VIRUS DYNAMICS IN THE PRESENCE OF CONTACT-MEDIATED HOST DORMANCY

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(23 July 2021)

Abstract: We investigate a stochastic individual-based model for the population dynamics of host–virus systems where the hosts may transition into a dormant state upon contact with virions, thus evading infection. Such a dormancy-based defence mechanism was described in Bautista et al (2015).

We first analyse the effect of the dormancy-related model parameters on the probability of invasion of a newly arriving virus into a resident host population. It turns out that the probability of dormancy initiation upon virus contact plays a crucial role, while the lengths of the dormancy periods or the death rate during dormancy are largely irrelevant.

Given successful invasion, we then show that the emergence of a persistent virus infection ('epidemic') in the host population corresponds to the existence of a coexistence equilibrium for the deterministic many-particle limit of our model. In this context, all dormancy-related parameters have a significant impact. Indeed, while related systems without dormancy may exhibit a Hopf bifurcation, giving rise to a variant of the ‘paradox of enrichment’, we argue that the inclusion of dormancy can prevent this loss of stability.

Finally, we show that the presence of contact-mediated dormancy enables the host population to maintain higher equilibrium sizes (resp. fitness values) – while still being able to avoid a persistent epidemic – than host populations without this trait, for which high fitness values would imply a high risk for the emergence of a persistent epidemic. This adds a twist to the relevance of ‘reproductive trade-offs’ usually associated with costly dormancy traits.

MSC 2010. 92D25, 60J85, 34D05, 37G15.

Keywords and phrases. Dormancy, host–virus dynamics, stochastic population model, multitype branching process, Hopf bifurcation, paradox of enrichment.

1. Introduction

Motivation and background. The abstract concept of ‘dormancy’ describes the ability of an organism to switch into a reversible state of low metabolic activity. This strategy to cope with adverse environmental conditions is wide-spread among many taxa, including plants, invertebrates, mammals and also micro-organisms \[1\], \[2\]. The resulting ‘seed banks’ comprised of dormant individuals have profound effects on the evolutionary and ecological behavior of populations, in particular increasing diversity and resilience against various forms of external stress.

The mathematical analysis of the effects of dormancy in ecology and evolution via dynamical systems, and increasingly also via stochastic individual based models, has been an active field of research for many years. One of the basic paradigms is that dormancy, and the resulting seed banks, can be highly

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beneficial in fluctuating environments, where they can often be understood as bet hedging strategies. This has been confirmed by abstract theory many times beginning with the delayed seed germination model of Cohen [C66]. Modelling has in fact grown rather complex in recent decades, incorporating the related concepts of ‘responsive transitioning’ and ‘phenotypic plasticity’, often in the context of microbial populations (e.g. [B04, KL05, MS08, DMB11]). Overall, environmental fluctuations can give rise to an interesting panorama of optimal dormancy initiation and resuscitation strategies, see e.g. [BHS21].

However, the assumption that external environmental fluctuations are absolutely necessary for dormancy to be an evolutionary successful strategy (given the high maintenance costs of such a trait) has also been challenged. Several mathematical models show that competitive pressure for resources [ES7, LR06, BT20, BT21] or certain predator-prey dynamics [T20] may also favor dormancy even in the absence of additional abiotic variation. For example, predator dormancy has been shown to be able to prevent the occurrence of the ‘paradox of enrichment’ [KMO09], thus stabilizing the coexistence regimes in predator-prey systems.

In this paper, we investigate a further and relatively novel scenario in which dormancy enters as a defence strategy of host cells against virus attacks. For example, it has been reported that infected bacteria can enter a dormant state as part of a CRISPR-Cas immune response, thereby curbing phage epidemics (cf. [JF19] resp. [MNM19]). Further, it has been suggested that dormancy of hosts may even be initiated upon mere contact of virus particles with their cell hull, so that the dormant host may entirely avoid infection, cf. Bautista et al. [B15]. Indeed, in experiments, Bautista et. al. observed that Sulfolobus islandicus (an archeon) populations may switch almost entirely into dormancy within hours after being exposed to the Sulfolobus spindle-shape virus SSV9, even when the initial virus-to-host ratio is relatively small. The authors argue that this highly sensitive anti-viral response should be taken into account in models for virus-host interactions so that its ecological consequences can be understood.

A first step in this direction was taken by Gulbudak and Weitz [GW16] who provide a biophysical model for the ‘early stages’ (covering a few hours) of the above host–virus dynamics. Indeed, their deterministic model can reproduce the observed rapid switches into dormancy for relatively small virus-to-host ratios.

However, their model is really tailored to a relatively short ‘time-window’ of host–virus dynamics and neither allows for a stochastic invasion analysis for low numbers of newly arriving virions (where random fluctuations play an important role), nor virus reproduction via host cells (lytic/budding or lysogenic), which would be necessary for a ‘long-time’ analysis of the system. Instead, their dynamical systems approach seems to implicitly require that both the host and the virus population sizes are initially sufficiently large to justify a deterministic model by a law-of-large-numbers argument (which seems fine if the host population is exposed artificially by sufficiently high numbers of virus particles during experiments, even if the virus-to-host ratio is relatively small).

Here, we follow up on the suggestion by [B15] to investigate the ecological consequences of contact-mediated dormancy by proposing a stochastic individual-based model that extends [GW16] in the two directions indicated above: i) We include explicit individual-based stochasticity, which is relevant during the early phases of an emerging virus epidemic (that is, when only few or even single virus particles arrive in the host population), and ii) incorporate a mechanism for lytic virus reproduction which allows an analysis of the coexistence / extinction regimes of the virus population. Once the virus epidemic becomes ‘macroscopic’ (that is, the number of virus particles is at least of the order of the resident population; a ‘successful invasion’), the stochastic model can then be well approximated by a deterministic dynamical system. This limiting deterministic system also extends a model of [BK98], where a lytic virus infection against single-cell hosts was studied. For their model, which is dormancy-free and also excludes the recovery of infected individuals, the authors provide a full bifurcation analysis of their system, which partially motivated our present analysis.
However, it should be said that our model is only one of several possible extensions of these previous models. Indeed, as mentioned before, we opt for lytic virus release after reproduction, always killing the host cell (as opposed to chronic infection of individual cells, cf. e.g. [GW18] for a related set-up). Other modelling choices may be taken regarding the contact-mechanics between virions and host (we opt for reversible host–virus contact), but we refrain from discussing all possible mechanisms here and leave them for future research.

**Main goals of the paper.** We now outline the main questions about our model that we will strive to answer in this paper. While we aim for mathematical rigour whenever possible, some questions regarding the long-term behaviour will be attacked ‘only’ via simulation, sometimes leading to mathematical conjectures that invite further theoretical work that is beyond the scope of the present manuscript.

Q a) Under which conditions is an invasion, starting with the arrival of a single virion, into a (large) resident host population possible with high probability? Here, by invasion we mean that the virus population reaches a level ‘visible’ on the scale of the carrying capacity of the host population, thus initiating a ‘macroscopic epidemic’. This refers to the first, stochastic phase of the infection dynamics, where random fluctuation play a crucial role for the establishment of the epidemic.

Q b) In the case that the virus invasion is successful, how long does this invasion process typically take (again expressed on the order of the size of the resident population)?

Q c) Given that the virus population reaches a level that is comparable to the resident host population (i.e., a successful invasion), a many-particle approximation becomes feasible. What is the dynamical system that corresponds to the many-particle limit of our stochastic individual based model? This system can then be used to describe the dynamics of the model after the initial ‘stochastic phase’, where now random fluctuations become negligible.

Q d) During this second deterministic phase, under which conditions does the virus epidemic either become persistent (both host- and virus populations maintain macroscopic sizes over ‘long’ time-intervals) or break down (extinction of the virus and potentially also the host population)?

Q e) In the case of persistence, what is a suitable classification of the long-term behaviour of the limiting dynamical system (i.e. stable coexistence vs. periodic/chaotic behaviour, emergence of a ‘paradox of enrichment’ phenomenon)? What are the novel effects introduced by contact-mediated dormancy (and also by the possible recovery of infected individuals, which were both absent from the deterministic model of [BK98])?

For all of these questions, we are particularly interested in the specific roles of the dormancy parameters (dormancy initiation probability upon virus contact, resuscitation rate, death rate during dormancy).

**Organization of the paper.** The paper is organized as follows. In Section 2 we define our model, prepare and present our main results, and discuss them in the context of existing literature. In particular, in Section 2.5 we provide explicit and mathematically rigorous answers to questions a)–d).

Section 3 is devoted to further results, conjectures, and simulations related to the underlying dynamical system that are no prerequisites of our main results, but help to get a further qualitative and quantitative understanding of the behaviour of our model, including a bifurcation analysis. In particular, we provide partial answers and a general conjecture for question e) in Section 3.1, present numerical simulations for various parameter regimes (Section 3.2), and investigate the emergence of the ‘paradox of enrichment’ in our model (Section 3.3).

Finally, the proofs of the main results are carried out in Section 4.
2. Model definition, heuristics and main results

2.1. A stochastic individual-based model for contact-mediated dormancy. We consider a host–virus population consisting of individuals of four types: Active hosts (type 1a), dormant hosts (type 1d), infected hosts (type 1i) and free virions (type 2). The stochastic dynamics of the system is given as follows:

- Active (1a) host cells reproduce via binary fission at rate $\lambda_1 > 0$ and die at rate $\mu_1 \in (0, \lambda_1)$. Dormant (1d) or infected (1i) cells do not reproduce. See Figure 1a (left panel).
- Virions (2) do not reproduce individually (but instead indirectly via infection of a host cell, see below) and die/degrade at rate $\mu_2 > 0$, see Figure 1a (right panel).
- Competition: Fix parameters $K > 0$ called carrying capacity and $C > 0$ called competition strength. For any ordered pair consisting of one active (1a) host cell and one other host cell (of either type 1a or 1i or 1d), at rate $C/K$, a death due to competition/overcrowding happens, affecting the active individual, which is removed from the population (cf. Figure 1b).
- Virus attack: Fix a parameter $q \in (0, 1)$ called dormancy initiation probability. For any ordered pair of individuals containing one active (1a) cell and one virion (2), a virus attack happens at rate $D/K$. In this case, with probability $q$, the attacked host (1a) sences the virion upon contact with its cell-hull and is able to switch into dormancy (from 1a to 1d) before infection, and with probability $1 - q$, the host cell gets infected (i.e. switches from 1a to 1i) and the free virus (2) is ‘removed’ (in the sense that it enters the cell), see Figure 1c.
- Infected cells (1i) either recover (at rate $r > 0$) or produce $m \in \mathbb{N}$ (where typically $m$ is large) new virions (2) and then dissolve (lysis), at rate $v > 0$ (see Figure 1d).
- Dormant cells (1d) resuscitate into (1a) at rate $\sigma > 0$ and die at rate $\kappa \mu_1$ for some $\kappa \geq 0$ (Figure 1e).

Note that in this model, there is no classical meaning of ‘fitness’ for the virions (type 2), since the reproduction of this type of individual rests entirely on host availability. As indicated in the introduction, such a reproduction mechanism reflects lysis, and we refer to $m$ as burst size (cf. e.g. [B09] for burst sizes in archea).

The corresponding population process is formally defined as a continuous time Markov chain $N = (N_t)$ on $\mathbb{N}_0^4$, where

$$ (N_t)_{t \geq 0} = (N_{1a,t}, N_{1d,t}, N_{1i,t}, N_{2,t})_{t \geq 0} $$

is interpreted as

$$ N_{x,t} = \# \{ \text{individuals of type } x \text{ alive at time } t \}, $$

for $x \in \{1a, 1d, 1i, 2\}$.

According to the above description, $N$ is then the unique Markov process with transitions

$$ (n_{1a}, n_{1d}, n_{1i}, n_2) \rightarrow \begin{cases} 
(n_{1a} + 1, n_{1d}, n_{1i}, n_2) \text{ at rate } n_{1a} \lambda_1, \\
(n_{1a} - 1, n_{1d}, n_{1i}, n_2) \text{ at rate } n_{1a} \mu_1 + (n_{1a} + n_{1d} + n_{1i})/K, \\
(n_{1a}, n_{1d}, n_{1i}, n_2 - 1) \text{ at rate } n_2 \mu_2, \\
(n_{1a}, n_{1d} - 1, n_{1i}, n_2) \text{ at rate } n_{1d} \kappa \mu_1, \\
(n_{1a} + 1, n_{1d}, n_{1i} - 1, n_2) \text{ at rate } n_{1d} \sigma, \\
(n_{1a}, n_{1d}, n_{1i} - 1, n_2 + m) \text{ at rate } v n_{1i}, \\
(n_{1a} + 1, n_{1d}, n_{1i} - 1, n_2) \text{ at rate } r n_{1i}, \\
(n_{1a} - 1, n_{1d} + 1, n_{1i}, n_2) \text{ at rate } q n_{1d} n_2/K, \\
(n_{1a} - 1, n_{1d}, n_{1i} + 1, n_2 - 1) \text{ at rate } (1 - q) n_{1a} n_2/K.
\end{cases} $$
VIRUS-INDUCED DORMANCY

(a) Clonal reproduction of active hosts (type 1a) at rate $\lambda_1$ resp. death at rate $\mu_1$ (left), and virus degradation at rate $\mu_2$ (right). The symbol $\dagger$ represents the ‘death state’.

(b) Competition events for pairs of host cells, involving the death of the first (type 1a) individual at rate $C/K$.

(c) Virus attack resulting in infection (rate $(1-q)D/K$) of host or dormancy (rate $qD/K$).

(d) Infected cells recover (at rate $r > 0$) or release $m$ virions after lysis, at rate $v > 0$.

(e) Leaving the dormant state 1d by resuscitation (rate $\sigma$) or death (rate $\kappa\mu_1$).

**Figure 1.** Overview of transitions of the host–virus model
Let us mention some elementary properties of this Markov chain. Its only absorbing state is \((0, 0, 0, 0)\), which corresponds to the extinction of all the four types. Moreover, if \(N_0 \in [0, \infty) \times \{0\}^3\), then \(N_t \in [0, \infty) \times \{0\}^3\) for all \(t > 0\), and if \(N_0 \in [0, \infty) \times \{0\}^2\), then \(N_t \in [0, \infty) \times \{0\}^2\) for all \(t > 0\). Finally, \(t \mapsto N_{1d,t}\) is monotonically decreasing and the expected time until it reaches 0 is finite. In other words, if there are initially neither infected individuals nor viruses, then this will also be the case for all positive times, and the dormant population will vanish rapidly.

Our goal is to analyze a situation where \(K\) is large (even the limit as \(K \to \infty\), corresponding to a many-particles limit), and the initial size of the (scaled) host population \(N_{1a,0}^K\) is close to its (virus-free) equilibrium. We will thus consider the rescaled process

\[(N^K_t)_{t \geq 0} = (N^K_{1a,t}, N^K_{1d,t}, N^K_{1i,t}, N^K_{2,t})_{t \geq 0},\]

which is defined via

\[N^K_{x,t} = \frac{1}{K} \#\{\text{individuals of type } x_i \text{ alive at time } t\},\]

so that \(N^K_t = N_t\) for all \(K, t > 0\), recalling that \(K > 0\) is the carrying capacity of the system. We also write

\[N^K_{1,t} = N^K_{1a,t} + N^K_{1d,t} + N^K_{1i,t}\]

for the total population size of the host individuals (scaled by \(K\)).

In this set-up, we later assume that a single virion (type 2) enters the host population and starts targeting the type 1a individuals. Using techniques of Freidlin–Wentzell type large deviations and multitype branching processes, we aim to identify the asymptotic probability that a ‘macroscopic’ epidemic emerges, i.e. that type 2 (and hence also types 1i and 1d) becomes ‘visible’ on the order of \(K\) instead of going extinct. The emergence of a macroscopic epidemic marks the end of the initial stochastic phase of the system. Instead, the scaled population sizes can from then on be uniformly approximated by a deterministic, non-linear dynamical system. We introduce this limiting system in the next subsection.

**Remark 2.1 (Contact-mediated dormancy vs. other types of dormancy initiation).** Dormancy initiation as the result of mere host–virus contact seems to be a new feature in population dynamic models and further extends the growing panorama of different dormancy mechanisms in the mathematical literature, each of them with different consequences for the dynamics of the underlying systems. Here, we briefly mention competition-induced dormancy as described in [BT20], where dormancy is incorporated into a stochastic individual based model as a means to escape from death by overcrowding due to the own or other species. A different variant is given by predator dormancy studied in predator-prey systems (e.g. in [KC09], [KMO09]), which serves as a way to resolve instabilities resulting from the paradox of enrichment, see also Section 3.3 below. Besides competition or rival species, other forms of environmental stress (heat, antibiotic treatment etc.) can lead to responsive switching into dormancy, which describes dormancy initiation as the result of an external trigger event, while also spontaneous dormancy initiation (without external trigger) has been observed. The latter can e.g. be understood in terms of stochastic bet-hedging strategies and is useful in particular in randomly fluctuating environments. See [LdHWB21] for an overview of dormancy attributes and further literature.

Note that our system shares some features with stochastic epidemic models, however, there are also significant differences, in particular regarding competition and the explicit modeling of the virus population. We will discuss these and comment on the notion and properties of the basic reproduction number in the context of our model in Section 2.6.3.
2.2. The limiting dynamical system for large populations. Once a macroscopic epidemic has emerged, that is, the population size of the virus particles and the host cells are both of order \( K \) (for large \( K \)), then the Markov chain \( (N^K_t)_{t \geq 0} \) satisfies a ‘functional law of large numbers’ and can be approximated by a limiting deterministic dynamical system. We now introduce this scaling limit. Assume that the initial population size of \( N^K_0 \) satisfies
\[
\frac{1}{K} N^K_0 = N^K_0 \xrightarrow{K \to \infty} n(0) = ((n_{1a}(0), n_{1d}(0), n_2(0)) \in [0, \infty)^3
\]
and fix some \( T > 0 \). Then, \([\text{EK86} \text{ Theorem 11.2.1, p. 456}]\) implies the weak convergence (uniformly on \([0, T])\)
\[
(N^K_t)_{t \in [0, T]} \xrightarrow{K \to \infty} (n(t))_{t \geq 0} = ((n_{1a}(t), n_{1d}(t), n_2(t)))_{t \in [0, T]}
\]
to the unique solution \((n(t))_{t \geq 0}\) of the dynamical system
\[
\begin{align*}
\frac{dn_{1a}(t)}{dt} &= n_{1a}(t)(\lambda_1 - \mu_1 - C(n_{1a}(t) + n_{1i}(t) + n_{1d}(t)) - Dn_2(t)) + \sigma n_{1d}(t) + rn_{1i}(t), \\
\frac{dn_{1d}(t)}{dt} &= qDn_{1a}(t)n_2(t) - (\kappa_1 + \sigma)n_{1d}(t), \\
\frac{dn_{1i}(t)}{dt} &= (1 - q)Dn_{1a}(t)n_2(t) - (r + v)n_{1i}(t), \\
\frac{dn_2(t)}{dt} &= mvn_{1i}(t) - (1 - q)Dn_{1a}(t)n_2(t) - \mu_2n_2(t)
\end{align*}
\tag{2.1}
\]
with parameters as above. It is easy to see that the positive orthant is positively invariant under this system. Define
\[
\bar{n}_{1a} := \frac{(\lambda_1 - \mu_1)v}{C}.
\]
Then, \((0, 0, 0, 0)\) (the zero or ‘death’ equilibrium) and \((\bar{n}_{1a}, 0, 0, 0)\) (the ‘virus-free’ equilibrium, e.g. after complete recovery) are equilibria of the dynamical system \((2.1)\), and they are distinct as long as \( \lambda_1 > \mu_1 \).

We now investigate under what conditions a ‘coexistence equilibrium’ \((n_{1a}, n_{1d}, n_{1i}, n_2)\) with four positive coordinates exists, which is a question that turns out to be closely related to the stability of \((\bar{n}_{1a}, 0, 0, 0)\).

**Lemma 2.2.** Assume that \( \lambda_1 > \mu_1 \). Then, the system has a coordinatewise positive coexistence equilibrium \((n_{1a}, n_{1d}, n_{1i}, n_2)\) if and only if the condition
\[
(mv - (r + v))(1 - q)D\bar{n}_{1a} > \mu_2(r + v).
\tag{2.2}
\]
holds. In this case, the coexistence equilibrium is unique, and its active coordinate \(n_{1a}\) is given by
\[
n_{1a} = \frac{\mu_2(r + v)}{(1 - q)D(mv - (r + v))}.
\tag{2.3}
\]

It is clear from \((2.2)\) and \((2.3)\) that if \((n_{1a}, n_{1d}, n_{1i}, n_2)\) exists, then \(n_{1a} < \bar{n}_{1a}\), i.e. a persistent virus epidemic always reduces the population size of type 1a (compared to its virus-free equilibrium). We refer the reader to Section \(\text{1.2}\) for the proof of this Lemma, which also provides an explicit characterization of the coordinates \(n_{1d}, n_{1i}, n_2\) of the coexistence equilibrium.

Condition \((2.2)\) has several interesting aspects and will be interpreted in detail in Section \(\text{2.6}.1\) whereas in Section \(\text{2.6}.2\) we discuss potential trade-offs between ‘fitness’ and ‘dormancy costs’, and in Section \(\text{2.6}.3\) we comment on the ‘reproduction number’ of the virus epidemic. Note further that the condition is not only equivalent to the existence of a coexistence equilibrium for \((2.1)\), but also guarantees the supercriticality of a three-type branching process approximating the dormant, infected, and virus population in the initial stochastic phase of the host–virus system, cf. Section \(\text{2.3}\) below.
Finally, we note that for $\lambda_1 > \mu_1$, (2.2) implies that $mv > r + v$. Here, the critical case where (2.2) holds with equality is given by
\[
\frac{\lambda_1 - \mu_1}{C} = \frac{\mu_2(r + v)}{(1 - q)D(mv - (r + v))}. 
\tag{2.4}
\]
It will be clear from the proof of Lemma 2.2 that if (2.4) holds, then $(\bar{n}_{1a}, 0, 0, 0)$ will be the only non-negative equilibrium.

