model, approaching the GAS E_5 as expected (Figure 4). At time 25, we use the final conditions of the 3-d simulation as initial conditions for the 4-d model, adding a small population of the evolved parasite, Q . The resulting time course shows that the original host is driven to extinction, while the solution approaches the LAS equilibrium E_7 .

7. Discussion and conclusions. We study a system of a host and parasite, along with a second potential host species that is not infected by the parasite. We demonstrate that if the parasite successfully expands its host range, only four outcomes are possible, as described below.

As expected, host-range expansion can drive the novel host to extinction (E_6). This result makes intuitive sense since, by definition, a host-range expansion occurs when the parasite becomes able to infect and kill the new host. Concerns in the ecological literature centering on the risks of host-range expansion typically address this outcome [1, 7, 27].

Alternatively, host-range expansion can cause the emergence of a new, generalist parasite that stably co-exists with both old and new hosts, and the original parasite (E_9). The evolution

of generalist parasites, via a “jump” to a new host, has been reported in many contexts [9, 27], most notably in the emergence of zoonotic disease [15]. Such expansions may be facilitated by genetic innovations, physiological or ecological stressors [35].

Rather than stably co-existing, however, the emergence of the generalist can also cause the extinction of the original, specialist parasite (E_8). Given that the two parasite species compete for hosts, this potential outcome is not surprising, and situations in which a generalist predator outcompetes a specialist predator have been previously described [33, 36].

Along with these three outcomes, however, our work reveals a fourth possibility: host-range expansion can, in some parameter regimes, drive the original host species to extinction (E_7), along with the original specialist parasite. This is unexpected, since the original host and its parasite were at stable equilibrium before the range expansion, and the range expansion involves death in the novel host species, a competitor for the original host.

What factors cause the original host to go extinct? While the stability conditions for E_7 make it clear that this behavior depends in a complex way on many parameters, we suggest that this can occur when the parasite density that is sustainable by the novel host is higher than the parasite density sustained by the original host. Thus, the parasite population markedly increases when the new host can be infected, driving the original host to extinction. This explanation only holds, however, if the parasite is a more important factor in regulating population sizes than the competition between the two species. The implications of this outcome are that relatively small populations may be at risk of extinction if their parasites gain the ability to infect a related species with a much larger population size. For example, native species could be driven extinct by parasites with which they have stably co-existed for centuries if those parasites become able to infect and thrive on species introduced and maintained by humans.

While we have focused in this section on the biological implications of our work, we note that achieving these results involved several technical challenges. Bifurcation analysis is widely applied to study nonlinear dynamical systems, yet in real-world applications these techniques have been mainly restricted to lower-dimensional systems. It is difficult to apply bifurcation analysis to higher-dimensional (e.g., 4-d or 5-d) models, in particular when a substantial number of system parameters are involved. In this paper, we explored the bifurcation behaviors for a 4-d model with 13 parameters, and derived all equilibria and their stability conditions, expressed explicitly in terms of the system parameters. In particular, we obtained the stability conditions for several Hopf bifurcations, which play an important role in the oscillatory behaviors of predator-prey systems. Thus, in addition to the biological insights made possible in this work, our study offers an important example of how to approach a full bifurcation analysis of a high-dimensional dynamical system.

Despite the relative complexity of the models we present here, our conclusions remain limited by a number of key simplifying assumptions. We assume well-mixed populations of parasites and hosts, ignoring any spatial considerations. We likewise use mass-action kinetics to describe the infection process, an assumption that could be invalid in parameter regimes with large numbers of hosts and few parasites, such that single parasites are modelled as infecting multiple hosts. Most importantly, we ignore transient dynamics and focus entirely on equilibrium and stability results. Each of these simplifying assumptions suggests a possible direction for further work.

It has long been recognized that adding a predator can stabilize the dynamics between competitor species [6, 28, 29]. In contrast, here we report the surprising result that adding a parasite, through host-range expansion, can in many cases destabilize the coexistence of two competing species. Our approach could also be applied to the question of host-range contraction, that is, the emergence of a specialist parasite through loss-of-function mutations in the generalist. This case would require the analysis of a 3-d model that includes only the generalist, rather than the specialist, before the host-range contraction. This simple idea points to a wealth of interesting and important problems surrounding dynamic changes in the host range of pathogens.

Acknowledgments. The authors are grateful to the reviewers for insightful comments that strengthened the work.

Author contributions. The first author conducted stability and bifurcation analyses and wrote the manuscript. The second author conducted equilibria and stability analyses. The third author designed the study, developed the models, and wrote the manuscript. The fourth author designed the study, developed the models, and wrote the manuscript.

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