Given all parameters but $m$, the value of $m$ ensuring that (2.4) holds will be denoted by $m^*$, the critical burst size, throughout the rest of the paper. Note that $m^*$ is not necessarily an integer, and also that if all parameters but $m$ are fixed, then (2.2) is equivalent to $m > m^*$. We also refer to $m^*$ as transcritical bifurcation point. In Section 3.1 we will justify this naming in view of the classical nomenclature of dynamical systems (as can be found e.g. in [KMO09]).

Let us now analyse the stability of the equilibria $(0,0,0,0)$, $(\bar{n}_{1a}, 0, 0, 0)$, and $(n_{1a}, n_{1d}, n_{1i}, n_2)$ of the system (2.1) (if they exist). While the local stability of $(0,0,0,0)$ and $(\bar{n}_{1a}, 0, 0, 0)$ can easily be determined via linearization (except for a few boundary cases), for the coordinatewise positive coexistence equilibrium $(n_{1a}, n_{1d}, n_{1i}, n_2)$ (if it exists) we have only partial results. As we will explain in Section 3.1 below, this equilibrium may be stable or unstable depending on the choice of the parameters.

**Lemma 2.3.** Let $\lambda_1 > \mu_1$. Then the following assertions hold for the dynamical system (2.1).

1. The equilibrium $(0,0,0,0)$ is unstable.
2. The equilibrium $(\bar{n}_{1a}, 0, 0, 0)$ is unstable if (2.2) holds and asymptotically stable if the strict reverse inequality of (2.2) holds, in other words,
\[
mv(1 - q)D\bar{n}_{1a} < ((1 - q)D\bar{n}_{1a} + \mu_2)(r + v). 
\tag{2.5}
\]
3. Under condition (2.2), the Jacobi matrix of the system at $(n_{1a}, n_{1d}, n_{1i}, n_2)$ has positive determinant and negative trace.

The proof of Lemma 2.3 will also be carried out in Section 4.2. Note that assertion (3) implies that the Jacobi matrix at $(n_{1a}, n_{1d}, n_{1i}, n_2)$ has either 2 or 4 eigenvalues with negative real parts. In fact, by Proposition 3.5 below, all eigenvalues have negative real parts and thus $(n_{1a}, n_{1d}, n_{1i}, n_2)$ is asymptotically stable for all $m > m^*$ if their difference is sufficiently small.

However, depending on the choice of the parameters, the coexistence equilibrium may also be unstable: For all parameters but $m$ fixed, it may undergo a Hopf bifurcation at some value $m = m^{**} > m^*$, giving rise to stable periodic trajectories. For $m$ very large, these periods may have minima arbitrarily close to zero. Hence, in the underlying stochastic system, the population may in fact die out due to random fluctuations. Indeed, in [BK98], the presence of such Hopf bifurcations was verified for the three-dimensional analogue of the system (2.1) without dormancy and also without the possibility of host recovery (i.e., for $q = r = 0$ and with $n_{1d}(t)$ absent).

We show (see Proposition 3.4 below) that for the same three-dimensional system with host recovery, for $r > v$, i.e., if infected cells are more likely to recover than to die via lysis, then the coexistence equilibrium is stable for all $m$ sufficiently large. The bifurcation analysis of the four-dimensional system (2.1) is unfortunately rather involved. In a nutshell, we expect that increasing the dormancy probability $q$ also increases the Hopf bifurcation point $m^{**}$, whereas increasing the recovery rate $r$ will lead to $m^{**} = \infty$. That is, thanks to dormancy, the system stays stable also for higher burst sizes than in the absence of dormancy, whereas increasing the recovery rate (also in absence of dormancy) may lead to stability irrespective of the burst size. See Section 3.1 for a general conjecture as well as for rigorous partial results in this direction, and Section 3.2 for numerical results.

Some of our simulations indicate that for the same choice of parameters as in [GW13], our extended model exhibits similar behaviour over short time-intervals in the deterministic phase. Indeed, one
can observe a high initial peak of the dormant population size shortly after artificial exposure to a virus-population, corresponding to the majority of active individuals quickly becoming dormant (see Example 3.11) as reported in [GW16].

For all choices of parameters where \((n_{1a}, n_{1d}, n_{1i}, n_2)\) exists with four positive coordinates, independently of whether Hopf bifurcations are present in the system or not, we can verify the following results, which will be crucial for our main theorems regarding the stochastic process \((N_t)_{t \geq 0}\) in the limit \(K \to \infty\). The first one tells us that starting from an initial condition with only positive coordinates, the one-type equilibrium \((\bar{n}_{1a}, 0, 0, 0)\) can never be reached under Condition (2.2).

**Proposition 2.4.** Consider the dynamical system (2.1). Assume that \(\lambda_1 > \mu_1\), (2.2) holds, and \((n_{1a}(0), n_{1d}(0), n_{1i}(0), n_2(0)) \in (0, \infty)^4\). Then \((n_{1a}(t), n_{1d}(t), n_{1i}(t), n_2(t))\) does not tend to \((\bar{n}_{1a}, 0, 0, 0)\) as \(t \to \infty\), not even along a diverging subsequence of time-points.

Since coordinatewise nonnegative solutions of (2.1) are bounded, Proposition 2.4 together with a simple compactness argument implies that started from any initial condition \((n_{1a}(0), n_{1d}(0), n_{1i}(0), n_2(0)) \in (0, \infty)^4\), there exists a \(\varrho > 0\) such that

\[
\liminf_{t \to \infty} \| (n_{1a}(t), n_{1d}(t), n_{1i}(t), n_2(t)) - (\bar{n}_{1a}, 0, 0, 0) \|_1 \geq \varrho. \tag{2.6}
\]

This assertion is known as \((\bar{n}_{1a}, 0, 0, 0)\) being a uniform strong repeller; cf. [BK98] Corollary 4.2 for its analogue in the recovery- and dormancy-free three-dimensional case. Next, the following corollary is analogous to [BK98], Lemma 2.3 and Theorem 4.2, but since that paper provides no explicit proof and our setting is more complex, we present a proof for the corollary.

**Corollary 2.5.** Consider the dynamical system (2.1). Assume that \(\lambda_1 > \mu_1\), (2.2) holds, and \((n_{1a}(0), n_{1d}(0), n_{1i}(0), n_2(0)) \in (0, \infty)^4\). Then

\[
\liminf_{t \to \infty} n_j(t) > 0
\]

holds for all \(j \in \{1a, 1d, 1i, 2\}\), and

\[
\limsup_{t \to \infty} n_{1a}(t) + n_{1d}(t) + n_{1i}(t) < \bar{n}_{1a}.
\]

Further,

\[
\limsup_{t \to \infty} n_2(t) < \frac{mv\bar{n}_{1a}}{\mu_2}.
\]

The positivity of the \(\liminf\)'s of the coordinates \(n_{1d}(t), n_{1i}(t), n_2(t)\) is called the uniform strong persistence of the system (2.1), as mentioned in [BK98]. By our uniform approximation result, in this case, the macroscopic virus epidemic will also be present for long times (with high probability) in the stochastic model with large enough carrying capacities \(K\).

**Remark 2.6** (Initial conditions in Corollary 2.5). Let us emphasize the role of the coordinatewise positivity of the initial condition: For example, if \(n_{1a}(0) > 0\) and \(n_{1d}(0) > 0\) but \(n_{1i}(0) = n_2(0) = 0\), then the solution will converge to \((\bar{n}_{1a}, 0, 0, 0)\). In contrast, if \((n_{1d}(0), n_{1i}(0), n_2(0)) \in [0, \infty)^3\) with \(\max\{n_{1i}(0), n_2(0)\} > 0\), then \(\min\{n_{1d}(t), n_{1i}(t), n_2(t)\} > 0\) holds for all \(t > 0\), and hence Proposition 2.4 and Corollary 2.5 also hold for such initial conditions.

The proof of Proposition 2.4 as well as the one of Corollary 2.5 can again be found in Section 4.2.
2.3. The approximating branching process(es) in the early stochastic phase. Assume that at time 0, a single virion arrives in a resident population of type 1a individuals with population size close to its equilibrium size $\bar{n}_{1a}$ (where we assume that $\lambda_1 > \mu_1$). Then, thanks to Freidlin–Wentzell type large deviation results (cf. Section 4.3 below), initially, the type 1a population size (divided by $K$) stays close to $\bar{n}_{1a}$ with high probability. Hence, the three-type population size process $(N_{1d,t}, N_{1i,t}, N_{2,t})$ is initially close to a three-type linear branching process $(\hat{N}(t))_{t \geq 0} = ((\hat{N}_{1d}(t), \hat{N}_{1i}(t), \hat{N}_{2}(t)))_{t \geq 0}$ with jump rates obtained by replacing $N_{1a,t}^K$ with the fixed value $\bar{n}_{1a}$ in the rates corresponding to $K\bar{n}_{1a}^K$. To be more precise, this branching process has the following transition rates for $(x,y,z) \in \mathbb{N}_0^3$:

- $(x, y, z) \rightarrow (x + 1, y, z)$ at rate $qD\bar{n}_{1a}z$,
- $(x, y, z) \rightarrow (x - 1, y, z)$ at rate $(\kappa\mu_1 + \sigma)x$,
- $(x, y, z) \rightarrow (x, y + 1, z - 1)$ at rate $(1 - q)D\bar{n}_{1a}z$,
- $(x, y, z) \rightarrow (x, y - 1, z)$ at rate $ry$,
- $(x, y, z) \rightarrow (x, y - 1, z + m)$ at rate $vy$,
- $(x, y, z) \rightarrow (x, y, z - 1)$ at rate $\mu_2 z$.

In which sense the two processes are ‘close’ to each other will be explained in Section 4.3; they are related via standard coupling arguments as in [CCLS17, CCLLS21]. It turns out that with high probability, this coupling holds as long as the population size $N_{1d,t} + N_{1i,t} + N_{2,t}$ of the infection-related types either reaches $\varepsilon K$ for some small (but fixed) $\varepsilon > 0$ or goes extinct. Once all sub-population sizes are of order $K$, the ‘early’ stochastic phase of the epidemic ends, and the ‘macroscopic phase’ starts.

The rescaled population size process of all the four types $N^K_t$ can then be approximated by the solution of the dynamical system (2.1) with the same initial condition. We visualize these phases in Figure 2 below. Here, note that refined results about (2.1) would immediately improve our results, as we will discuss in Remark 3.6 below.

We now briefly analyse the approximating branching process(es) and introduce some notation that is necessary in order to state our main results. Note that $(\hat{N}(t))_{t \geq 0}$ is not a pure birth-and-death process. Its number of ‘offspring’ is bounded by $m$. If we define a two-dimensional branching process with the same rates as for the $y$- and $z$-coordinates of $(\hat{N}(t))_{t \geq 0}$, ignoring all jumps of the form $(x, y, z) \rightarrow (x + 1, y, z)$ and $(x, y, z) \rightarrow (x - 1, y, z)$, then we obtain a further two-type linear branching process. Started from the same initial condition, this is the same process as the two-dimensional projection $((\hat{N}_{1i}(t), \hat{N}_{2}(t)))_{t \geq 0}$ of the branching process $(\hat{N}(t))_{t \geq 0}$.

According to [AN72, Section 7.2], the mean matrix of $(\hat{N}(t))_{t \geq 0}$ is given as follows:

$$J = \begin{pmatrix} -\kappa\mu_1 - \sigma & 0 & 0 \\ 0 & -r - v & mv \\ qD\bar{n}_{1a} & (1 - q)D\bar{n}_{1a} & -(1 - q)D\bar{n}_{1a} + \mu_2 \end{pmatrix}. \quad (2.7)$$

We immediately see that $-\kappa\mu_1 - \sigma < 0$ is an eigenvalue of $J$ (with left eigenvector $(1,0,0)^T$). Hence, $J$ having a positive eigenvalue is equivalent to its last $2 \times 2$ block

$$J_2 = \begin{pmatrix} -r - v & (1 - q)D\bar{n}_{1a} \\ mv & -(1 - q)D\bar{n}_{1a} + \mu_2 \end{pmatrix}, \quad (2.8)$$

having a positive eigenvalue. Note that $J_2$ is the mean matrix of $((\hat{N}_{1i}(t), \hat{N}_{2}(t)))_{t \geq 0}$. To put it differently, $(\hat{N}(t))_{t \geq 0}$ is supercritical if and only if $((\hat{N}_{1i}(t), \hat{N}_{2}(t)))_{t \geq 0}$ is supercritical. On a related note, it is easy to see that the mean matrix $J$ is not irreducible but $J_2$ is irreducible. Now, we have the following lemma, the proof of which will be carried out in Section 4.4.

**Lemma 2.7.** The eigenvalues of $J_2$ are real, and the largest eigenvalue is given as follows:

$$\tilde{\lambda} = \frac{-(r + v + (1 - q)D\bar{n}_{1a} + \mu_2) + \sqrt{(r + v + (1 - q)D\bar{n}_{1a} + \mu_2)^2 - 4((r + v)(1 - q)D\bar{n}_{1a} + (r + v)\mu_2)}}{2}. \quad (2.9)$$
This is positive if and only if the condition (2.2) holds.

This lemma shows a correspondence between the branching processes and the dynamical system (2.1): \( \tilde{\lambda} > 0 \) holds, i.e., the branching processes are supercritical (and thus have a nonzero survival probability) if and only if the dynamical system has a coordinatewise coexistence equilibrium. Note that if \( \tilde{\lambda} = 0 \), then both branching processes are critical, and for \( \lambda < 0 \) they are subcritical. Since \(-\kappa\mu - \sigma < 0\), the largest eigenvalue of \( J \) is always equal to \( \lambda \) if \( \lambda \geq 0 \), otherwise it may be equal to \(-\kappa\mu - \sigma\). On the other hand, if the strict reverse inequality of (2.2) holds, then \( \lambda < 0 \), and thus the branching processes are subcritical. In particular, with high probability as \( K \to \infty \), \( (N_{1i,t}, N_{2,t}) \) will die out before \( (N_{1a,t}^K, N_{1d,t}^K) \) leaves a small neighbourhood of the `two-coordinate equilibrium size' \((\tilde{n}_{1a}, 0)\), and then eventually \( N_{1d,t} \) will also be absorbed at zero. Finally, if \( \lambda = 0 \), when (2.2) holds with an equality, the branching processes are critical. This case is difficult to analyse, and we will exclude it from our further investigations.

The extinction probability of the three-type branching process \((\tilde{N}(t))_{t \geq 0}\) is defined as
\[
s_2 = P(\exists t < \infty: \tilde{N}_{1d}(t) + \tilde{N}_{1i}(t) + \tilde{N}_2(t) = 0 | (\tilde{N}_{1d}(0), \tilde{N}_{1i}(0), \tilde{N}_2(t)) = (0, 0, 1)),
\]
given that the branching process is started with one virus (type 2 individual) and no infected or dormant type 1 individuals at time \( t = 0 \). By [AN72] Section 7.2, \( s_2 \) equals 1 if \( \lambda < 0 \), whereas if \( \lambda > 0 \), then \( s_2 \) equals the last coordinate of the coordinatewise smallest nonnegative solution \((s_{1d}, s_{1i}, s_2)\) of the system of generating equations
\[
(\kappa\mu_1 + \sigma)(1 - s_{1d}) = 0, \quad r(1 - s_{1i}) + v(s_2^0 - s_{1i}) = 0, \quad qD\tilde{n}_{1a}s_2(s_{1d} - 1) + (1 - q)D\tilde{n}_{1a}(s_{1i} - s_2) + \mu_2(1 - s_2) = 0.
\]
Here, \( s_{1d} \) and \( s_{1i} \) are the extinction probabilities of the branching process \((\tilde{N}(t))_{t \geq 0}\) started from \((1, 0, 0)\) and \((0, 1, 0)\), respectively. In particular, a crucial property, which obviously follows from the first equation in (2.11), is that \( s_{1d} = 1 \). I.e. started with one dormant individual (or any positive number of dormant individuals) and no infected individuals or virions, the branching process dies out almost surely, as anticipated before. Indeed, dormant individuals are created only in presence of type 2, and they can only produce type 1a individuals (this is resuscitation) but not type 1d, 1i or 2 ones. In Section 2.6.5 we will discuss how this feature of the branching process impacts on the proof of our main results.

We will comment on the relation of \( s_{1i} \) to \( s_2 \) in Section 2.6.4. There, we will also characterize \( s_2 \) in terms of a single-Indeterminate polynomial and explain why \( s_{1i}, s_2 \) are both always positive in the supercritical case. By construction, \( s_{1i} \) and \( s_2 \) equal the extinction probabilities of \((\tilde{N}_{1i}(t), \tilde{N}_2(t))_{t \geq 0}\) started from \((1, 0)\) respectively \((0, 1)\).

**Remark 2.8** (Role of the dormancy-related parameters). The approximating branching processes are supercritical if and only if (4.1) holds. Interestingly, among the parameters related to dormancy, this condition only involves the probability \( q \) of dormancy initiation during each cell–virus contact event, but not the death rate \( \kappa \) or the resuscitation rate \( \sigma \) of dormant individuals. We will discuss this observation further in Section 2.6.1 in the context of condition (2.2).

2.4. The phases of a `successful' virus epidemic. A `successful' virus epidemic consists of a first, stochastic phase, in which a newly arriving virion invades the resident population so that both the free virions and the infected cells reach a population size `visible' on the order of the carrying capacity \( K \). We formalize this time-point for \((N_t)_{t \geq 0}\) by introducing a suitable stopping time (with respect to its canonical filtration). For \( \varepsilon > 0 \), we define
\[
T_{\varepsilon}^2 := \inf \{ t \geq 0: N_{1i,t} + N_{2,t} = \lfloor \varepsilon K \rfloor \}.
\]
If $\varepsilon$ is small, then with high probability as $K \to \infty$, until time $T_\varepsilon^2$ the rescaled population size $N_{1a,t}^K$ of type 1a stays close to the equilibrium $\bar{n}_{1a}$, and the rescaled population size $N_{1d,t}^K$ of type 1d stays near zero (up to some error terms that are at most proportional to $\varepsilon$), given that $T_\varepsilon^2$ is finite. After successful invasion, the second, deterministic phase begins, where the system can be approximated by the deterministic dynamical system (2.1). Note that the system could as well already be started in this second phase, for example by the artificial exposure of the host cells to large numbers of virions, as e.g. in the experiments in [B15]. In the deterministic phase, we could further distinguish between an ‘early phase’, in which the reproduction of viruses does not yet play a role (as is the scenario considered in [GW16]), and its ‘long-term’ behaviour, in which a persistent epidemic may emerge.

To describe the latter, we further define, for $\beta > 0$ the persistence set

$$S_\beta := \{ (\bar{n}_{1a}, \bar{n}_{1d}, \bar{n}_{1i}, \bar{n}_2) \in (0, \infty)^4 : n_v \geq \beta, \forall v \in \{1a, 1d, 1i, 2\}, \bar{n}_{1a} + \bar{n}_{1d} + \bar{n}_{1i} \leq \bar{n}_{1a} - \beta, \bar{n}_2 \leq \frac{\mu \bar{n}_{1a}}{\mu_2} - \beta \} \quad (2.13)$$

Inside this persistence set, all sub-populations will have size at least $\beta > 0$, and the total host population size will already be below its virus-free equilibrium. The last condition ensures that the virus load is not too high, thus this set describes a scenario with a currently persistent but not overwhelming virus infection. Note that $S_\beta$ is always well-defined and non-empty if $\lambda_1 > \mu_1$ and $\beta \in (0, \bar{n}_{1a})$. Further, we expect that starting from time $S_{\beta}$, the rescaled population size process $(N^K_{1i,t})_{t \geq 0}$ allows us to consider uniform approximations after such random stopping times.

Moreover, $(N^K_{t})_{t \geq 0}$ does not only spend a short period of time in the set $S_{\beta}$, but for $T > 0$ large enough and independent of $K$, $N^K_{T_{S_{\beta}} + T} \in S_{\beta}$ holds with high probability as $K \to \infty$ (cf. Corollary 2.13 below). Note that the strong Markov property of $(N^K_{t})_{t \geq 0}$ allows us to consider uniform approximations after such random stopping times.

We expect that starting from time $T_{S_{\beta}}$, the stability of the coexistence equilibrium $(n_{1a}, n_{1d}, n_{1i}, n_2)$ already matters for the dynamics of our stochastic process. In Figure 2 we illustrate these phases of a successful virus invasion in two different scenarios: (i) when the coexistence equilibrium $(n_{1a}, n_{1d}, n_{1i}, n_2)$ is globally asymptotically stable and thus between $T_{S_{\beta}}$ and $T_{S_{\beta}} + T$, the rescaled population size process $N^K_{t}$ stays close to this equilibrium, (ii) when the coexistence equilibrium is unstable, giving rise to approximately periodic behaviour also in the stochastic system after time $T_{S_{\beta}}$.

2.5. Statement of the main results. Now, we formulate our main results. To this aim, we define a further stopping time as follows:

$$T_0^2 := \inf\{t \geq 0 : (N^K_{1i,t}, N^K_{2,t}) = (0,0)\}. \quad (2.15)$$
(a) The case when the coexistence equilibrium of (2.1) is globally asymptotically stable.

(b) The case when the coexistence equilibrium is unstable and a stable periodic trajectory attracts the coordinatewise positive solutions.

Figure 2. Schematic illustration of the behaviour of \((N^K_t)_{t \geq 0}\) in case of a successful invasion. We sketch two cases: stable coexistence (Figure 2a) and periodic behaviour (Figure 2b). Each label has the same colour as the graph of the corresponding subpopulation. Black labels correspond to multiple types. The orange ‘dormancy peak’ corresponds to a similar peak described in [GW16] (see Figure 8 for a quantitative result), and gray dotted curves depict the total host size \(N_1,t = N_{1u,t} + N_{1d,t} + N_{1i,t}\).

This is the time of *extinction of the epidemic*, i.e. when all infected individuals and virions have disappeared. Finally, let

\[
U_0^2 := \inf \left\{ t \geq 0 : (N^K_{1d,t}, N^K_{1i,t}, N^K_{2,t}) = (0, 0, 0) \right\}.
\]  
(2.16)

Our first theorem states that the probability of successful invasion of the virus particles (that is, when a macroscopic epidemic emerges and becomes persistent), i.e. of reaching \(S^\beta\) for some \(\beta > 0\) before
extinction of the invaders, converges to the survival probability $s_2$ of the approximating branching process as $K \to \infty$. For this, recall that the eigenvalue $\lambda$ from (2.9) is positive if and only if (2.2) holds. Also recall the extinction probability $s_2$ of the approximating branching process $((\tilde{N}_{1a}(t), N_2(t)) _{t \geq 0}$ started from $(0,1)$.

**Theorem 2.9.** Assume that $\lambda_1 > \mu_1$ and $\lambda \neq 0$. Assume further that
\[ N_{1a}^K(0) \to \tilde{n}_{1a} \]
and
\[ (N_{1a}^K(0), N_{1i}^K(0), N_2^K(0)) = (0, 0, 1/K) . \]
Then for all sufficiently small $\beta > 0$, we have
\[ \lim_{K \to \infty} \mathbb{P}(T_{S_\beta} < T_0^2) = 1 - s_2. \]

The next theorem shows that in case of a macroscopic/persistent epidemic, the time until reaching a small neighbourhood of the coexistence equilibrium of the dynamical system behaves like $1/\lambda \log K$.

**Theorem 2.10.** Under the assumption that $\lambda_1 > \mu_1$ and (2.2) holds (equivalently, $s_2 < 1$), we have that on the event \{ $T_{S_\beta} < T_0^2$ \},
\[ \lim_{K \to \infty} \frac{T_{S_\beta}}{\log K} = \frac{1}{\lambda} \]
in probability.

The final theorem provides information about the time of the extinction of the epidemic and implies that with high probability, the rescaled active population size stays close to its virus-free equilibrium $\tilde{n}_{1a}$ and the dormant population stays small until this extinction (after which it decreases to 0). This theorem also holds for $\lambda > 0$ where both persistence and non-persistence of the epidemic have a positive probability.

**Theorem 2.11.** Under the assumption that $\lambda_1 > \mu_1$ and (2.2) holds (equivalently, $s_2 < 1$), we have that on the event \{ $T_0^2 < T_{S_\beta}$ \},
\[ \lim_{K \to \infty} \frac{T_0^2}{\log K} = 0 \]
and
\[ 1 \{ T_{S_\beta} > T_0^2 \} \| (N_{1a}^K(t_0, T_0^2), N_{1i}^K(t_0, T_0^2)) - (\tilde{n}_{1a}, 0) \|_{K \to \infty} \to 0, \]
both in probability, where $\| \cdot \|$ is an arbitrary (but fixed) norm on $\mathbb{R}^2$.

**Remark 2.12** (Dormant individuals and the extinction of the epidemic). Recall the stopping time $U_0^2$ from (2.16) which is the first time at which all the types 1d, 1i, and 2 are extinct. A slight modification of the proof of Theorem 2.11 implies the following assertions regarding $U_0^2$. For $\beta$ as in the theorem, the event \{ $U_0^2 < T_{S_\beta}$ \} also has probability tending to $s_2$, and on this event, $U_0^2$ is also sub-logarithmic in $K$, further $N_{1a}(t_0, U_0^2)$ tends to $\tilde{n}_{1a}$ as $K \to \infty$. Similarly, Theorems 2.9 and 2.10 hold with $T_0^2$ replaced by $U_0^2$ everywhere. A formal proof requires the use of the three-dimensional approximating branching process instead of the two-dimensional one. This also has extinction probability $s_2$, and either $\lambda$ is the only nonnegative eigenvalue of its mean matrix $J$, or $J$ has no nonnegative eigenvalue, see Section 2.3. However, the methods of the proof would be the same as in our case, hence we refrain from presenting the full details here. See Section 2.6.5 for a related discussion about the use of the two- and the three-dimensional branching process in our proofs.

In view of Theorem 2.11 on the event \{ $T_0^2 < T_{S_\beta}$ \} for suitably chosen $\beta > 0$, at time $T_0^2$ the type 1d population is nearly extinct with high probability, and the rescaled type 1a population is very close to
Assume that Corollary 2.13.

result, whose proof is now immediate.

2.6. Discussion of the main results.

will discuss how finer results about the dynamical system could give rise to extended versions of the theorems. In Remark 3.6 below we will discuss how finer results about the dynamical system could give rise to extended versions of the theorems.

Corollary 2.13. Assume that $\lambda_1 > \mu_1$ and (2.2) holds. Then for all sufficiently small $\beta > 0$ and sufficiently large $T > 0$, we have

$$\lim_{K \to \infty} \mathbb{P}(N_{T_{S_{\beta}}+T} \in S_{\beta} | T_{S_{\beta}} < T_0^2) = 1.$$ (2.21)

Note that (2.21) is equivalent to the fact that the assertions

$$\lim_{K \to \infty} \mathbb{P}(N_{1a,T_{S_{\beta}}+T}^K + N_{1d,T_{S_{\beta}}+T}^K + N_{1i,T_{S_{\beta}}+T}^K \leq \bar{n}_{1a} - \beta | T_{S_{\beta}} < T_0^2) = 1,$$

$$\lim_{K \to \infty} \mathbb{P}(N_{2,T_{S_{\beta}}+T}^K \leq \frac{m \bar{n}_{1a}}{\mu_2} - \beta | T_{S_{\beta}} < T_0^2) = 1,$$

and

$$\lim_{K \to \infty} \mathbb{P}(N_{v,T_{S_{\beta}}+T}^K \geq \beta | T_{S_{\beta}} < T_0^2) = 1, \quad \forall v \in \{1a, 1d, 1i, 2\}$$

hold. I.e., we have persistence of the epidemic on intervals starting at $T_{S_{\beta}}$ whose length does not scale with $K$. The proofs of Theorems 2.9, 2.10 and 2.11 will be carried out in Section 4.

Remark 2.14 (Concepts of proofs). For the first (stochastic) phase, we are able to use several proof techniques of the paper [CCLLS21], however with an unusual role distribution of ‘residents’ and ‘invaders’ (i.e., considering not only type 1a but also type 1d as ‘resident’); see also Section 2.6.5. However, there are some steps in this proof where a direct application of the aforementioned methods are not possible, especially regarding the precise description of the coupling of the 1d, 1i and 2 between two 3-type linear branching processes. The second (macroscopic) phase is based on Proposition 2.4 and Corollary 2.5. Once we can guarantee that a suitable initial condition has been reached, an approximation by the dynamical system (2.1) will quickly imply our main theorems. See Figure 2 for a visualisation of these phases of the host–virus dynamics and the relevant stopping times. In Remark 3.6 below we will discuss how finer results about the dynamical system could give rise to extended versions of the theorems.

2.6. Discussion of the main results.
2.6.1. Interpretation of the supercriticality condition. Condition (2.2) is equivalent to
\[
\left( \frac{\nu}{r + \nu} m - 1 \right) (1 - q) D \tilde{n}_{1a} > \mu_2. \tag{2.22}
\]

To understand this intuitively, imagine that our population process is observed shortly after time 0 so that it consists of approximately $K \tilde{n}_{1a}$ type 1a individuals and only a few virions. Then, the right-hand side is the death rate of each single virion, whereas the left-hand side is the rate at which it produces new virus particles (via infection and subsequent lysis). Indeed, $(1 - q) D \tilde{n}_{1a}$ is the rate at which the virion successfully invades a type 1a individual, the $-1$ corresponds to the loss of this invader during the attack, the fraction $\frac{\nu}{r + \nu}$ is the probability that the infected individual does not recover, and $m$ is the number of new virions released from the infected cell. This is precisely the approximation of the population size that corresponds to the definition of the branching process $(\tilde{N}(t))_{t \geq 0}$ (or its projection to types 1i and 2). Thus, we see that (2.22) ensures that the branching process is supercritical, or equivalently, that (2.1) has a coordinatewise positive equilibrium. Also recall from the proof of Lemma 2.2 that (2.22) is equivalent to $\tilde{n}_{1a} > n_{1a}$; else, the epidemic is not persistent. The fact that $\tilde{n}_{1a} > n_{1a}$ whenever coexistence is possible also indicates that coexistence with type 2 is always detrimental for type 1 (not surprisingly).

It is remarkable that Condition (2.22) neither depends on the death rate factor $\kappa$ nor the resuscitation rate $\sigma$ of dormant individuals. That is, for fixed $q \in (0, 1)$, we get the same probability for the persistence of the epidemic in the limit $\kappa = \infty, \sigma \geq 0$ (where an unsuccessful virus attack kills the affected type 1a individual without giving a chance to reproduction of viruses) as well as in the opposite limit $\kappa \geq 0, \sigma = \infty$ (where an unsuccessful virus attack keeps the affected individual alive and active). This is the consequence of the fact that the dynamics of type 1d does not directly affect the one of types 1i and 2 (cf. (1,0,0) is a left eigenvector of J), but only via type 1a, which has a nearly constant rescaled population size during the first (very early) phase of the invasion. By Remark 2.12, $\kappa$ and $\sigma$ do not influence the time until a successful invasion either since the principal eigenvalue $\lambda$ does not depend on these parameters.

After successful invasion, in the second phase of the epidemic, the values of $\kappa$ and $\sigma$ play a more prominent role, governing important properties of the coexistence equilibrium. For example, it follows from the proof of Lemma 2.2 (see Section 4.2 below) that under the condition (2.22), the dormant coordinate $n_{1d}$ of the coexistence equilibrium $(n_{1a}, n_{1d}, n_{1i}, n_2)$ satisfies
\[
n_{1d} = \frac{q D n_{1a} n_2}{\kappa \mu_1 + \sigma}. \tag{2.23}
\]

Thus, $n_{1d}$ is an increasing function of $q$ and a decreasing function of $\kappa \mu_1 + \sigma$. See Example 3.12 for a related discussion and simulation about the dynamical system (2.1) in the case of diverging $\sigma$.

It is also clear that given $\lambda_1 > \mu_1$, (2.22) can only hold if $mv > r + v$, else the left-hand side is nonpositive, whereas the right-hand side is positive by assumption. This condition says that each virus attack increases the number of viruses on average, i.e. the mean number of viruses that is created when the infected individual leaves state 1i (which equals $m$ in case the individual dies and 0 if it recovers) exceeds 1 (which is the number of viruses lost at each virus attack). If $\frac{mv}{r + v} \leq 1$, then $(\tilde{N}(t))_{t \geq 0}$ will be strictly subcritical, regardless of the values of $\tilde{n}_{1a}, D, q,$ and $\mu_2$.

2.6.2. Dormancy-related reproductive trade-offs in the light of the threat of persistent epidemics. Note that microbial dormancy is a costly trait that requires resources e.g. to maintain the switching machinery of cells required to transition into and out of dormancy. Hence it is natural to assume that it should come with a ‘reproductive trade-off’ (see [11] for further details). A simple caricature of this effect is to assume that the maintenance of a costly dormancy trait reduces the reproduction rate of the cell (in comparison to a hypothetical cell lacking this trait), in our model leading to a reduction of the value of $\lambda_1$. 

\[
(\frac{\nu}{r + \nu} m - 1) (1 - q) D \tilde{n}_{1a} > \mu_2.
\]
However, note that condition \(2.22\) implies that large reproduction rates \(\lambda_1\) can be hazardous when facing a virus infection (with or without dormancy mechanism). Hence there are hypothetical scenarios where a population threatened by recurring virus invasions might not realize its full reproductive potential in order to avoid persistent epidemics. The way to maximize its long-term average fitness in the face of virus epidemics could then be to invest remaining resources into a dormancy-defense, which allows for higher carrying capacities during infections, and the ‘reproductive trade-off’ vanishes (at least to some degree). Investigating the balance of classical fitness (in competition with other species) and strategies (e.g. dormancy-based) reducing reproductive rates in order to cope with recurring infections could be a topic for future work.

2.6.3. The reproduction number of the epidemic, and relation to stochastic epidemic models. The distinction between an initial stochastic phase, where an invader can be compared to a branching process, followed by deterministic behaviour, where the whole system is well-described by a deterministic dynamical system, is reminiscent of stochastic and deterministic epidemic modelling (see e.g. [AB00] for an overview). In stochastic epidemic models like the standard SIR (susceptible–infected–removed) model, the basic reproduction number \(R_0\) of the epidemic is defined as the expected number of infections generated by one infectious individual in a large susceptible population, cf. [AB00] Section 2.1]. The SIR model and many of its variants are individual-based, but they do not directly model pathogens as ‘individuals’, and the infection is spread by interactions between susceptible and infected individuals, unlike in the model in the present paper. Further, these epidemic models typically make the simplifying assumption that individuals do not reproduce or compete, and deaths are either also excluded or only possible due to the infectious disease itself. A consequence of this assumption is that the total population is constant (at least if we also take dead individuals into account). In contrast, in our model, the population size is regulated by logistic competition, whence even in absence of viruses, a constant population size can only be obtained after rescaling by the carrying capacity \(K\). As already discussed, in the presence of a macroscopic epidemic, the total type 1 population is substantially reduced (cf. Corollary 2.5 as well as Theorems 2.9 and 2.10).

Despite these differences, we can still define \(R_0\) in our model in such a way that it still fulfills the heuristic definition of [AB00] (where we always assume that \(\lambda_1 > \mu_1\)). In order to obtain ‘a large susceptible population’, we will have to assume that \(K\) is large, since the equilibrium population size scales like \(K(\bar{n}_{1a} + o(1))\) as \(K \to \infty\). Then, similarly to the branching process approximation of types 1d, 1i, and 2 during the initial phase of the epidemic, we will assume that the rescaled susceptible population size is fixed as \(\bar{n}_{1a}\) (ignoring also the question of whether this number is an integer). Let us now look at an infected individual in this situation. It either recovers with probability \(r/(r + v)\) or dies due to lysis, giving rise to \(m\) new virions, with probability \(v/(m + v)\). Each of these new virions will eventually either degrade, which happens at rate \(\mu_2\), or successfully attack a susceptible individual. Since there are \(K\bar{n}_{1a}\) susceptibles, the probability that the latter event occurs is \((1-q)(1-q)D\bar{n}_{1a}\). The number of infected individuals emerging from attacks by these \(m\) viruses is the average number of infections generated by the originally infected individual. Thus, we obtain the expression

\[
R_0 = \frac{mv(1-q)D\bar{n}_{1a}}{(r + v)((1-q)D\bar{n}_{1a} + \mu_2)}
\]

reproduction number in our model. Note that \(R_0\) depends on \(q\) but not on \(\kappa\) and \(\mu\), and in particular it is the same as for a dormancy-free epidemic with lower infectivity if we replace \(q\) by 0 and \(D\) by \((1-q)D\). This gives a rather natural interpretation of the effect of dormancy from an epidemiological point of view.

Note that our virus epidemic has a positive probability to become macroscopic if and only if \(R_0 > 1\), in analogy to e.g. the standard SIR model. Indeed, \(R_0 > 1\) holds if and only if

\[(mv - (r + v))(1-q)D\bar{n}_{1a} > (r + v)\mu_2,\]
which is precisely our coexistence condition \((2.2)\).

Note further that \(R_0\) can also be interpreted as the average number viruses who are the ‘offspring’ of a single given virus, obtained via infection of a susceptible individual producing secondary viruses via lysis. Indeed, we see that \(R_0 > 1\) is equivalent to condition \((2.22)\), which we interpret as the average number of ‘offspring’ of a given virus being at least 1. This provides a heuristic reason why \(s_{1i} \ne 1\) is equivalent to \(s_2 \ne 1\), which we will verify in Section \(2.6.4\).

2.6.4. Host–virus dynamics started with a single infected individual. We have seen that in equation \((2.11)\), \(s_{1d}, s_{1i}, s_2\) correspond to the extinction probability of the approximating branching process \((\hat{N}(t))_{t \ge 0} = (\hat{N}_{1d}(t), \hat{N}_{1i}(t), \hat{N}_2(t))_{t \ge 0}\) started from the states \((1, 0, 0), (0, 1, 0), (0, 0, 1)\) respectively, and that \(s_{1d} = 1\). Let us now argue that \(s_{1i}\), which is the extinction probability of the process started from \((0, 1, 0)\), equals one if and only if \(s_2\) equals one. According to the second equation in \((2.11)\), we have
\[
s_{1i} = \frac{r + vs_2^m}{r + v}.
\]
(2.24)

This equation can easily be interpreted with the help of a first-step analysis of \((\hat{N}(t))_{t \ge 0}\). Indeed, if at time zero there is one infected individual, this one will recover with probability \(\frac{r}{r+v}\), and conditional on this recovery, \((\hat{N}(t))_{t \ge 0}\) immediately gets absorbed at the state \((0,0,0)\). On the complementary event, i.e. with probability \(\frac{v}{r+v}\), the infected individual will die and give birth to \(m\) viruses, which leads to the state \((0,0,m)\). Hence, in order for the epidemic to get extinct, now \(m\) independent copies of \((\hat{N}(t))_{t \ge 0}\) started from \((0,0,1)\) all have to die out, which has probability \(s_2^m\).

Substituting \((2.24)\) and \(s_{1d} = 1\) into the last equation of \((2.11)\), we obtain
\[
(1-q)D\hat{n}_{1a}\left(\frac{r + vs_2^m}{r + v} - s_2\right) + \mu_2 (1 - s_2) = 0,
\]
and hence \(s_2\) must be equal to the smallest nonnegative root of the polynomial
\[
f(x) = (1-q)D\hat{n}_{1a}\frac{v}{r+v}x^m - ((1-q)D\hat{n}_{1a} + \mu_2)x + \left(\mu_2 + (1-q)D\hat{n}_{1a}\frac{r}{r+v}\right),
\]
of order \(m\). Although for \(m \ge 5\) an explicit solution of the roots of \(f\) cannot be given, we can easily convince ourselves that \(s_2 \in (0,1)\) holds under the condition \((2.2)\). Indeed, it is clear that \(f(0) > 0\) and \(f(1) = 0\). Now, if \(m = 1\) (note that in this case, \((2.2)\) cannot be satisfied), then \(f\) is linear, hence its only root is 1, which implies that \(s_2 = 1\). Else, \(f\) is convex on \([0,\infty)\) because its second derivative is a nonzero monomial with a positive coefficient. Hence, there can be at most two roots in \((0,\infty)\), one of which is equal to 1. Further, we have
\[
f'(1) = \frac{(1-q)D\hat{n}_{1a}(mv - (r+v)) - \mu_2(r+v)}{r+v},
\]
which is positive under the condition \((2.2)\). Thus, since \(f\) is convex and \(0 = f(1) < f(0)\), \(f\) must have a unique root in \((0,1)\). Since the smallest nonnegative root of \(f\) equals \(s_2\), we conclude that \(s_2 \in (0,1)\).

2.6.5. Individual subcritiality of the dormant coordinate of the branching processes. For \(\lambda_1 > \mu_1\), assume that the rescaled type 1a population is initially very close to the equilibrium size \(\hat{n}_{1a}\), and there is just one virus and no infected or dormant individuals. Then, the analysis of the early ‘stochastic phase’ of the virus invasion consists in showing that the resident population stays close to its virus-free equilibrium for a large amount of time (thanks to Freidlin–Wentzell type large deviation results), and as long as this holds, the ‘invader’ sub-populations can be approximated by a multitype branching process. A naive adaptation of the approach followed in the papers \([CCLS17, CCLLS21, BT20, BT21]\) would be to consider only type 1a as resident and types 1d, 1i, and 2 as invader. Then, the total time until the total size \(N_{1d,t} + N_{1i,t} + N_{2,t}\) of these sub-populations reaches size \(\varepsilon K\) or dies out, as
well as the probability of extinction respectively invasion, could be estimated using classical results on multitype branching processes [AN72].

The problem is that in our case, one coordinate of the arising branching process is always subcritical when being on its own: When the branching process is started with dormant individuals only, it will die out almost surely. In contrast, in the aforementioned papers, if the multitype branching process is supercritical, then started with one individual of any of the types, it will survive with positive probability. In our setting, in the extreme case when the total size $\varepsilon K$ of types 1d, 1i, and 2 consists almost exclusively of dormant individuals, with high probability the total population of these three types will die out before type 1a leaves equilibrium, and the epidemic will not be persistent. To put it differently, the multitype branching processes appearing in the aforementioned papers have irreducible mean matrices, whereas our mean matrix, $J$ is not irreducible (unlike the two-dimensional one, $J_2$).

Hence, we have to adapt the proof strategy in the following way. We will consider type 1d also as resident, with its ‘equilibrium size’ being just 0 (which corresponds to the case when there are no viruses or infected cells in the system), and only types 1i and 2 as invaders. We then show that with high probability, these two types die out or reach size $\varepsilon K$ before the other two types leave a small neighbourhood of their equilibrium sizes. Here, we will approximate types 1i and 2 by a two-type branching process, which can in turn be chosen as the two-dimensional projection $(\tilde{N}_{1i}(t), \tilde{N}_{2}(t))_{t \geq 0}$ of the three-type branching process $(\tilde{N}_{1d}(t), \tilde{N}_{1i}(t), \tilde{N}_{2}(t))_{t \geq 0}$. If one of these branching processes is supercritical, then so is the other.

Once the size $\varepsilon K$ has been reached by the total population size of types 1i and 2, we are in a position where the rescaled population size process $N^K_t$ can be well approximated by the dynamical system (2.1), which turns out to have a coexistence equilibrium if and only if the approximating two- (or three-) type branching process is supercritical. In view of Remark 2.6 Corollary 2.5 also applies for initial conditions $(n_{1a}(0), n_{1d}(0), n_{1i}(0), n_{2}(0)) \in [0, \infty)^4$ such that $n_{1a}(0) > 0$, $n_{1d}(0) + n_{1i}(0) > 0$. This is already a strong indication for our main results, including also Corollary 2.13 but the arguments of the proof will have to be made rigorous, see Section 4.4.

3. THE DYNAMICAL SYSTEM: FURTHER RESULTS, CONJECTURES, AND SIMULATIONS

Unfortunately, the stability of the coexistence equilibrium and the associated question whether bifurcations emerge in the system (2.1) are in general difficult (and tedious) to analyse. In Section 3.1 we present a general conjecture and some partial results in this regard. These are supported by numerical results for various parameter regimes, see Section 3.2. Finally, in Section 3.3 we recall the notion of paradox of enrichment for predator–prey systems and explain its relation to our model.

3.1. Stability of the coexistence equilibrium, Hopf bifurcations. We first adapt the notion of a simple supercritical Hopf bifurcation (see e.g. [L94]) to the context of our particular setting. Recall from Section 2.2 that $m^*$ is the transcritical bifurcation point for which $(n_{1a}, n_{1d}, n_{1i}, n_{2})$ and $(\tilde{n}_{1a}, 0, 0, 0)$ coincide.

Definition 3.1. Fix all parameters but $m$. We say that the system (2.1) undergoes a supercritical Hopf bifurcation at some value $m^{**} > m^*$ if the following conditions are satisfied:

1. The Jacobi matrix of the system at $(n_{1a}, n_{1d}, n_{1i}, n_{2})$ has four eigenvalues with negative real parts for all $m \in (m^*, m^{**})$;
2. precisely two such eigenvalues for all $m \in (m^{**}, \infty)$, and
3. in an open neighbourhood of $m^{**}$, the remaining two eigenvalues are complex, being purely imaginary and nonzero at $m = m^{**}$.

Further, the supercritical Hopf bifurcation at $m^{**}$ is called simple if the real part of any of the eigenvalues of the Jacobi matrix has a nonvanishing derivative at $m^{**}$. 
Note that having a simple Hopf bifurcation in particular means that the equilibrium \((n_{1a}, n_{1d}, n_{1i}, n_2)\) is asymptotically stable for \(m \in (m^*, m^{**})\) and unstable for \(m \in (m^{**}, \infty)\). For simple supercritical Hopf bifurcations the periodic limiting trajectories that arise in the unstable phase can be observed numerically, cf. \[L94\, p.1\]. Here is our main conjecture regarding the system \((2.1)\).

**Conjecture 3.2.** Consider the solution of the dynamical system \((2.1)\) started from an arbitrary coordinatewise positive initial condition. Let us fix all parameters but \(m, r\) and assume that \(\lambda_1 > \mu_1\) and \(\lambda \neq 0\). Then there exists \(r^* > 0\) such that the following assertions hold.

1. For \(m \in (0, m^*)\), for any \(r > 0\), the aforementioned solution converges to \((\bar{n}_{1a}, 0, 0, 0)\) as \(t \to \infty\), in other words, \((\bar{n}_{1a}, 0, 0, 0)\) is globally asymptotically stable on \((0, \infty)^4\). Further, each coordinate of the solution becomes monotone eventually.
2. If \(r > r^*\), then the coexistence equilibrium \((n_{1a}, n_{1d}, n_{1i}, n_2)\) is asymptotically stable for any \(m > m^*\). The solution converges to \((n_{1a}, n_{1d}, n_{1i}, n_2)\).
3. If \(r \in (0, r^*)\), then there is a simple supercritical Hopf bifurcation at some value \(m^{**} > m^*\). The coexistence equilibrium is asymptotically stable for all \(m \in (m^*, m^{**})\) and unstable for all \(m > m^{**}\), and the solution converges to a periodic trajectory that is bounded away from 0 in each coordinate.
4. There exists \(m^{***} \in (m^*, m^{**})\) such that the solution tends to \((n_{1a}, n_{1d}, n_{1i}, n_2)\) so that each coordinate of the solution eventually becomes monotone for all \(m \in (m^*, m^{***})\), and it converges to it in a coordinatewise oscillatory way (i.e., so that none of the coordinates ever becomes monotone) for all \(m \in (m^{***}, m^{**})\), where we put \(m^{**} = \infty\) in case \(r < r^*\).

Note that although in our individual-based model it is reasonable to assume that the burst size \(m\) is an integer, the dynamical system \((2.1)\) is well-defined for general \(m > 0\), and hence just as \(m^*, m^{**}, m^{***}\) are also not necessary integers (and according to the conjecture, \(m^{**}\) may not even be finite).

The main results of this paper do not use this conjecture but only preliminary results that have actually been verified. However, as we will explain below, given the conjecture, how our main results could immediately be improved without substantial changes in their proof.

Let us point out that it follows immediately from preliminary work that there are indeed cases when the coexistence equilibrium loses its stability for large \(m\), and thus part \((3)\) of Conjecture 3.2 is not without any reason. To this end, consider the ‘dormancy-free’ three-dimensional variant

\[
\begin{align*}
\frac{dn_{1a}(t)}{dt} &= n_{1a}(t)(\lambda_1 - \mu_1 - C(n_{1a}(t) + n_{1i}(t)) - Dn_2(t)) + rn_{1i}(t), \\
\frac{dn_{1i}(t)}{dt} &= Dn_{1a}(t)n_2(t) - (r + v)n_{1i}(t), \\
\frac{dn_2(t)}{dt} &= mn_{1i}(t) - Dn_{1a}(t)n_2(t) - \mu_2n_2(t).
\end{align*}
\]  

(3.1)

of the system \((2.1)\). For \(r = 0\) (i.e., for a virus infection with a lethality of 100%) and with a slightly different form of logistic competition, (3.1) is the main object of study of the paper \[BK98\]. It is easy to see that this system exhibits a coordinatewise positive coexistence equilibrium, denoted as \((n_{1a}, n_{1i}, n_2)\), if and only if the condition \((2.2)\) holds for \(q = 0\). Clearly, this equilibrium is equal to \((n_{1a}, n_{1i}, n_2)\) corresponding to the coexistence equilibrium \((n_{1a}, n_{1d}, n_{1i}, n_2)\) of \((2.1)\) for \(q = 0\) (and \(\kappa \geq 0, \sigma > 0\) arbitrary). Now we have the following assertion (which is in analogy to the ‘paradox of enrichment’ discussed in Section 3.3 below).

**Proposition 3.3.** Fix all parameters of the model but \(r, m\). If \(q \in (0, 1)\) is sufficiently small, then there exists an \(r^* > 0\) such that for all \(r \in (0, r^*)\), the coexistence equilibrium \((n_{1a}, n_{1d}, n_{1i}, n_2)\) of \((2.1)\) is unstable for all sufficiently large \(m > m^*\). This assertion also holds in the degenerate case \(q = 0\) for (3.1) instead of (2.1) and \((n_{1a}, n_{1i}, n_2)\) instead of \((n_{1a}, n_{1d}, n_{1i}, n_2)\) (where we define \(m^*\) the same way as for (2.1) with \(q = 0\)).
Proof. For $q = r = 0$, the existence of $m > m^*$ such that $(n_{1a}, n_{1i}, n_2)$ is unstable follows from Proposition 3.2. By continuity of the right-hand side of (3.1) in $r$, it also follows for sufficiently small $r > 0$. Finally, since (3.1) is equal to the projection of (2.1) to the active, infected, and virus coordinates for $q = 0$ in case the dormant coordinate $n_{id}(0)$ of the initial condition is also zero, thanks to continuity of the right-hand side of (2.1) in $q$ we also obtain the assertion for sufficiently small $q > 0$ (both in the degenerate case $r = 0$ and for sufficiently small $r > 0$).

Next, let us point out that recovery indeed has a qualitative effect on the behaviour of the dynamical system. Namely, if $r$ is sufficiently large compared to $v$, then for all sufficiently large $m$ the coexistence equilibrium is asymptotically stable, at least for $q$ small. For $q = 0$, it is actually satisfied if recovery is more frequent than death by lysis (i.e. if the virus infection has mortality less than 50%).

Proposition 3.4. Fix all parameters of the model but $r, m$. If $q \in (0, 1)$ is sufficiently small, then there exists an $r^* > 0$ such that for all $r \in (r^*, \infty)$, the coexistence equilibrium $(n_{1a}, n_{id}, n_{1i}, n_2)$ of (2.1) is asymptotically stable for all sufficiently large $m > m^*$.

This assertion also holds in the degenerate case $q = 0$ for (3.1) instead of (2.1) and for $(n_{1a}, n_{id}, n_{1i}, n_2)$ replaced by $(n_{1a}, n_{1i}, n_2)$ (where we define $m^*$ the same way as for (2.1) with $q = 0$). In that case, $r > v$ is sufficient for this to hold.

Finally, we show that irrespective of the relation between $r$ and $v$, for $m$ being just slightly bigger than $m^*$, the coexistence equilibrium will be asymptotically stable.

Proposition 3.5. Fix all parameters of the model but $m$. Then, for all $m > m^*$ sufficiently small, the coexistence equilibrium $(n_{1a}, n_{id}, n_{1i}, n_2)$ of (2.1) is asymptotically stable. In the degenerate case $q = 0$, the same holds for the coexistence equilibrium $(n_{1a}, n_{1i}, n_2)$ of (3.1).

Propositions 3.4 and 3.5 will be proved in Appendix A. We see that even for the restricted parameter regime corresponding to Proposition 3.3, the proposition is weaker than part (3) of Conjecture 3.2 because it does not imply the existence of a simple supercritical Hopf bifurcation but just instability of the coexistence equilibrium for large $m$, and it does not tell anything about periodic limiting solutions. Similarly, Proposition 3.4 is weaker than part (2) of the conjecture, not only due to the restriction of the parameter regime but also because it only implies that $(n_{1a}, n_{id}, n_{1i}, n_2)$ is locally asymptotically stable for large $m$ (instead of globally), and it does not tell anything about the case of smaller values $m > m^*$. However, from Proposition 3.5 it follows that for $m > m^*$ very close to $m^*$, $(n_{1a}, n_{id}, n_{1i}, n_2)$ is indeed asymptotically stable. In other words, we have a transcritical bifurcation (cf. e.g. [KMO09, Proposition 2.1]) at $m = m^*$, meaning that the previously stable equilibrium $(\bar{n}_{1a}, 0, 0, 0)$ loses its stability and a new, stable equilibrium $(n_{1a}, n_{id}, n_{1i}, n_2)$ emerges, the two equilibria being equal at the critical point $m = m^*$. Hence, it is plausible to think that parts (2) and (3) of Conjecture 3.2 hold, and the only value of $m \in (m^*, \infty)$ where the stability of $(n_{1a}, n_{id}, n_{1i}, n_2)$ may change is the Hopf bifurcation point (if it exists).

Part (1) of the conjecture is also plausible and perhaps not even difficult to prove. However, in the analysis of our stochastic model we will never come across a situation where we would need this assertion, since for $m \in (0, m^*)$, with high probability the epidemic dies out before becoming macroscopic, and hence our rescaled population size process $(N^K_t)_{t \geq 0}$ will not be amenable to approximation by a solution of (2.1).

Remark 3.6 (Potential extensions of our main results). Having Conjecture 3.2 at hand, we would immediately be able to verify Theorems 2.9 and 2.10 with the rather large ‘persistence set’ $S_\beta$ replaced by a much more specific set $\tilde{S}_\beta$ everywhere for $r \neq r^*$ and $m \notin \{m^*, m^{**}\}$, using the same proof techniques as before. Indeed, $\tilde{S}_\beta$ could be chosen as a closed $\beta$-neighbourhood of $(n_{1a}, n_{id}, n_{1i}, n_2)$ in the $\ell^1$-norm for $r < r^*$, and as a closed spatio-temporal $\beta$-neighbourhood of the limiting periodic trajectory.
Table 1. Choice of the parameters for the simulations of the dynamical systems (2.1) and (3.1), where $n_I(0) = n_{1d}(0) + n_{1i}(0) + n_2(0)$.

| Parameter | Value |
|-----------|-------|
| $\lambda_1$ | $\tilde{\sigma}$ |
| $\mu_1$ | 4 |
| $C$ | 1 |
| $\kappa$ | default: $q = 0.1$, large: $q = 0.9$, dormancy-free case: $q = 0$ |
| $q$ | default: $r = 0.001$, large: $r = 1.1$ for default/zero $q$, large: $r = 2$ for large $q$ |
| $\nu$ | 1 |
| $\mu_2$ | 0.3 |
| $n_{1a}(0)$ | 1 ($= \bar{n}_{1a}$) |
| $n_I(0)$ | 0.1 |
| $n_{1d}(0)$ | $\pi_{1d}$ $n_I(0)$ |
| $n_{1i}(0)$ | $\pi_{1i}$ $n_I(0)$ |
| $n_2(0)$ | $\pi_2$ $n_I(0)$ |
| $\sigma$ | default: $\sigma = 2$, large: $\sigma = 100$ |
| $D$ | 0.5 |

for $r > r^*$. This would yield a complete analogue of the main results of [CCLLS21, BT20, BT21] for the model of the present paper.

3.2. Visualization and further discussion of the behaviour of the dynamical system. To gain an understanding of the concrete behaviour of the dynamical system (2.1) and its three-dimensional variant (3.1), in particular on the effects of dormancy and recovery, we now provide numerical simulations of the solutions of these systems for various parameter regimes. The code can be found in Appendix B. These results support and illustrate Conjecture 3.2. We will work with the choice of parameters presented in Table 1 (abbreviating $n_I(0) := n_{1d}(0) + n_{1i}(0) + n_2(0)$).

Here, $\pi_{1d}$, $\pi_{1i}$, and $\pi_2$ are the dormant, infected, and virus coordinates of the coordinatewise positive (‘Kesten–Stigum’) left eigenvector of the mean matrix $J$ associated to the eigenvalue $\bar{\lambda}$ normalized so that $\bar{\lambda} > 0$, conditional on survival of the approximating branching process $(\bar{N}(t))_{t \geq 0}$, the proportions of its dormant, infected, and virus coordinates converge to the corresponding proportions of $(\pi_{1d}, \pi_{1i}, \pi_2)$ thanks to the Kesten–Stigum theorem (cf. e.g. [GB03]). We refrain from making a precise connection between the Kesten–Stigum proportions and our rescaled stochastic population size process $(\tilde{N}_t^K)_{t \geq 0}$ in the present paper; see [CCLLS21, Section 3.2] for further details in a similar model of invasion dynamics. The value of the burst size $m$ will change from figure to figure to demonstrate monotonicity respectively non-monoticity of the solution and presence respectively absence of Hopf bifurcations.

Example 3.7 (Hopf bifurcation in the case when recovery is weak compared to death by lysis). We consider the ‘default’ parameters from our parameter table, and we observe the change of behaviour of the numerical solution of (2.1) upon gradual increase of the burst size $m$, see Figure 3. For $m = 1$, the condition (2.2) does not hold yet, hence $\bar{\lambda} < 0$. The solution converges to $(\bar{n}_{1a},0,0,0)$, and the convergence of the dormant, infected, and virus coordinates to zero is rapid. However, we observe that at least the active coordinate of the solution is not monotone on $[0,\infty)$ but only on $[T,\infty)$ for $T$ sufficiently large. For $m = 2$, condition (2.2) already holds (i.e., the transcritical bifurcation point $m^*$ lies in (1, 2)), and the solution converges to the coexistence equilibrium $(n_{1a}, n_{1d}, n_{1i}, n_2)$ in a way that is at least eventually coordinatewise monotone, whereas for $m = 4, 5, 7$ it converges in an oscillatory way, just as in described in part 1 of Conjecture 3.2 where the amplitude of the oscillation increases with $m$. Further, since the rate $\nu$ of death by lysis is large compared to the recovery rate $r$, we observe a supercritical Hopf bifurcation at some value $m^{**} \in (7, 12)$, and for $m = 12$ the solution tends to a stable periodic trajectory (all this aligns with part 3 of the conjecture).

In order to investigate the effect of contact-mediated dormancy in the system, it is also important to consider the dormancy-free analogue of the model, i.e. the solution of the three-dimensional system (3.1) with similar choices of parameters. For this system, we have shown that if $r$ small compared...
Figure 3. First line: solutions of (2.1) with default parameters and $m = 1, 2$. Second line: same for $m = 4, 5$. Third line: same for $m = 7, 12$.

To $v$, then for large $m$ the coexistence equilibrium is unstable, whereas for (2.1), the same holds for small $q > 0$ (see Proposition 3.3), and we conjecture that this holds for all $q \in (0, 1)$ (see part 3 of Conjecture 3.2).

Example 3.8 (Hopf bifurcation when recovery is weak, in the dormancy-free case). We consider the model again with default parameters, but in the dormancy-free case $q = 0$ (ignoring the dormant coordinate). For $m = 1$ the epidemic goes extinct, for $m = 2$ we have monotone convergence to the coexistence equilibrium, and for $m = 4, 5$ we have oscillatory convergence, just as in the case with dormancy. However, already for $m = 7$ (and of course also for $m = 12$), the coexistence equilibrium is unstable and the solution converges to a periodic trajectory, unlike in the case with dormancy. This shows that dormancy, already with a moderate value of $q$ like $q = 0.1$, can substantially increase the critical value $m^{**}$ of the burst size where the coexistence equilibrium loses its stability. See Figure 4.

Next, we consider the case when $r$ is large compared to $v$. If Conjecture 3.2 holds, then there exists $r^* > 0$ such that if $r > r^*$, the coexistence equilibrium stays stable for all $m > m^*$, whereas for $r < r^*$ it becomes unstable for large $m$. In Proposition 3.4 we verified part of this assertion in the dormancy-free case: If $r > v$, i.e. if the infection of an individual is more likely to end with recovery than with death (and subsequent lysis), then the coexistence equilibrium is stable at least for large enough $m$ (and also for $m > m^*$ sufficiently close to $m$). As we indicate in Proposition 3.4, for $q > 0$ small, $r$ can also be
made sufficiently large such that the same assertion holds, and we expect that the same holds for all $q \in (0, 1)$ but $r > v$ may not be sufficient for that (depending also on $q$).

Example 3.9 (No Hopf bifurcation in case recovery dominates). First we consider the default parameters, apart from $r$ where we choose the larger value $r = 1.1$. In this case, even for $m = 35$, and according to part (4) of Conjecture 3.2 also for any $m > 35$, the solution converges to the coexistence equilibrium (in an oscillatory way), whereas for the default choice $r = 0.001$ the coexistence equilibrium was already unstable for $m = 12$. For $m = 3$ the epidemic still dies out rapidly, and for $m = 5$ there is already stable coexistence, but the solution is still nearly monotone in each coordinate, unlike for small $r$ where we already had stable coexistence (with eventual monotonicity) for $m = 2$ and oscillation for $m = 4$. See Figure 5.

Similar effects can be observed in the dormancy-free case $q = 0$, where we also choose $r = 1.1 > v$ as an example of a large value of recovery rate. Here $m = 3$ still corresponds to extinction of the epidemic (even though $mv > r + v$), whereas for $m = 35$ we again observe oscillatory convergence. See Figure 6.

Summarizing, in terms of Conjecture 3.2 it is plausible to think that for both (2.1) and (3.1), the result of increasing $r$ is not just that $m^{**}$ becomes infinite but also that $m^*$ and $m^{***}$ increase. In other words, both persistence of the epidemic and loss of eventual monotonicity of solutions in the persistence phase require much higher burst sizes. Comparing the cases $m = 35$ in Figures 5 and 6.
indicates that increasing the dormancy probability $q$ has a similar effect (although we expect that it cannot make $m^{**}$ infinite on its own), which we investigate further in the next example.

Example 3.10 (Effects of large $q$; portion of individuals becoming dormant). Now we turn back to our default choice of parameters, apart from the probability $q$ of contact-mediated dormancy, which we choose large ($q = 0.9$). Since a large value of $q$ corresponds to ‘thinning out’ the successful virus attacks, it is not surprising that $m^*$, $m^{**}$, and $m^{***}$ (given that they are well-defined as finite numbers) all increase. For $m = 8$ we still have eventually coordinatewise monotone convergence to the coexistence equilibrium, while for $q = 0.1$ this was not the case anymore for $m = 4$. Further, for $m = 50$ we observe oscillatory convergence, while for $q = 0.1$, this was not true anymore for $m = 12$. Finally, since $r$ is small compared to $v$, for $m$ very large, the system becomes periodic. The Hopf bifurcation point $m^{**}$ lies slightly below 300. See Figure 7.

If $r$ and $q$ are both large, then the simulations again show that there is no Hopf bifurcation and the coexistence equilibrium stays stable for all $m > m^*$, as depicted in the last image of Figure 7.
Figure 7. First line: solutions of (2.1) with large \( q \) (\( q = 0.9 \)) for \( m = 8 \) and \( m = 50 \). Second line: same for \( m = 300 \) (left), and solution of (2.1) with large \( q \) (\( q = 0.9 \)) and large \( r \) (\( r = 2 \)) for \( m = 195 \) (right).

Example 3.11 (The dormancy peak). As previously observed in [GW16], for the choice of parameters of that paper, at time close to zero, the virus population triggers dormancy in the active population, with the majority of the active population becoming dormant after a short time (orange line), given that \( q \) is close enough to 1. The images of Figure 8 depict the total population sizes of all types (1a, 1d, 1i, and 2), the proportion of dormant individuals among all host (type 1, i.e. type 1a, 1d or 1i) individuals, and the total amount of type 1 individuals, respectively. In terms of our stochastic process that is approximated by (2.1), this means that in the beginning of the early macroscopic phase, shortly after the dynamical system approximation has become applicable, the majority of the active individuals becomes dormant.

Finally, let us comment on the case of quick resuscitation of dormant cells, that is, diverging \( \sigma \).

Example 3.12 (Effects of large \( \sigma \)). The case of very large \( \sigma \) corresponds to almost instantaneous resuscitation of dormant individuals after falling dormant. Thus, it is plausible to think that the qualitative behaviour of the active, infected, and virus coordinates of the system (2.1) behave very similarly to the case where there is no dormancy but the parameter \( D \) of virus attacks is reduced by a factor of \( 1 - q \). On a heuristic level, this is of course not only true for the dynamical system (2.1) but also for our rescaled stochastic population process on time intervals where the dynamical system approximates the stochastic process well, as we pointed out in Section 2.6.1. In Figure 9 we consider a solution of (2.1) with the default choice of parameters, apart from \( \sigma \) which we choose as very large (\( \sigma = 100 \), as opposed to the default value \( \sigma = 2 \)), also in comparison to the value of \( \kappa \) (being equal to 1). We see that the behaviour of this solution is very similar to the one of (3.1) with the same initial condition and with the same choice of the parameters apart from \( q \) being altered to 0 and \( D \) to \( (1 - q)D \).

3.3. Paradox of enrichment. The fact that the coexistence equilibrium can lose its stability is a variant of the phenomenon called paradox of enrichment in ecology, which is well-known from the context of predator–prey type dynamical systems, originating from [R71] [GR72] (whereas the case with
Figure 8. Here, the parameters are chosen according to [GW16] Figures 5a, 5b, 6]:
\[ \lambda_1 - \mu_1 = 0.23, \quad C = \frac{\lambda_1 - \mu_1}{\gamma}, \quad D = 1.02 \times 10^{-7}, \quad q = 50/51, \quad \sigma = r = 1/72, \quad \kappa = v = 1/24, \quad \mu_2 = 1/12, \quad \text{and} \quad m = 10. \]
The dormant, infected, and virus coordinates of the initial condition are given analogously to the other simulations in Section 3.2. Let us note that in this case, any \( m \geq 2 \) leads to periodic behaviour for the dynamical system (2.1).

Predator dormancy was studied e.g. in [KC09]). It rests on a bifurcation that appears in our model as well as in the variant studied in [BK98] in the following way: When the burst size \( m \) reaches a critical threshold, the coexistence equilibrium emerges and is initially stable. However, further increase in the burst size destabilizes it, giving rise to periodic limiting behaviour.

In the predator–prey context, the analogue of the burst size expresses how much energy the predator can gain out of a consumed unit prey, and the analogue of the equilibrium population size \( \bar{n}_{1a} \) of active hosts is the carrying capacity of the prey population.

Now, increasing the carrying capacity of the system leads to periodic cycles with increasing amplitudes, where the lowest population size during a period approaches zero for both for the prey and the predators. This corresponds to an increased danger of extinction due to small stochastic fluctuations.
Figure 9. Solution of (2.1) with large $\sigma$ ($\sigma = 100$) (left) and the one of the corresponding solution of (3.1) (right), for $m = 5$. In the solution of (3.1) there is no dormant coordinate, whereas the dormant coordinate of the solution of (2.1) stays very close to zero.

in the underlying individual-based model. The ‘paradox’ consist in the counter-intuitive effect that increasing carrying capacities may actually increase the risk of extinction for the whole system.

In our model, for $r$ small compared to $v$, a similar high-amplitude periodicity (with low minimum value) can be observed (see e.g. Figures 3 and 4). It is further remarkable that in our model, as long as the coexistence equilibrium exists, its active coordinate $n_{1a}$ does not depend on $\bar{n}_{1a}$. This is in analogy to the fact that in certain predator–prey models, the prey coordinate of the coexistence equilibrium between predators and prey does not depend on the carrying capacity of the prey, see e.g. [KC09, Section 2].

In [KC09], the particular effect of predator dormancy is studied. The authors showed that this evolutionary trait can help avoid periodic behaviour or at least decrease the amplitude of the periods, even in the case where dormant predators never resuscitate. This is a clear analogy to our model, where we also observe that dormancy may prevent bifurcations (see Section 3.2). Here, virions correspond to the predators and active individuals to the prey. However, there are also significant differences between the two models, for example the lack of an analogue of the infected state in the predator–prey setting. Further, in our setting, the burst size $m$ and the active equilibrium size $\bar{n}_{1a}$ are two independent parameters, both of which correspond to the carrying capacity of prey. In turn, the predator–prey interaction in [KC09] is more complex than the quadratic interaction between viruses and active individuals in (2.1).

4. Proofs

In this section, we first prove the assertions of Section 2.2 regarding the dynamical system (2.1) in Section 4.2 and Lemma 2.7 regarding the mean matrix of the approximating branching processes in Section 4.1, and then we turn to the analysis of our original stochastic process $(N_t)_{t \geq 0}$. Section 4.3 contains the proofs of results about the ‘very early’ (stochastic) phase of the host–virus dynamics, whereas in Section 4.4 we put these together with the assertions about the dynamical system to conclude Theorems 2.9, 2.10, and 2.11.

4.1. The eigenvalues of the mean matrices of the branching processes. In this section, we carry out the proof of Lemma 2.7.

Proof of Lemma 2.7. The trace of $J_2$ is strictly negative by assumption, hence $J_2$ can have at most one eigenvalue with positive real part. We claim that there is such an eigenvalue with positive real part if and only if $\det J_2 < 0$, in other words,

$$\begin{align*}
(mv - (r + v))(1 - q)D\bar{n}_{1a} > \mu_2(r + v),
\end{align*}
$$

(4.1)
i.e., (2.2) holds. Indeed, if the determinant is negative, then the two eigenvalues must be real because the product of two complex (and hence conjugate) eigenvalues would be positive. This implies that one of the eigenvalues must be positive and the other negative.

The largest eigenvalue \( \lambda \) of \( J_2 \) is given as the largest solution \( \lambda \) to

\[
\lambda^2 + (r + v + (1 - q)D\tilde{n}_{1a} + \mu_2)\lambda + (r + v)((1 - q)D\tilde{n}_{1a} + \mu_2) - (1 - q)D\tilde{n}_{1a}mv = 0,
\]

and thus it is given by (2.9).

\[4.2\]. \textbf{Proofs of preliminary results regarding the dynamical system.} In this section we verify our results regarding the system (2.1). We start with the proof of Lemma 2.2

\textbf{Proof of Lemma 2.2} Let us compute the coordinates of the coexistence equilibrium \((n_{1a}, n_{1d}, n_{1i}, n_2)\); this will also yield its uniqueness. Making the second and the third line of (2.1) equal to zero, we obtain

\[ n_{1d} = \frac{qDn_{1a}n_2}{\kappa\mu_1 + \sigma} \]  \hspace{1cm} (4.2)

and

\[ n_{1i} = \frac{(1 - q)Dn_{1a}n_2}{r + v} \]  \hspace{1cm} (4.3)

Hence, according to the fourth line of the same dynamical system,

\[ n_{1i} = \frac{(1 - q)Dn_{1a}n_{1i}(mv - (r + v))}{\mu_2(r + v)}. \]

Under the condition that \( n_{1i} \neq 0 \), this is equivalent to

\[ n_{1a} = \frac{\mu_2(r + v)}{(1 - q)D(mv - (r + v))}, \]  \hspace{1cm} (4.4)

which is (2.3). Under the condition that \( mv > r + v \), we have \( n_{1a} > 0 \). Hence, by (4.2) and (4.3), \( n_{1d} \), \( n_{1i} \), and \( n_2 \) all have the same sign. If \( mv = r + v \), then \( n_{1a} \) is not well-defined under our assumption that \( n_{1i} \neq 0 \). In particular, a coordinatewise positive equilibrium cannot exist. Finally, if \( mv < r + v \), then \( n_{1i} \neq 0 \) implies \( n_{1a} < 0 \) and thus there is no coordinatewise positive equilibrium.

Let us now assume that \( mv > r + v \). Then, making the first equation of (2.1) equal to zero and substituting the equations (4.2) and (4.3) into it, we obtain

\[ 0 = n_{1a}(\lambda_1 - \mu_1 - C(n_{1a} + n_{1d} + n_{1i}) - Dn_2) + \sigma n_{1d} + rn_{1i} \]

\[ = n_{1a}(\lambda_1 - \mu_1 - C(n_{1a} + \frac{qDn_{1a}n_2}{\kappa\mu_1 + \sigma} + \frac{(1 - q)Dn_{1a}n_2}{r + v}) - Dn_2) + \frac{\sigma qDn_{1a}}{\kappa\mu_1 + \sigma}n_2 + \frac{r(1 - q)Dn_{1a}}{r + v}n_2. \]  \hspace{1cm} (4.5)

From this equation and (4.4), an explicit expression for \( n_2 \) can be obtained, and this together with (4.2) and (4.3) can be used in order to derive explicit formulas for \( n_{1d} \) and \( n_{1i} \).

Now we can complete the proof of Lemma 2.2. Making the right-hand side of (4.3) (which is equal to the right-hand side of the first equation in (2.1)) equal to zero and dividing both sides by \( n_{1a} \) implies that

\[ \lambda_1 - \mu_1 - C(n_{1a} + n_{1d} + n_{1i}) = n_2D\left(1 - \frac{q\sigma}{\kappa\mu_1 + \sigma} - \frac{(1 - q)r}{r + v}\right). \]  \hspace{1cm} (4.6)

Now, since \( q \in (0, 1) \), \( \kappa \geq 0 \), and \( r, v, \sigma > 0 \), we have that \( 1 - \frac{q\sigma}{\kappa\mu_1 + \sigma} - \frac{(1 - q)r}{r + v} \) is strictly positive. Further, by (4.2) and (4.3), \( n_{1d}, n_{1i}, n_2 \) all have the same sign. Hence, thanks to (4.6), we have the following.

(i) Assume that \( n_{1a} + n_{1d} + n_{1i} \geq \tilde{n}_{1a} = \frac{\lambda_1 - \mu_1}{C} \). Then \( n_2 \leq 0 \). Hence, \( n_{1d} \leq 0 \) and \( n_{1i} \leq 0 \). Thus, \( n_{1a} \geq \tilde{n}_{1a} \).
(ii) On the other hand, assume that \( n_{1a} + n_{1d} + n_{1i} \leq \bar{n}_{1a} \). Then \( n_2 \geq 0 \). Hence, \( n_{1d} \geq 0 \) and \( n_{1i} \geq 0 \). Thus, \( n_{1a} \leq \bar{n}_{1a} \).

In particular, we have obtained that if \( n_{1a} + n_{1d} + n_{1i} = \bar{n}_{1a} \), then \( n_{1d}, n_{1i}, n_2 \) must be zero and hence \( n_{1a} = \bar{n}_{1a} \). Finally, the arguments [i] and [ii] also hold with ‘\( \geq \)’ replaced by ‘\( > \)’ and ‘\( \leq \)’ by ‘\( < \)’ everywhere. From this we derive that \( n_{1d}, n_{1i}, n_2 \) and \( \lambda_1 - \mu_1 - Cn_{1a} \) have the same sign, which implies the lemma. □

We continue with the proof of Lemma 2.3.

**Proof of Lemma 2.3** At \((0,0,0,0)\) we have the Jacobi matrix

\[
A(0,0,0,0) = \begin{pmatrix}
\lambda_1 - \mu_1 & \sigma & r & 0 \\
0 & -\kappa \mu_1 - \sigma & 0 & 0 \\
0 & 0 & -(r + v) & 0 \\
0 & 0 & mw & -\mu_2 \\
\end{pmatrix}.
\]

Clearly, the eigenvalues of this matrix are its diagonal entries. Thanks to the assumptions that \( \lambda_1 > \mu_1 > 0 \), \( \kappa \geq 0 \), \( \sigma, r, v, \mu_2 > 0 \), we see that \( A(0,0,0,0) \) has precisely one positive eigenvalue: \( \lambda_1 - \mu_1 \), whereas all other eigenvalues are strictly negative. Hence, the equilibrium \((0,0,0,0)\) is unstable, as claimed in part (1) of the lemma. On the other hand, at \((\bar{n}_{1a},0,0,0)\), the Jacobi matrix is given as follows

\[
A(\bar{n}_{1a},0,0,0) = \begin{pmatrix}
-(\lambda_1 - \mu_1) & \sigma & r & -D\bar{n}_{1a} \\
0 & -\kappa \mu_1 - \sigma & 0 & qD\bar{n}_{1a} \\
0 & 0 & -(r + v) & (1 - q)D\bar{n}_{1a} \\
0 & 0 & mw & -\mu_2 - (1 - q)D\bar{n}_{1a} \\
\end{pmatrix}.
\] (4.7)

We immediately see that \( -(\lambda_1 - \mu_1) < 0 \) is an eigenvalue of this matrix (with eigenvector \((1,0,0,0)^T\)). The remaining three eigenvalues are the ones of the last \(3 \times 3\) block of \( A(\bar{n}_{1a},0,0,0) \). We recognize this block as the transpose of the mean matrix \( J \) defined in (2.7), which has the same eigenvalues as \( J \). Consequently, if the condition (2.2) holds, then \( A(\bar{n}_{1a},0,0,0) \) is indefinite with three negative eigenvalues and one positive one, and hence \((\bar{n}_{1a},0,0,0)\) is unstable. In contrast, if (2.5) holds, then all eigenvalues of \( A(\bar{n}_{1a},0,0,0) \) are strictly negative, and thus \((\bar{n}_{1a},0,0,0)\) is asymptotically stable. Thus, part (2) of the lemma follows.

Let us finally consider the coexistence equilibrium \((n_{1a},n_{1d},n_{1i},n_2)\) under condition (2.2). Writing \( n_1 = n_{1a} + n_{1d} + n_{1i} \), the Jacobi matrix is given as follows

\[
A(n_{1a},n_{1d},n_{1i},n_2) = \begin{pmatrix}
\lambda_1 - \mu_1 - Cn_{1a} - Dn_2 & \sigma - Cn_{1a} & r - Cn_{1a} & -Dn_{1a} \\
qDn_2 & -\kappa \mu_1 - \sigma & 0 & qDn_{1a} \\
(1 - q)Dn_2 & 0 & -r - v & (1 - q)Dn_{1a} \\
-(1 - q)Dn_2 & 0 & mw & -(1 - q)Dn_{1a} - \mu_2 \\
\end{pmatrix}.
\]

Our first goal is to show that the determinant of this matrix is positive. Subtracting \( \frac{q}{1-q} \) times the third row from the second row, we obtain the matrix

\[
\tilde{A}(n_{1a},n_{1d},n_{1i},n_2) = \begin{pmatrix}
\lambda_1 - \mu_1 - Cn_{1a} - Dn_2 & \sigma - Cn_{1a} & r - Cn_{1a} & -Dn_{1a} \\
0 & -\kappa \mu_1 - \sigma & \frac{q(r + v)}{1-q} & 0 \\
(1 - q)Dn_2 & 0 & -r - v & (1 - q)Dn_{1a} \\
-(1 - q)Dn_2 & 0 & mw & -(1 - q)Dn_{1a} - \mu_2 \\
\end{pmatrix}.
\]
which has the same determinant as $A(n_{1a}, n_{1d}, n_{1i}, n_2)$. We now claim that the last $3 \times 3$ block of $\tilde{A}(n_{1a}, n_{1d}, n_{1i}, n_2)$ has determinant zero. Indeed, we have

$$\det \begin{pmatrix}
\frac{q}{1-q} (r + v) & 0 & 0 \\
0 & -r - v & (1 - q) Dn_{1a} \\
0 & mv & (1 - q) Dn_{1a} - \mu_2.
\end{pmatrix}$$

$$= (-\kappa_1 - \sigma)((1 - q)Dn_{1a} + \mu_2)(r + v) - (1 - q)mvDn_{1a}$$

$$= (-\kappa_1 - \sigma)((1 - q)Dn_{1a}(r + v - mv) + \mu_2(r + v)) = 0,$$

where in the last step we used the definition (2.3) of $n_{1a}$. Hence, by Laplace’s expansion theorem applied to the first column of $\tilde{A}(n_{1a}, n_{1d}, n_{1i}, n_2)$, we have

$$\det A(n_{1a}, n_{1d}, n_{1i}, n_2) = \det \tilde{A}(n_{1a}, n_{1d}, n_{1i}, n_2)$$

$$= (1 - q)Dn_2 \left[ (\sigma - Cn_{1a}) \frac{q}{1-q}(r + v)(-1)Dn_{1a} - \mu_2 + Dn_{1a}(\kappa_1 + \sigma)mv \\
- (r - Cn_{1a})(\kappa_1 + \sigma)((1 - q)Dn_{1a} + \mu_2) + (\sigma - Cn_{1a}) \frac{q}{1-q}(r + v)(1 - q)Dn_{1a} \\
- Dn_{1a}(\kappa_1 + \sigma)(r + v) + (\kappa_1 + \sigma)(r - Cn_{1a})(1 - q)Dn_{1a} \right]$$

$$= (1 - q)Dn_2 \left[ Cn_{1a} \frac{q}{1-q}(r + v)\mu_2 + Cn_{1a}(\kappa_1 + \sigma)\mu_2 - \sigma \frac{q}{1-q}(r + v)\mu_2 + Dn_{1a}(\kappa_1 + \sigma)mv \\
- r(\kappa_1 + \sigma)mv - r(\kappa_1 + \sigma)\mu_2 - Dn_{1a}(\kappa_1 + \sigma)(r + v) \right]$$

$$= (1 - q)Dn_2 \left[ Cn_{1a} \frac{q}{1-q}(r + v)\mu_2 + Cn_{1a}(\kappa_1 + \sigma)\mu_2 \right.$$  

$$+ (\kappa_1 + \sigma) \left( \frac{\mu_2(r + v)}{1-q} - \mu_2 r \right) - \sigma \frac{q}{1-q}\mu_2(r + v) \right]$$

$$= Dn_2[Cn_{1a} q(r + v)\mu_2 + Cn_{1a}(1 - q)(\kappa_1 + \sigma)\mu_2$$

$$+ \kappa_1\mu_2 r + \kappa_1\mu_2 v + \sigma\mu_2 r + \sigma\mu_2 v - \kappa_1(1 - q)\mu_2 r - \sigma(1 - q)\mu_2 r - \sigma q\mu_2 r - \sigma q\mu_2 v]$$

$$= Dn_2[Cn_{1a} q(r + v)\mu_2 + Cn_{1a}(1 - q)(\kappa_1 + \sigma)\mu_2 + \kappa_1\mu_2 q + \sigma v(1 - q) + \kappa_1 v] > 0.$$  

(4.8)

where in the third equality we again used (2.3) and in the last step we used the positivity of $n_{1a}$ and $n_2$. Further, the trace of the matrix is negative because all its diagonal entries are negative. Indeed, also the first entry of the first column is negative, which follows from the fact that since $(n_{1a}, n_{1d}, n_{1i}, n_2)$ is an equilibrium of (2.1) with four positive coordinates, we have

$$\lambda_1 - \mu_1 - C(n_{1a} + n_{1d} + n_{1i}) - Dn_2 = -\frac{\sigma n_{1d} + rn_{1i}}{n_{1a}},$$

and hence

$$\lambda_1 - \mu_1 - 2Cn_{1a} - C(n_{1d} + n_{1i}) - Dn_2 < -\frac{\sigma n_{1d} + rn_{1i}}{n_{1a}} < 0.$$  

This concludes the proof of the lemma. □

Next, we carry out the proof of Proposition 2.4.

Proof of Proposition 2.4 Proposition 2.4 is the analogue of the assertion [BK98, Lemma 4.1] that treated the case without dormancy or recovery and slightly with different competition. Our proof is indeed the analogue of the one in [BK98], which relies on the idea of Chetaev’s instability theorem [C61]. The main additional step of our proof is that the dormant coordinate should not be treated analogously to the infected and the virus coordinate, but it should just be ignored. Since it is possibly not straightforward to see that this approach works out, we present a self-contained proof as follows.
Let $V : [0, \infty)^4 \to \mathbb{R}$, $(\bar{n}_{1a}, \bar{n}_{1d}, \bar{n}_{i1}, \bar{n}_{i2}) \mapsto w_1 \bar{n}_{1i} + w_2 \bar{n}_{2}$ for some $w_1, w_2 > 0$. Let us write the system (2.1) as $\mathbf{n}(t) = f(\mathbf{n}(t))$ and fix $\varepsilon > 0$. Then, the standard Euclidean scalar product of the gradient of $V$ and $f$ at $(\bar{n}_{1a}, \bar{n}_{1d}, \bar{n}_{i1}, \bar{n}_{i2}) \in [0, \infty)^4$ with $\bar{n}_{1a} > n_{1a} - \varepsilon$ equals

$$\langle \nabla V, f \rangle(\bar{n}_{1a}, \bar{n}_{1d}, \bar{n}_{i1}, \bar{n}_{i2}) = w_1((1 - q)D\bar{n}_{1a}\bar{n}_{2} - \bar{n}_{1i}(r + v)) + w_2(-(1 - q)D\bar{n}_{1a}\bar{n}_{2} + mv\bar{n}_{i1} - \mu_2\bar{n}_{2})$$

$$= \bar{n}_{1i}[mvw_2 - w_1i(r + v)] + \bar{n}_{2}((1 - q)D\bar{n}_{1a}w_{1i} - (1 - q)D\bar{n}_{1a}w_{2i} - \mu_2w_{2i})$$

$$> \bar{n}_{1i}[mvw_2 - w_1i(r + v)] + \bar{n}_{2}((1 - q)D(\bar{n}_{1a} - \varepsilon)w_{1i} - (1 - q)D\bar{n}_{1a}w_{2i} - \mu_2w_{2i}).$$

Hence, the function $V$ is positive definite once

$$mvw_2 > (r + v)w_{1i} \quad \text{and} \quad (1 - q)w_{1i}D(\bar{n}_{1a} - \varepsilon) > ((1 - q)D(\bar{n}_{1a} - \varepsilon) + \mu_2)w_{2i}, \quad (4.9)$$

in other words,

$$\frac{mv}{r + v}w_2 > w_1((1 - q) + \frac{\mu_2}{D(\bar{n}_{1a} - \varepsilon)} = w_2\left[1 + \frac{\mu_2}{(1 - q)D(\bar{n}_{1a} - \varepsilon)}\right].$$

Since $w_1i > 0, w_2i > 0$, this requires

$$\bar{n}_{1a} - \varepsilon > \frac{\mu_2(r + v)}{(1 - q)D(mv - (r + v))},$$

which holds whenever $\varepsilon \in (0, \bar{n}_{1a} - n_{1a})$, where we recall that $\bar{n}_{1a} > n_{1a}$ under the condition (2.2). Then we can indeed choose $w_1i, w_2i > 0$ satisfying (4.9), and thus we can find $d > 0$ such that for such a choice of $w_1i, w_2i$, and $\varepsilon$, we have

$$\nabla V > dV \quad \text{on } B_{\varepsilon}(\bar{n}_{1a}, 0, 0, 0) \cap (0, \infty)^4 \quad (4.10)$$

where for $x \in \mathbb{R}^4$ and $\rho > 0$, $B_{\rho}(x)$ denotes the open $\ell^2$-ball of radius $\rho$ around $x$.

Now, let us assume that $(n_{1a}(0), n_{1d}(0), n_{i1}(0), n_{i2}(0)) \in (0, \infty)^4$. Then it is clear that for all $t > 0, n_{1i}(t) \neq 0$ and $n_{2i}(t) \neq 0$. Now, if $\lim_{t \to \infty}(n_{1a}(t), n_{1d}(t), n_{i1}(t), n_{i2}(t)) = (\bar{n}_{1a}, 0, 0, 0)$, there exists $\varepsilon > 0$ such that for all $t > 0$, $(n_{1a}(t), n_{1d}(t), n_{i1}(t), n_{i2}(t)) \in B_{\varepsilon}(\bar{n}_{1a}, 0, 0, 0) \cap (0, \infty)^4$. Hence, by (4.10), $\lim_{t \to \infty}V(n_{1a}(t), n_{1d}(t), n_{i1}(t), n_{i2}(t)) = \infty$, which contradicts the assumption that $\lim_{t \to \infty}(n_{1a}(t), n_{i2}(t)) = (0, 0)$.

From this it is in fact easy to derive that $(n_{1a}(t), n_{1d}(t), n_{i1}(t), n_{i2}(t))$ cannot even converge to $(\bar{n}_{1a}, 0, 0, 0)$ along any diverging sequence of times, but let us provide the details for completeness. Since $V$ is positive definite on $B_0 := B_{\varepsilon}(\bar{n}_{1a}, 0, 0, 0) \cap (0, \infty)^4$, the $\omega$-limit set $\Omega_0$ of any solution of (2.1) (i.e., the set of subsequential limits of the solution as $t \to \infty$) started from $B_0$ satisfies

$$\Omega_0 \cap \overline{B_0} \subseteq \{\nabla V, f, \varepsilon \} = 0\}$$

where $\overline{B_0}$ is the closure of $B_0$. In terms of these objects, we have already verified that $(\bar{n}_{1a}, 0, 0, 0) \in \{\nabla V, f, \varepsilon \} = 0\}$ and that $(\bar{n}_{1a}, 0, 0, 0) \notin \Omega_0 \cap \overline{B_0}$.

Using the definition of $V$ and the fact that $(0, \infty)^4$ is positively invariant under (2.1), we conclude that $\Omega_0 \cap \overline{B_0}$ contains only points of the form $(\bar{n}_{1a}, \bar{n}_{1d}, 0, 0)$, where $\bar{n}_{1a}, \bar{n}_{1d} > 0$. However, if a coordinatewise nonnegative solution of (2.1) started from $(0, \infty)^4$ is such that its infected and virus coordinate tend to zero, then its dormant coordinate must also tend to zero and hence its active coordinate to $\bar{n}_{1a}$. We conclude that $\Omega_0 \cap \overline{B_0} \subseteq \{(\bar{n}_{1a}, 0, 0, 0)\}$. But since $(\bar{n}_{1a}, 0, 0, 0) \notin \Omega_0 \cap \overline{B_0}$, it follows that $\Omega_0 \cap \overline{B_0} = \emptyset$, and thus the proposition is proven.

Now, we verify Corollary 2.5.

Proof of Corollary 2.5: According to the properties of the linearized variant of the system (2.1) near $(0, 0, 0, 0)$ (see the Jacobi matrix $A(0, 0, 0, 0)$ in the proof of Lemma 2.3), if $(n_{1a}(0), n_{1d}(0), n_{i1}(0), n_{i2}(0)) \in (0, \infty)^4$ with $n_{1a}(0) > 0$, then $\liminf_{t \to \infty} n_{1a}(t) > 0$. 

\[ \square \]
Next, note that if \( \mathbf{n}(0) \in [0, \infty)^4 \) with \( n_{1a}(0) > 0 \), then there are two possibilities. Either \( \max\{n_{1i}(0), n_{2}(0)\} > 0 \) and hence \( n_{1d}(t), n_{1i}(t), n_{2}(t) > 0 \) for all \( t > 0 \), or \( \max\{n_{1i}(0), n_{2}(0)\} = 0 \) and hence \( \lim_{t \to \infty} \mathbf{n}(t) = (\bar{n}_{1a}, 0, 0, 0) \). Thanks to the invariance of \( \omega \)-limit sets, this implies that if the \( \omega \)-limit set of \( (\mathbf{n}(t))_{t \geq 0} \) contains a point with a zero coordinate (which is necessarily not the type 1a coordinate), then in fact the \( \omega \)-limit set contains \( (\bar{n}_{1a}, 0, 0, 0) \), i.e. the solution converges to \( (\bar{n}_{1a}, 0, 0, 0) \) at least along a subsequence of times. But for a coordinatewise positive initial condition, that would contradict Proposition 2.4, hence the positivity part of the proposition.

Next, let us verify that \( \limsup_{t \to \infty} n_{1a}(t) + n_{1d}(t) + n_{1i}(t) < \bar{n}_{1a} \). Summing the first three lines of (2.1), we obtain
\[
\dot{n}_{1a}(t) + \dot{n}_{1d}(t) + \dot{n}_{1i}(t) = n_{1a}(t)(\lambda_1 - \mu_1 - C(n_{1a}(t) + n_{1d}(t) + n_{1i}(t)) - \kappa n_{1d}(t) - v n_{1i}(t).
\]
Let us choose \( \varepsilon > 0 \) such that \( \liminf_{t \to \infty} \kappa n_{1d}(t) + v n_{1i}(t) > \varepsilon \). Then if for some \( t > 0 \) we have \( n_{1a}(t) + n_{1d}(t) + n_{1i}(t) \geq \bar{n}_{1a} - \delta \), then we have
\[
\frac{d}{dt}(n_{1a}(t) + n_{1d}(t) + n_{1i}(t)) < -\varepsilon.
\]
Now, solutions of (2.1) are continuously differentiable thanks to the Picard–Lindelöf theorem, and hence we obtain that there exists \( \delta > 0 \) such that whenever \( n_{1a}(t) + n_{1d}(t) + n_{1i}(t) \geq \bar{n}_{1a} - \delta \), we have
\[
\frac{d}{dt}(n_{1a}(t) + n_{1d}(t) + n_{1i}(t)) < -\varepsilon/2.
\]
This implies the time
\[
t_{\bar{n}_{1a} - \delta} = \inf \{ t \geq 0: n_{1a}(t) + n_{1d}(t) + n_{1i}(t) < \bar{n}_{1a} - \delta \}
\]
is finite, and for all \( t > t_{\bar{n}_{1a} - \delta} \) we have \( n_{1a}(t) + n_{1d}(t) + n_{1i}(t) \leq \bar{n}_{1a} - \delta < \bar{n}_{1a} \). Thus, \( \limsup_{t \to \infty} n_{1a}(t) + n_{1d}(t) + n_{1i}(t) < \bar{n}_{1a} \).

Finally, the asymptotic upper bound on \( n_{2}(t) \) as \( t \to \infty \) is the analogue of [BK98] Lemma 2.3 in our model. Relying on the already proven parts of Corollary 2.5, we can now provide a short proof for it. Recall that under the assumptions of the corollary we have
\[
\limsup_{t \to \infty} n_{1a}(t) + n_{1d}(t) + n_{1i}(t) < \bar{n}_{1a}, \quad \liminf_{t \to \infty} n_{j}(t) > 0, \forall j \in \{1a, 1i, 2\},
\]
and hence there exists \( \beta > 0 \) such that
\[
\limsup_{t \to \infty} n_{1i}(t) \leq \bar{n}_{1a} - \beta.
\]
Thus, we obtain for all \( t \) sufficiently large
\[
\dot{n}_{2}(t) = -(1 - q) D n_{1a}(t) n_{2}(t) + m v n_{1i}(t) - \mu_2 n_{2}(t) < m v (\bar{n}_{1a} - \beta) - \mu_2 n_{2}(t).
\]
This shows that for such \( t \), if \( n_{2}(t) \geq \frac{m v (\bar{n}_{1a} - \beta)}{\mu_2} \), then \( s \mapsto n_{2}(s) \) is decreasing at \( t \). Consequently,
\[
\limsup_{t \to \infty} n_{2}(t) \leq \frac{m v (\bar{n}_{1a} - \beta)}{\mu_2} < \frac{m v \bar{n}_{1a}}{\mu_2},
\]
as wanted. \( \square \)

4.3. First phase: growth or extinction of the epidemic. Our first goal is to prove that during the first phase of the virus invasion, with high probability, the rescaled type 1a population stays close to equilibrium \( \bar{n}_{1a} \) and the type 1d population stays small compared to \( K \) until the total type 1i and 2 population reaches a size of order \( K \) or goes extinct. Recall the stopping time \( T_{\varepsilon}^{0} \) from (2.15) and for \( \varepsilon > 0 \) the stopping time \( T_{\varepsilon}^{2} \) from (2.12). Let us further define the stopping time
\[
Q_{\varepsilon} = \inf \{ t \geq 0: (N_{1a,t}^{K}, N_{1d,t}^{K}) \notin [\bar{n}_{1a} - \varepsilon, \bar{n}_{1a} + \varepsilon] \times [0, \varepsilon] \},
\]
the first time when the rescaled type 1a population leaves a neighbourhood of radius \( \varepsilon \) around the equilibrium \( \bar{n}_{1a} \) or the rescaled 1d population reaches size \( \varepsilon \). Our main results regarding the first phase are summarized in the following proposition.

**Proposition 4.1.** Assume that \( \lambda_1 > \mu_1 \) and \( \bar{\lambda} \neq 0 \). Let \( K \rightarrow m_{1a}^K \) be a function from \((0, \infty)\) to \([0, \infty)\) such that \( m_{1a}^K \in \frac{1}{K} N_0 \) and \( \lim K \rightarrow \infty m_{1a}^K = \bar{n}_{1a} \). Then there exists a constant \( b \geq 2 \) and a function \( f: (0, \infty) \rightarrow (0, \infty) \) tending to zero as \( \varepsilon \downarrow 0 \) such that

\[
\limsup_{K \rightarrow \infty} \mathbb{P}\left(T^2_{\varepsilon} < T_0^2 \land Q_{bc}, \frac{T_{\varepsilon}^2}{\log K} - \frac{1}{\lambda} \leq f(\varepsilon) \left| N_0^K = (m_{1a}^K, 0, 0, \frac{1}{K}) \right. \right) - (1 - s_2) = o_{\varepsilon}(1) \tag{4.12}
\]

and

\[
\limsup_{K \rightarrow \infty} \mathbb{P}\left(T_0^2 < T_{\varepsilon}^2 \land Q_{bc}, \left| N_0^K = (m_{1a}^K, 0, 0, \frac{1}{K}) \right. \right) - s_2 = o_{\varepsilon}(1), \tag{4.13}
\]

where \( o_{\varepsilon}(1) \) tends to zero as \( \varepsilon \downarrow 0 \).

In order to prove the proposition, we first verify the following lemma.

**Lemma 4.2.** Under the assumptions of Proposition 4.1 there exist constants \( \varepsilon_0 > 0, b \geq 2 \) such that for any \( \varepsilon \in (0, \varepsilon_0] \),

\[
\limsup_{K \rightarrow \infty} \mathbb{P}(Q_{bc} \leq T_{\varepsilon}^2 \land T_0^2) = 0.
\]

**Proof.** We follow the approach of the proof of [CCLLS21, Lemma 3.2], with the main difference being that instead of considering only types that are initially of size comparable to \( K \) as ‘resident’ types and all other types as ‘mutant’, we also consider the initially microscopic type 1d like as resident (as we discussed in Section 2.6.5), which requires a bit more care.

We verify our lemma via coupling the rescaled population size \((N_{1a,t}, N_{1d,t})_{t \geq 0}\) of types 1a and 1d with two birth-and-death processes, \((N_{1a}, N_{1d}) = ((N_{1a,t}, N_{1d,t})_{t \geq 0}) \) and \((N_{1a}^2, N_{1d}^2) = ((N_{1a,t}^2, N_{1d,t}^2))_{t \geq 0}\), on time scales where the total population of types 1i, and 2 is still small compared to \( K \). (These processes will also depend on \( K \), but we omit the notation \( K \) from their nomenclature for simplicity.) To be more precise, we want to choose \(((N_{1a,t}, N_{1d,t}^2))_{t \geq 0}\) and \(((N_{1a,t}^2, N_{1d,t}^2))_{t \geq 0}\) so that

\[
N_{1a,t}^1 \leq N_{1a,t}^K \leq N_{1d,t}^2, \quad \text{a.s.} \quad \forall t \leq T_{\varepsilon}^2 \land T_0^2, \quad \forall v \in \{1a, 1d\}. \tag{4.14}
\]

In order to satisfy \(4.14\), for all \( \varepsilon > 0 \) small enough, the processes \(((N_{1a,t}, N_{1d,t}))_{t \geq 0}\) and \(((N_{1a,t}^2, N_{1d,t}^2))_{t \geq 0}\) can be chosen with the following birth and death rates, for all \( i, j \in N_0 \) (where certain kinds of transitions occur for only one of the two processes):

\[
(N_{1a}, N_{1d}): \begin{cases}
\left( \frac{i}{K}, \frac{j}{K} \right) \rightarrow \left( \frac{i + 1}{K}, \frac{j}{K} \right) & \text{at rate } i\lambda_1, \\
\left( \frac{i}{K}, \frac{j}{K} \right) \rightarrow \left( \frac{i - 1}{K}, \frac{j}{K} \right) & \text{at rate } i(\mu_1 + C\left( \frac{i}{K} + \varepsilon \right) + D\varepsilon), \\
\left( \frac{i}{K}, \frac{j}{K} \right) \rightarrow \left( \frac{i}{K}, \frac{j - 1}{K} \right) & \text{at rate } j\kappa\mu_1, \\
\left( \frac{i}{K}, \frac{j}{K} \right) \rightarrow \left( \frac{i + 1}{K}, \frac{j - 1}{K} \right) & \text{at rate } j\sigma,
\end{cases}
\]
and

\[
(N^2_{1a}, N^2_{1d}) : \begin{align*}
(i/K, j/K) &\to (i+1/K, j/K) \quad \text{at rate } i\lambda_1 + r\varepsilon, \\
(i/K, j/K) &\to (i-1/K, j/K) \quad \text{at rate } i(\mu_1 + C i/K), \\
(i/K, j/K) &\to (i/K, j+1/K) \quad \text{at rate } iqD\varepsilon, \\
(i/K, j/K) &\to (i/K, j-1/K) \quad \text{at rate } j\kappa\mu_1, \\
(i/K, j/K) &\to (i+1/K, j-1/K) \quad \text{at rate } j\sigma,
\end{align*}
\]

both started from \((m^K_{1a}, 0)\) at time zero. Indeed, given the initial conditions, \(((N^1_{1a,t}, N^1_{1d,t}))_{t \geq 0}\) has a dormant coordinate absorbed at zero, since it starts at zero and is monotonically decreasing. In particular, in this process, active individuals that would become dormant (having a chance to resuscitate) in our original population process \((N^K_t)_{t \geq 0}\) just die immediately, and recoveries are also ignored. The rate of death of individuals of type 1a due to competition is maximized under the constraint that the total population of types 1i and 2 is at most \(\varepsilon K\). In contrast, in the process \(((N^1_{1a,t}, N^1_{1d,t}))_{t \geq 0}\), successful virus attacks are ignored, whereas the birth rate is increased by the maximal possible amount of recovered individuals on \([0, T^2_\varepsilon \wedge T^2_{\varepsilon}]\). Unsuccessful virus attacks are replaced by events where a dormant individual emerges but no active individual gets lost. Further, deaths of type 1a individuals due to competition with other types (i.e. 1d or 2) are ignored. Together with the fact that the rates for birth, natural death of actives, death by competition, death of dormant individuals, and resuscitation rates are the same for all three these processes, it follows that the coupling \([1.14]\) is satisfied.

Let us estimate the time until which the processes \((N^1_{1a}, N^1_{1d})\) and \((N^2_{1a}, N^2_{1d})\) stay close to the value \((\bar{n}_{1a}, 0)\). We define the stopping times

\[
Q^j_{\varepsilon} := \inf \left\{ t \geq 0 : N^j_{1a,t} \notin [\bar{n}_{1a} - \varepsilon, \bar{n}_{1a} + \varepsilon] \text{ or } N^j_{1d,t} > \varepsilon \right\}, \quad j \in \{1, 2\}, \varepsilon > 0.
\]

As \(K \to \infty\), according to \([1.14]\) (Theorem 2.1, p. 456), uniformly on any fixed time interval of the form \([0, T]\), \(T > 0\), \((N^1_{1a,t}, N^1_{1d,t})\) converges in probability to the unique solution to

\[
\begin{align*}
\dot{n}_{1a,1}(t) & = n_{1a,1}(t)(\lambda_1 - \mu_1 - C(n_{1a,1}(t) + \varepsilon) - D\varepsilon) + \sigma n_{1d,1}(t), \\
\dot{n}_{1d,1}(t) & = - (\kappa\mu_1 + \sigma)n_{1d,1}(t),
\end{align*}
\]

(4.15)

given that the initial conditions converge in probability to the initial condition of the limiting differential equation. Similarly, for large \(K\), the dynamics of \((N^2_{1a,t}, N^2_{1d,t})\) is close to the one of the unique solution to

\[
\begin{align*}
\dot{n}_{1a,2}(t) & = n_{1a,1}(t)(\lambda_1 - \mu_1 - Cn_{1a,2}(t) + \sigma n_{1d,2}(t) + r\varepsilon, \\
\dot{n}_{1d,2}(t) & = qDn_{1a,2}(t) - (\kappa\mu_1 + \sigma)n_{1d,2}(t),
\end{align*}
\]

(4.16)

where for both systems of ODEs, the corresponding initial condition is \((\bar{n}_{1a}, 0)\). Both systems are such that all their coordinatewise nonnegative solutions are bounded (whereas the positive orthant is positively invariant under both systems). Further, if \(\varepsilon > 0\) is sufficiently small, then the equilibrium \((0, 0)\) is unstable, and there is a unique additional coordinatewise nonnegative equilibrium, given as \((\bar{n}^{(1)}_{1a}, \bar{n}^{(1)}_{1d}) := (\lambda_1 - \mu_1 - C + D\varepsilon)\varepsilon, 0\) (for \([4.15]\)) respectively as \((\bar{n}^{(2)}_{1a}, \bar{n}^{(2)}_{1d})\) characterized by

\[
\bar{n}^{(2)}_{1d} = \frac{qD\bar{n}^{(2)}_{1a}\varepsilon}{\kappa\mu_1 + \sigma}
\]

and thus \(\bar{n}^{(2)}_{1a}\) being the unique positive zero locus of the quadratic polynomial

\[
h(x) = x(\lambda_1 - \mu + \frac{\sigma qD\varepsilon}{\kappa\mu_1 + \sigma} - Cx) + r\varepsilon = 0
\]
and thus in particular
\[ \lim_{\varepsilon \downarrow 0} (n^{(1)}_{1a}, n^{(1)}_{1d}) = \lim_{\varepsilon \downarrow 0} (\bar{n}^{(2)}_{1a}, \bar{n}^{(2)}_{1d}) = (\bar{n}_{1a}, 0), \]
and thus in particular
\[ 0 \leq \bar{n}^{(2)}_{1d} = \frac{qD\bar{n}_{1a}}{\kappa \mu + \sigma} (1 + o(1)) = O(\varepsilon). \]
We can therefore find \( \varepsilon_0 > 0 \) and \( b \geq 2 \) such that for all \( \varepsilon \in (0, \varepsilon_0), j \in \{1, 2\}, \) and \( v \in \{1a, 1d\} \) we have
\[ |\bar{n}_v - \bar{n}^{(j)}_v| \leq b\varepsilon \quad \text{and} \quad 0 \notin [\bar{n}_{1a} - b\varepsilon, \bar{n}_{1a} + b\varepsilon], \quad (4.17) \]
where we wrote \( \bar{n}_{1d} = 0. \)

Now, thanks to a result about exit of jump processes from a domain by Freidlin and Wentzell [FW84, Chapter 5] (see [C06, Section 4.2] for details in a very similar situation), there exists a family (over \( K \)) of Markov jump processes \( (\tilde{N}^{1}_{1a}, \tilde{N}^{1}_{1d}) = (\tilde{N}^{1}_{1a,t}, \tilde{N}^{1}_{1d,t}))_{t \geq 0} \) with positive, bounded, Lipschitz continuous transition rates that are uniformly bounded away from 0 such that for
\[ \tilde{Q}^j_v := \inf \{ t \geq 0 : \tilde{N}^{j}_{1a,t} \notin [\bar{n}_{1a} - \varepsilon, \bar{n}_{1a} + \varepsilon] \text{ or } \tilde{N}^{j}_{1d,t} \geq \varepsilon \}, \quad j \in \{1, 2\}, \varepsilon > 0, \]
there exists \( V > 0 \) such that
\[ \mathbb{P}(Q^j_{be} > e^{KV}) = \mathbb{P}(\tilde{Q}^j_{be} > e^{KV}) \xrightarrow{K \to \infty} 0. \quad (4.18) \]
Using similar arguments for \( N^2_{1a} \), we derive that for \( \varepsilon > 0, V > 0 \) small enough, we have that
\[ \mathbb{P}(Q^j_{be} > e^{KV}) \xrightarrow{K \to \infty} 0. \quad (4.19) \]
Now, on the event \( \{Q_{be} \leq T^0_\varepsilon \wedge T^2_\varepsilon \} \) we have \( Q_{be} \geq \tilde{Q}^1_{be} \wedge \tilde{Q}^2_{be} \). Using (4.18) and (4.19), we derive that
\[ \limsup_{K \to \infty} \mathbb{P}(Q_{be} \leq e^{KV}, Q_{be} \leq T^0_\varepsilon \wedge T^2_\varepsilon) = 0. \]
Moreover, using Markov’s inequality,
\[ \mathbb{P}(Q_{be} \leq T^0_\varepsilon \wedge T^2_\varepsilon) \leq \mathbb{P}(Q_{be} \leq e^{KV}, Q_{be} \leq T^0_\varepsilon \wedge T^2_\varepsilon) + \mathbb{P}(Q_{be} \wedge T^0_\varepsilon \wedge T^2_\varepsilon \geq e^{KV}) \]
\[ \leq \mathbb{P}(Q_{be} \leq e^{KV}, Q_{be} \leq T^0_\varepsilon \wedge T^2_\varepsilon) + e^{-KV} \mathbb{E}(Q_{be} \wedge T^0_\varepsilon \wedge T^2_\varepsilon). \]
Since we have
\[ \mathbb{E}[Q_{be} \wedge T^0_\varepsilon \wedge T^2_\varepsilon] \leq \mathbb{E} \left[ \int_0^{T^0_\varepsilon \wedge T^2_\varepsilon} K(N^K_{11,t} + N^K_{21,t})dt \right], \]
it suffices to show that there exists \( \tilde{C} > 0 \) such that
\[ \mathbb{E} \left[ \int_0^{Q_{be} \wedge T^0_\varepsilon \wedge T^2_\varepsilon} K(N^K_{11,t} + N^K_{21,t})dt \right] \leq \tilde{C} \varepsilon K. \quad (4.20) \]
This can be done similarly to [CCLLS21, Section 3.1.2], the only difference being again that type 1d is considered as ‘resident’ and not as ‘mutant’ type, but for the reader’s convenience we provide the details. We claim that it is enough to show that there exists a function \( g : (\frac{1}{K} N_0)^4 \to \mathbb{R} \) defined as
\[ g(n_{1a}, n_{1d}, n_{2}) = \gamma_1 n_{1i} + \gamma_2 n_{2} \quad (4.21) \]
for suitably chosen \( \gamma_1, \gamma_2 \in \mathbb{R}, \) such that
\[ \mathcal{L} g(N^K_t) \geq N^K_{11,t} + N^K_{21,t} \quad (4.22) \]
where $\mathcal{L}$ is the infinitesimal generator of $(N^K_t)_{t \geq 0}$. Indeed, if (4.22) holds, then thanks to Dynkin’s formula we have

$$
\mathbb{E}\left[\int_0^{Q_{be} \wedge T_0^2 \wedge T_2^L} K(N_{1,t}^K + N_{2,t}^K)dt\right] \leq \mathbb{E}\left[\int_0^{Q_{be} \wedge T_0^2 \wedge T_2^L} K\mathcal{L}g(N^K_t)dt\right]
$$

$$
= \mathbb{E}[Kg(N^K_{Q_{be} \wedge T_0^2 \wedge T_2^L}) - Kg(N^K_0)] \leq (|\gamma_1| + |\gamma_2|)(\varepsilon K - 1),
$$

which implies the existence of $\varepsilon > 0$ such that (4.20) holds for all $\varepsilon > 0$ small enough, independently of the signs of $\gamma_1, \gamma_2$. Here, Dynkin’s formula can indeed be applied because $\mathbb{E}[Q_{be} \wedge T_0^2 \wedge T_2^L]$ is finite. That holds because given our initial conditions, with positive probability the single initial type 2 individual dies due to natural death within a unit length of time before any event of the process $N^K_t$ occurs, and hence already $T_2^L$ is stochastically dominated by a geometric random variable, which has all moments. We now apply the infinitesimal generator $\mathcal{L}$ to the function $g$ introduced in (4.21) once again. The infinitesimal generator $\mathcal{L}$ is such that $\tilde{\mathcal{L}}(\cdot) = \mathcal{L}(K\cdot)$ maps a bounded measurable function $h: \mathbb{N}^4 \to \mathbb{R}$ to $\tilde{L}h: \mathbb{N}^4 \to \mathbb{R}$ defined as follows

$$
\tilde{L}h(x, y, z, w) = (h(x + 1, y, z, w) - h(x, y, z, w))\lambda_1 x
$$

\begin{align*}
+ (h(x - 1, y, z, w) - h(x, y, z, w))\mu_1 + C^x(y+z)K \\
+ (h(x - 1, y + 1, z, w) - h(x, y, z, w))D_{xzw}K \\
+ (h(x - 1, y, z + 1, w - 1) - h(x, y, z, w))D_{1-q}xwK \\
+ (h(x + 1, y - 1, z, w) - h(x, y, z, w))\sigma y + (h(x, y - 1, z, w) - h(x, y, z, w))\kappa_1 y \\
+ (h(x, y, z - 1, w + m) - h(x, y, z, w))v z + (h(x + 1, y, z - 1, w) - h(x, y, z, w))r z \\
+ (h(x, y, z, w - 1) - h(x, y, z, w))\mu_2 w.
\end{align*}

This yields

$$
\mathcal{L}g(N^K_t) = DN^K_{1a,t}N^K_{2,t}(1 - q)(\gamma_1 - \gamma_2) + (m\gamma_2 - \gamma_1)vn_{11,t}N^K_{11,t} - \gamma_1 r n_{11,t} - \gamma_2 \mu_2 n_{2,t}.
$$

Hence, according to (4.21), it suffices to show that there exist $\gamma_1, \gamma_2 \in \mathbb{R}$ such that the following system of inequalities is satisfied:

\begin{align*}
-(r + v)n_{11,t}\gamma_1 + mv n_{2,t} \gamma_2 > 1, \\
(1 - q)dn_{1a,t}n_{2,t} \gamma_1 - ((1 - q)dn_{1a,t}n_{2,t} + \mu_2) \gamma_2 > 1.
\end{align*}

(4.23)

We claim that as long as $t \leq Q_{be} \wedge T_0^2 \wedge T_2^L$, the matrix

$$
J^K_2(t) = \begin{pmatrix}
-r - v & mv \\
(1 - q)dn_{1a,t} & -(1 - q)dn_{1a,t} - \mu_2
\end{pmatrix}
$$

is entrywise close to the $2 \times 2$ mean matrix $J_2$ introduced in (2.8). This is certainly true because the first rows of the two matrices are equal, and for $t \leq Q_{be} \wedge T_0^2 \wedge T_2^L$ we have that

$$
|(J^K_2(t) - J_2)_{ij}| \leq Db\varepsilon, \quad \forall j, l \in \{1, 2\}.
$$

(4.24)

Let us now choose $(\gamma_1, \gamma_2)$. Thanks to the assumption that $\lambda_1 > \mu_1$, given that $\varepsilon > 0$ is sufficiently small, $J^K_2(t) + (r + v + (1 - q)dn_{1a} + \mu_2)Id$ is a matrix with positive entries, where $Id$ denotes the $2 \times 2$ identity matrix. Hence, writing $u_0 = r + v + (1 - q)dn_{1a} + \mu_2$, it follows from the Perron–Frobenius theorem that there exists a strictly positive right eigenvector $\vec{\Gamma} = \vec{\gamma}_1, \vec{\gamma}_2) \cdot J + u_0 Id$ corresponding to the eigenvalue $\vec{\lambda} + u_0$. Then we have

$$
(J_2 + u_0 Id)^T \vec{\Gamma} = (\vec{\lambda} + u_0)\vec{\Gamma},
$$

and thus also $J_2 \vec{\Gamma}^T = \vec{\lambda} \vec{\Gamma}^T$. Since by assumption $\vec{\lambda} \neq 0$ and $\vec{\Gamma}$ has two positive coordinates, we obtain that

$$
\Gamma := (\vec{\gamma}_1, \vec{\gamma}_2) := 2(\vec{\lambda}(\vec{\gamma}_1 \wedge \vec{\gamma}_2))^{-1}\vec{\Gamma}
$$
is well-defined, and it solves
\[ J_2 \Gamma^T = \widetilde{\lambda} \Gamma^T, \]  
(4.25) further, \( \tilde{\lambda} \gamma_j \geq 2 \) holds for all \( j \in \{1i, 2\} \). Now, using (4.24) and (4.25), we obtain
\[ |((1-q)DN_{1a,i}^K(\gamma_{1i} - \gamma_2) - \mu_2) - ((1-q)\tilde{n}_{1a}(\gamma_{1i} - \gamma_2) - \mu_2)| \leq D \varepsilon (|\gamma_{1i}| + |\gamma_2|). \]
Finally, since \( \tilde{\lambda} \gamma_j \geq 2 \) holds for all \( j \in \{1i, 2\} \), it follows that if \( \varepsilon > 0 \) is small enough, then as long as \( t \leq Q_{bc} \wedge T_{0}^2 \wedge T_{\varepsilon}^2 \), the inequality (4.23) is satisfied. This, together with the fact that \( J_2 \) and \( J_2^K(t) \) have the same first rows, implies (4.22), and hence the proof of Lemma 4.2 is concluded. \( \square \)

**Proof of Proposition 4.4** Now, similarly to the proof of Proposition [CCLLS21, Proposition 3.1], we consider our population process on the event
\[ A_{\varepsilon} := \{ T_{0}^2 \wedge U_{\varepsilon}^2 < Q_{bc} \} \]
for sufficiently small \( \varepsilon > 0 \), where we fix \( b \geq 2 \) corresponding to Lemma 4.2 for the rest of the proof. On this event, the invasion or extinction of the type 1i and 2 populations will happen before the rescaled type 1a population leaves a small neighbourhood of the equilibrium \( \hat{n}_{1a} \) of radius \( b \varepsilon \) or the rescaled type 1d population reaches size \( b \varepsilon \). On \( A_{\varepsilon} \) we couple the process \( (KN_{1i,t}^K, KN_{2i,t}^K) \) with two 2-type branching processes \( N_{\varepsilon,-}^z = ((N_{1i,t}^{\varepsilon,-}, N_{2i,t}^{\varepsilon,-}))_{t \geq 0} \) and \( N_{\varepsilon,+}^z = ((N_{1i,t}^{\varepsilon,+}, N_{2i,t}^{\varepsilon,+}))_{t \geq 0} \) (which also depend on \( K \), but we omit this from the notation for readability) such that almost surely, for any \( 0 \leq t < t_\varepsilon := T_{0}^2 \wedge T_{\varepsilon}^2 \wedge Q_{bc} \),
\[ N_{j,t}^{\varepsilon,-} \leq \hat{N}_j(t) \leq N_{j,t}^{\varepsilon,+}, \quad \forall j \in \{1i, 2\}, \]  
(4.26)
\[ N_{j,t}^{\varepsilon,-} \leq KN_{j,t}^{\varepsilon,+} \leq N_{j,t}^{\varepsilon,+}, \quad \forall j \in \{1i, 2\} \]  
(4.27)
where we again recall the approximating branching process \( (\hat{N}(t))_{t \geq 0} = ((\hat{N}_{1i,t}, \hat{N}_{1d,t}, \hat{N}_{2i,t}))_{t \geq 0} \) defined in Section 2.3, more precisely its two-dimensional projection \( ((\hat{N}_{1i,t}, \hat{N}_{2i,t}))_{t \geq 0} \). We claim that in order to satisfy (4.26) and (4.27), these processes can be defined as follows: \( N_{\varepsilon,-}^z \) having transition rates
- \( (y, z) \rightarrow (y+1, z-1) \) at rate \( (1-q)D(\hat{n}_{1a} - b \varepsilon)z \),
- \( (y, z) \rightarrow (y-1, z) \) at rate \( ry \),
- \( (y, z) \rightarrow (y-1, z+m) \) at rate \( vy \),
- \( (y, z) \rightarrow (y, z-1) \) at rate \( \mu_2 z + 2b \varepsilon (1-q)Dz \); and
\( N_{\varepsilon,+}^z \) having transition rates
- \( (y, z) \rightarrow (y+1, z-1) \) at rate \( (1-q)D(\hat{n}_{1a} - b \varepsilon)z \),
- \( (y, z) \rightarrow (y+1, z) \) at rate \( 2b \varepsilon (1-q)Dz \),
- \( (y, z) \rightarrow (y-1, z) \) at rate \( ry \),
- \( (y, z) \rightarrow (y-1, z+m) \) at rate \( vy \),
- \( (y, z) \rightarrow (y, z-1) \) at rate \( \mu_2 z \),
for \( y, z \in \mathbb{N}_0 \).

Let us now argue that this construction is suitable for the coupling (4.26) and (4.27). All the four processes involved in these two chains of inequalities have the same rates for reproduction, death by lysis, and death of viruses. The only difference is the infection mechanism in case of successful virus attacks. Indeed, for all the four processes involved, starting from a state \( (y, z) \in \mathbb{N}_0^2 \) at rate at least \( (1-q)D(\hat{n}_{1a} - b \varepsilon)z \) a successful virus attack happens. However, at additional rate \( 2b \varepsilon (1-q)Dz \), for the two coupled branching processes different events occur: \( N_{\varepsilon,-}^z \) has additional death of viruses without infecting any active individual, whereas \( N_{\varepsilon,+}^z \) has additional successful virus attacks where the involved virus does not even die. At the same time, for the approximating branching process \( ((\hat{N}_{1i,t}, \hat{N}_{2i,t}(t)))_{t \geq 0} \), at additional rate \( b \varepsilon (1-q)Dz \), successful virus attacks happen. These are less beneficial for types 1i and 2 than the additional events of \( N_{\varepsilon,+}^z \), since each successful virus attack kills a virus, and the total rate of virus attacks is reduced. Hence the second inequality in (4.26). On the other hand, any
of these additional virus attacks of \((\tilde{N}_{1,t}, \tilde{N}_{2}(t))\) is better for the type 1 and 2 population than the additional virus deaths of \(N_{1}^{ε,-}\), and even no event at all is better than those virus deaths, which implies the first inequality in (4.26). As for our original population process, on the event \(A_{ε}\), on the time interval \([0, T_{ε}^{2} \wedge T_{ε}^{2} \wedge Q_{ε}]\), starting from \((y, z)\), \((N_{11,t}, N_{21,t}^{K})\) has successful virus attacks at rate between \((1 - q)D(\tilde{n}_{1a} - bε)z\) and \((1 - q)D(\tilde{n}_{1a} + bε)z\). Hence, in (4.27), the second inequality follows analogously to the one of (4.26). Recalling that an additional successful virus attack or an event where nothing happens is better for types 1 and 2 than a virus death (without virus attack), also the first inequality of (4.27) follows.

For \(\diamond \in \{+, -\}\), let \(s_{2}^{(ε,\diamond)}\) denote the extinction probability of the process \(N_{t}^{ε,\diamond}\) started from \(N_{0}^{ε,\diamond} = (0, 1)\). The extinction probability of a 2-type branching process having the same kind of transitions as \((\tilde{N}_{1}(t), \tilde{N}_{2}(t))\) \(t \geq 0\) is continuous with respect to the rates of virus-induced dormancy, death of dormant individuals, resuscitation of dormant individuals, infection, recovery, lysis, and death of viruses, further, if additionally there are \((y, z) \rightarrow (y + 1, z)\) (i.e. ‘infection without death of the involved virus’) type transitions, then the extinction probability is also continuous with respect to the rate of these. These assertions can be proven analogously to [CCILS21, Section A.3].

Hence, it follows from (4.26) that for fixed \(ε > 0\),

\[
s_{2}^{(ε,+)} \leq s_{2} \leq s_{2}^{(ε,-)}
\]

and for \(\diamond \in \{+, -\}\),

\[
0 \leq \liminf_{ε \downarrow 0} |s_{2}^{(ε,\diamond)} - s_{2}| \leq \limsup_{ε \downarrow 0} |s_{2}^{(ε,\diamond)} - s_{2}| \leq \limsup_{ε \downarrow 0} |s_{2}^{(ε,-)} - s_{2}^{(ε,+)}| = 0,
\]

where we recall the extinction probability \(s_{2}\) of the approximating branching process \((N_{1}(t), N_{2}(t))_{t \geq 0}\) started from \((0, 1)\) (equivalently, the one of \((\tilde{N}(t))_{t \geq 0}\) started from \((0, 0, 1)\), see (2.10)).

Next, we show that the probabilities of extinction and invasion of the infected and virus coordinates \((N_{11,t}, N_{21,t}^{K})\) of the original population process \((N_{11,t}^{K}, 0, 0, 1/K)\) also converge to \(s_{2}\) and \(1 - s_{2}\), respectively, with high probability as \(K \rightarrow \infty\). We define the stopping times, for \(\diamond \in \{+, -\}\),

\[
T_{2}^{(ε,\diamond),2} := \inf\{t > 0 : N_{11,t}^{(ε,\diamond)} + N_{21,t}^{(ε,\diamond)} = [Kx]\}, \quad x \geq 0.
\]

Using the coupling in (4.27), which is valid on \(A_{ε}\), we have

\[
\mathbb{P}(T_{2}^{(ε,-),2} \leq T_{0}^{(ε,-),2}, A_{ε}) \leq \mathbb{P}(T_{2}^{(ε,-)} \leq T_{0}^{(ε,-)}, A_{ε}) \leq \mathbb{P}(T_{2}^{(ε,+)} \leq T_{0}^{(ε,+),2}, A_{ε}).
\]

Indeed, if a process reaches the size \(Kε\) before dying out, then the same holds for a larger process as well. However, \(A_{ε}\) is independent of \((N_{11,t}, N_{21,t}^{K})\) \(t \geq 0\) both for \(\diamond = +\) and for \(\diamond = -\), and thus

\[
\liminf_{K \rightarrow \infty} \mathbb{P}(T_{2}^{(ε,-),2} \leq T_{0}^{(ε,-),2}, A_{ε}) = \liminf_{K \rightarrow \infty} \mathbb{P}(A_{ε})\mathbb{P}(T_{2}^{(ε,-),2} \leq T_{0}^{(ε,-),2}) \geq (1 - s_{2}^{(ε,-)})(1 - o_{ε}(1))
\]

(4.30) and

\[
\limsup_{K \rightarrow \infty} \mathbb{P}(T_{2}^{(ε,+),2} \leq T_{0}^{(ε,+),2}, A_{ε}) = \limsup_{K \rightarrow \infty} \mathbb{P}(A_{ε})\mathbb{P}(T_{2}^{(ε,+),2} \leq T_{0}^{(ε,+),2}) \leq (1 - s_{2}^{(ε,+)})(1 + o_{ε}(1)).
\]

(4.31)

Letting \(K \rightarrow \infty\) in (4.29) and applying (4.30) and (4.31) yields that

\[
(1 - q_{2}^{(ε,-)})(1 - o_{ε}(1)) \leq \liminf_{K \rightarrow \infty} \mathbb{P}(T_{2}^{(ε,-),2} \leq T_{0}^{(ε,-),2}, A_{ε}) \leq \limsup_{K \rightarrow \infty} \mathbb{P}(T_{2}^{(ε,+),2} \leq T_{0}^{(ε,+),2}, A_{ε}) \leq (1 - q_{2}^{(ε,+)})(1 + o_{ε}(1)).
\]

Hence,

\[
\limsup_{K \rightarrow \infty} |\mathbb{P}(T_{2}^{2} \leq T_{0}^{2}, A_{ε}) - (1 - q_{2})| = o_{ε}(1),
\]

as required. The equation (4.13) can be derived similarly.
Finally, we show that in the case when the epidemic becomes macroscopic (which happens with probability tending to $1 - s_2$), the time before the mutant population reaches size $K \varepsilon$ is of order $\log K / \lambda$, where we recall the largest eigenvalue $\lambda$ of the mean matrix $J_2$, which was defined in (2.9).

Having (4.13), we can without loss of generality assume that $s_2 < 1$, which is equivalent to the condition (2.2) and the one $\tilde{\lambda} > 0$.

For $\diamond \in \{+,-\}$, let $\tilde{\lambda}(\epsilon,\diamond)$ denote the largest eigenvalue of the mean matrix corresponding to the branching process $N_2^{\epsilon,\diamond}$. Since $s_2 < 1$, this eigenvalue is positive for all sufficiently small $\varepsilon > 0$ and converges to $\lambda$ as $\varepsilon \downarrow 0$. In other words, there exists a nonnegative function $f: (0, \infty) \to (0, \infty)$ with $\lim_{\varepsilon \downarrow 0} f(\varepsilon) = 0$ such that for any $\varepsilon > 0$ small enough,

$$\left| \frac{\tilde{\lambda}(\varepsilon,\diamond)}{\lambda} - 1 \right| \leq \frac{f(\varepsilon)}{2}. \quad (4.32)$$

Let us fix $\varepsilon$ small enough such that (4.32) holds. Then from the coupling (4.27) we deduce that

$$\mathbb{P}\left( T_\varepsilon^{(\varepsilon,-),2} \leq T_0^{(\varepsilon,-),2} \land \frac{\log K}{\lambda} (1 + f(\varepsilon)), A_\varepsilon \right) \leq \mathbb{P}\left( T_\varepsilon^{2} \leq T_0^{2} \land \frac{\log K}{\lambda} (1 + f(\varepsilon)), A_\varepsilon \right).$$

Using this together with the independence between $A_\varepsilon$ and $(N_2^{\varepsilon,\diamond})_{t \geq 0}$ and employing [AN72, Section 7.5], we obtain for $\varepsilon > 0$ small enough (in particular such that $f(\varepsilon) < 1$)

$$\lim_{K \to \infty} \inf \mathbb{P}\left( T_\varepsilon^{(\varepsilon,-),2} \leq T_0^{(\varepsilon,-),2} \land \frac{\log K}{\lambda} (1 + f(\varepsilon)), A_\varepsilon \right) \geq \lim_{K \to \infty} \inf \mathbb{P}\left( T_\varepsilon^{(\varepsilon,-),2} \leq \frac{\log K}{\lambda} (1 + f(\varepsilon)) \right) \mathbb{P}(A_\varepsilon)$$

$$\geq \lim_{K \to \infty} \inf \mathbb{P}\left( T_\varepsilon^{(\varepsilon,-),2} \leq \frac{\log K}{\lambda(\varepsilon,-)} (1 - f(\varepsilon) / 2)(1 + f(\varepsilon)) \right) \mathbb{P}(A_\varepsilon)$$

$$\geq \lim_{K \to \infty} \inf \mathbb{P}\left( T_\varepsilon^{(\varepsilon,-),2} \leq \frac{\log K}{\lambda(\varepsilon,-)} \right) \mathbb{P}(A_\varepsilon) \geq (1 - q_2^{(\varepsilon,-)}(1 - o_\varepsilon(1))). \quad (4.33)$$

Similarly, using the coupling (4.27), we derive that for all sufficiently small $\varepsilon > 0$

$$\mathbb{P}\left( T_\varepsilon^{(\varepsilon,+),2} \leq T_0^{(\varepsilon,+),2} \land \frac{\log K}{\lambda} (1 - f(\varepsilon)), A_\varepsilon \right) \geq \mathbb{P}\left( T_\varepsilon^{2} \leq T_0^{2} \land \frac{\log K}{\lambda} (1 - f(\varepsilon)), A_\varepsilon \right),$$

and arguments analogous to the ones used in (4.33) imply that

$$\lim_{K \to \infty} \inf \mathbb{P}\left( T_\varepsilon^{(\varepsilon,+),2} \leq T_0^{(\varepsilon,+),2}, T_\varepsilon^{2} \geq \frac{\log K}{\lambda} (1 - f(\varepsilon)), A_\varepsilon \right) \geq (1 - q_2^{(\varepsilon,+)}(1 - o_\varepsilon(1))).$$

These together imply (4.12), which concludes the proof of the proposition.

4.4. Proof of Theorems 2.9, 2.10 and 2.11. Putting together Propositions 4.1 and 2.4 and Corollary 2.5, we now prove our main results, employing some arguments from [CCLLS21, Section 3.4], somewhat similarly to the case of stable coexistence in [BT21, Section 6.4]. The differences from these proofs stem from the fact that in the model of the present paper there is no case where the formerly resident type (here type 1a) goes extinct, and that we cannot verify a convergence of the dynamical system to the convergence equilibrium. Recall from Proposition 3.3 that in some cases, such a convergence cannot hold for large $m$, due to a Hopf bifurcation.

Our proof strongly relies on the coupling (4.26)-(4.27). To be more precise, we define a Bernoulli random variable $B$ as the indicator of nonextinction

$$B := \mathbb{1}\{\forall t > 0, \hat{N}_{1,t} + \hat{N}_{2,t} > 0\}$$

of the two-type approximating branching process $((\hat{N}_{1,t}, \hat{N}_{2,t}))_{t \geq 0}$ defined Section 2.3, which is initially coupled between the same two branching processes $N_{1,-}$ and $N_{2,+}$ as $((K N_{1,t}, N_{2,t}))_{t \geq 0}$, according to (4.26). Let $f$ be a function such that Proposition 4.1 holds for $f/3$ (and hence also for
Throughout the rest of the proof, we will assume that $\varepsilon > 0$ is so small that $f(\varepsilon) < 1$, further, we fix $b \geq 2$ such that Proposition 4.1 holds for $b$.

Our goal is to show that

$$\liminf_{K \to \infty} \mathcal{E}(K, \varepsilon) \geq s_2 - o_\varepsilon(1) \tag{4.34}$$

holds for

$$\mathcal{E}(K, \varepsilon) := \mathbb{P}\left(\frac{T_0^2}{\log K} \leq f(\varepsilon), T_0^2 < T_{S_\beta}, B = 0\right),$$

where we recall the stopping times $T_0^2$ and $T_{S_\beta}$ from Section 2.5. Further, we want to show that in case $s_2 < 1$,

$$\liminf_{K \to \infty} \mathcal{I}(K, \varepsilon) \geq 1 - s_2 - o_\varepsilon(1), \tag{4.35}$$

where we define

$$\mathcal{I}(K, \varepsilon) := \mathbb{P}\left(\frac{T_{S_\beta} \wedge T_0^2}{\log K} - \frac{1}{\lambda} \leq f(\varepsilon), T_{S_\beta} < T_0^2, B = 1\right).$$

Throughout the proof, $\beta > 0$ is to be understood as sufficiently small; later we will explain what conditions precisely it has to satisfy.

The assertions (4.34) and (4.35) together will imply Theorem 2.9, Theorem 2.10, and Equation (2.19) in Theorem 2.11. The other assertion of Theorem 2.11, Equation (2.20), follows already from (4.13).

Let us start with the case of extinction of the epidemic in the first phase of the invasion and verify (4.34). Clearly, we have

$$\mathcal{E}(K, \varepsilon) \geq \mathbb{P}\left(\frac{T_0^2}{\log K} \leq f(\varepsilon), T_0^2 < T_{S_\beta}^2, B = 0, T_0^2 > T_{S_\beta}^2 \wedge Q_{be}\right),$$

where we recall the stopping times $T_0^2$ and $T_{S_\beta}^2$ from Section 4.3. Now, considering our initial conditions, one can choose $\beta > 0$ sufficiently small such that for all sufficiently small $\varepsilon > 0$ we have

$$T_{S_\beta}^2 \wedge T_{be} < T_{S_\beta},$$

almost surely. We assume further on during the whole section that $\beta$ satisfies this condition. Then,

$$\mathcal{E}(K, \varepsilon) \geq \mathbb{P}\left(\frac{T_0^2}{\log K} \leq f(\varepsilon), B = 0, T_0^2 < T_{S_\beta}^2 \wedge Q_{be}\right). \tag{4.36}$$

Moreover, similarly to the proof of Proposition 4.1, we obtain

$$\limsup_{K \to \infty} \mathbb{P}\left\{\{B = 0\} \Delta \{T_0^2 < T_{S_\beta}^2 \wedge Q_{be}\}\right\} = o_\varepsilon(1), \tag{4.37}$$

where $\Delta$ denotes symmetric difference, and

$$\limsup_{K \to \infty} \mathbb{P}\left\{\{B = 0\} \Delta \{T_0^{(e,2)} \wedge Q_{be}\}\right\} = o_\varepsilon(1).$$

Together with (4.36) and the coupling (4.26)–(4.27), it follows that

$$\liminf_{K \to \infty} \mathcal{E}(K, \varepsilon) \geq \liminf_{K \to \infty} \mathbb{P}\left(\frac{T_0^2}{\log K} \leq f(\varepsilon), B = 0, T_0^2 \leq T_{S_\beta}^2 \wedge Q_{be}\right) \geq \liminf_{K \to \infty} \mathbb{P}\left(\frac{T_0^{(e,2)}}{\log K} \leq f(\varepsilon), B = 0, T_0^{(e,2)} \leq T_{S_\beta}^2 \wedge Q_{be}\right) \geq \liminf_{K \to \infty} \mathbb{P}\left(\frac{T_0^{(e,2)}}{\log K} \leq f(\varepsilon), T_0^{(e,2)} < \infty\right) + o_\varepsilon(1), \tag{4.38}$$

Thus, employing (4.28), we obtain (4.34), which implies (2.19).
Let us continue with the case of persistence of the epidemic and verify (4.35). Let us fix a constant $b \geq 2$ satisfying the condition of Lemma 3.2. Arguing analogously to (4.37), we get

$$\limsup_{K \to \infty} \mathbb{P}\left( \{ B = 1 \} \Delta \{ T^2_\varepsilon < T^2_0 \land Q_{be} \} \right) = o_\varepsilon(1).$$

Thus,

$$\liminf_{K \to \infty} I(K, \varepsilon) = \liminf_{K \to \infty} \mathbb{P}\left( \left| \frac{T_{S_\beta}}{\log K} - \frac{1}{\lambda} \right| \leq f(\varepsilon), T_{S_\beta} < T^2_0, T^2_\varepsilon < T^2_0 \land Q_{be} \right) + o_\varepsilon(1).$$

Now, (4.39) implies that

$$\liminf_{K \to \infty} I(K, \varepsilon) \geq \mathbb{P}\left( \left| \frac{T_{S_\beta}}{\log K} - \frac{1}{\lambda} \right| \leq f(\varepsilon), T^2_\varepsilon < T^2_0 \land Q_{be}, T_{S_\beta} < T^2_0 \right) + o_\varepsilon(1)$$

$$\geq \mathbb{P}\left( \left| \frac{T^2_\varepsilon}{\log K} - \frac{1}{\lambda} \right| \leq \frac{f(\varepsilon)}{3}, \frac{T^2_{S_\beta} - T^2_\varepsilon}{\log K} \leq \frac{f(\varepsilon)}{3}, T^2_\varepsilon < T^2_0 \land Q_{be}, T_{S_\beta} < T^2_0 \right) + o_\varepsilon(1),$$

Note that for $\beta > 0$ sufficiently small and $\varepsilon > 0$ sufficiently small chosen accordingly, $Q_{be} \leq T_{S_\beta}$ almost surely. We assume during the rest of the proof that $\beta$ satisfies this condition. Hence, defining

$$M_\varepsilon = \{ (n^0_{1a}, n^0_{1d}, n^0_{i1}, n^0_{i2}) \in [0, \infty)^4 : |n^0_{1a} - \bar{n}_{1a}| \leq \varepsilon, |n^0_{1d}| \leq b_\varepsilon, n^0_{i1} + n^0_{i2} = \varepsilon \}$$

and for $K > 0$

$$M_\varepsilon(K) = \{ (n^0_{1a}, n^0_{1d}, n^0_{i1}, n^0_{i2}) \in [0, \infty)^4 : |n^0_{1a} - \bar{n}_{1a}| \leq \varepsilon, |n^0_{1d}| \leq b_\varepsilon, n^0_{i1} + n^0_{i2} = \frac{|\lambda K|}{\lambda} \},$$

the strong Markov property applied at time $T^2_\varepsilon$ implies

$$\liminf_{K \to \infty} I(K, \varepsilon) \geq \liminf_{K \to \infty} \mathbb{P}\left( \left| \frac{T^2_\varepsilon}{\log K} - \frac{1}{\lambda} \right| \leq \frac{f(\varepsilon)}{3}, T^2_\varepsilon < T^2_0 \land Q_{be} \right)$$

$$\times \inf_{(n^0_{1a}, n^0_{1d}, n^0_{i1}, n^0_{i2}) \in M_\varepsilon(K)} \mathbb{P}\left( \frac{T^2_{S_\beta} - T^2_\varepsilon}{\log K} \leq \frac{f(\varepsilon)}{3}, T^2_{S_\beta} > T^2_0 \middle| N^K_0 = (n^0_{1a}, n^0_{1d}, n^0_{i1}, n^0_{i2}) \right).$$

(4.40)

It remains to show that the right-hand side of (4.40) is close to $1 - s_2$ as $K \to \infty$ if $\varepsilon$ is small. The fact the times inferior of the first factor on the right-hand side of (4.40) is at least $1 - s_2 + o_\varepsilon(1)$ follows analogously to (4.39) (since Proposition 4.1 holds not only for $f$ but also for $f/3$).

Now, let us treat the second, nearly deterministic phase of the epidemic. For $m = (m_{1a}, m_{1d}, m_{i1}, m_{i2}) \in [0, \infty)^4$, let $n(m) = (n^m_{1a}(t), n^m_{1d}(t), n^m_{i1}(t), n^m_{i2}(t))$ denote the unique solution of the dynamical system (2.1) with initial condition $m$. Note that for any $\varepsilon > 0$, for any initial condition $n^0$ contained in $M_\varepsilon$ or in $M_\varepsilon(K)$ in some $K > 0$, for any $t > 0$, $n^m(t)$ is a suitable initial condition for Proposition 2.4 and Corollary 2.5. Indeed, starting from a coordinatewise nonnegative initial condition with nonzero active coordinate and nonzero sum of infected and virus coordinate, for all positive times, all coordinates of the solution of (2.1) will be positive. Then, thanks to Corollary 2.5 and the continuity of flows of the dynamical system with respect to the initial condition, we deduce that if $\beta, \varepsilon > 0$ are small enough and $K_0 > 0$ is large enough, then there exists $t_{\beta, \varepsilon} > 0$ such that for all $n^0 \in M_\varepsilon \cup (\bigcup_{K \geq K_0} M_\varepsilon(K))$ there exists $t \leq t_{\beta, \varepsilon}$ satisfying

$$n^0_{1a}(t), n^0_{1d}(t) > \beta, n^0_{i1}(t) \in (\beta, \bar{n}_{1a} - \beta), \text{ and } n^0_{i2}(t) \in (\beta, \frac{m \bar{n}_{1a}}{\mu_2} - \beta),$$

in other words, $n^0(t) \in S^\varepsilon_\beta$, where for $A \subseteq \mathbb{R}^4$, $A^\circ$ denotes the interior of the set $A$. We assume for the rest of the proof that $\beta, \varepsilon, K$ satisfy this assumption.

Now, using [EKS86] Theorem 2.1, p. 456 and the strong Markov property, we conclude that if $\varepsilon, \beta$ are sufficiently small, then the following holds:

$$\lim_{K \to \infty} \mathbb{P}\left( T_{S_\beta} - T^2_\varepsilon \leq t_{\beta, \varepsilon} \right) = \lim_{K \to \infty} \mathbb{P}\left( T_{S_\beta} \leq t_{\beta, \varepsilon} \middle| N^K_0 \in M_\varepsilon(K) \right) = 1 - o_\varepsilon(1).$$
Thus, the second term on the right-hand side of (4.40) is close to 1 when $K$ tends to $\infty$, $\beta$ is small, and $\varepsilon > 0$ is small enough chosen according to $\beta$. Hence, together with the fact that the first factor on the right-hand side of (4.40) is asymptotically at least $1 - s_2 - o_\varepsilon(1)$, we have obtained

$$\liminf_{K \to \infty} \mathcal{I}(K, \varepsilon) \geq 1 - s_2 - o_\varepsilon(1),$$

which implies (2.18) and (2.17).

**APPENDIX A. PROOF OF PROPOSITIONS 3.3 AND 3.5**

In the following, we carry out the proof of Proposition 3.4.

**Proof of Proposition 3.4** Let us first start with the three-dimensional case, i.e. let us put $q = 0$, consider the dynamical system (3.1) and show that for $r > v$, $(n_{1a}, n_{1i}, n_2)$ is asymptotically stable for all sufficiently small $m > m^*$. From this, one can derive the assertion of the proposition regarding the four-dimensional system (2.1) for small $q$ and large $r$ using continuity, analogously to the proof of Proposition 3.3 (where we considered the case of small $q$ and small $r$).

Let $q = 0$ and $r > v$. Now for fixed $m$, we consider the Jacobi matrix $A_m(n_{1a}, n_{1i}, n_2)$ corresponding to (3.1) at the coexistence equilibrium, which defined analogously to $A(n_{1a}, n_{1d}, n_{1i}, n_2)$ but with $q = 0$ (where the coexistence equilibrium corresponds to the same $m$ as the Jacobi matrix), ignoring the dormant coordinate:

$$A_m(n_{1a}, n_{1i}, n_2) = \begin{pmatrix} \lambda_1 - \mu_1 - 2Cn_{1a} - Cn_{1i} - Dn_2 & r - Cn_{1a} & -Dn_{1a} \\ Dn_2 & -(r + v) & Dn_{1a} \\ -Dn_2 & mv & -Dn_{1a} - \mu_2 \end{pmatrix}.$$ 

Note that several entries of this matrix depend on $m$, but we ignore this in the notation for simplicity. We want to analyse the stability of $(n_{1a}, n_{1i}, n_2)$ for large $m$ using the Routh–Hurwitz criterion (see e.g. [BK98 Section 3]). We write the characteristic equation of $A_m(n_{1a}, n_{1i}, n_2)$ as

$$\lambda^3 + a_1(m)\lambda^2 + a_2(m)\lambda + a_3(m) = 0.$$ 

Then, we have that $a_1(m) = -\text{Tr} \ A_m(n_{1a}, n_{1i}, n_2)$, $a_2(m)$ is the factor of $-\lambda$ in the characteristic polynomial when writing it as $\det(A_m(n_{1a}, n_{1i}, n_2) - \lambda I)$, and $a_3(m) = -\det A_m(n_{1a}, n_{1i}, n_2)$, where $I$ is the $3 \times 3$ identity matrix. Then all eigenvalues of $A_m(n_{1a}, n_{1i}, n_2)$ have a strictly negative real part if and only if $a_1(m) > 0$, $a_1(m) a_2(m) > a_3(m)$, and $a_3(m) > 0$. Further, if $a_1(m) > 0$, $a_3(m) > 0$, and $a_1(m) a_2(m) < a_3(m)$, then the matrix is strictly unstable: since its determinant and trace are negative, its eigenvalue with the largest absolute value is negative, but the other two eigenvalues have strictly positive real parts (of course, these eigenvalues are either both real or complex conjugate).

Note that according to (2.3) (for $q = 0$), we have $\lim_{m \to \infty} n_{1a} = 0$. For $m > m^*$, the right-hand side of the first equation of (3.1) equal to zero, and dividing it with $n_{1a} > 0$ we obtain

$$\lambda_1 - \mu_1 - C(n_{1a} + n_{1i}) - Dn_2 = \frac{r}{r + v} Dn_2.$$ 

Hence, it follows that

$$\lim_{m \to \infty} \lambda_1 - \mu_1 - Cn_{1i} - \frac{v}{r + v} Dn_2 = 0,$$

and thus in particular

$$\limsup_{m \to \infty} n_2 \leq \frac{\lambda_1 - \mu_1 r + v}{D} \frac{1}{v}.$$ 

In particular, $n_2$ is bounded as a function of $m$. Hence, from (4.3) we conclude that $\lim_{m \to \infty} n_{1i} = 0$ and thus

$$\lim_{m \to \infty} n_2 = \frac{\lambda_1 - \mu_1 r + v}{D} \frac{1}{v}.$$ 


Hence, we obtain
\[
\lim_{m \to \infty} a_1(m) = \lim_{m \to \infty} -(\lambda_1 - \mu_1 - Dn_2) + r + v + \mu_2 = (\lambda_1 - \mu_1)\frac{r}{v} + (r + v) + \mu_2 > 0,
\]
further,
\[
\lim_{m \to \infty} a_2(m) = \lim_{m \to \infty} -(\lambda_1 - \mu_1 - Dn_2)(r + v) - Dn_2r + (\lambda_1 - \mu_1)\frac{r}{v} \mu_2 + \mu_2(r + v) - Dn_1a mv = (\lambda_1 - \mu_1)\frac{r}{v} \mu_2,
\]
and
\[
\lim_{m \to \infty} a_3(m) = - \lim_{m \to \infty} (\lambda_1 - \mu_1 - Dn_2)(r + v)\mu_2 - Dn_2n_1a mv - (\lambda_1 - \mu_1 - Dn_2)mv Dn_1a + Dn_2r \mu_2
\]
for \( \lambda_1 > \mu_1 \). Therefore, for \( r > v \) we obtain that
\[
\liminf_{m \to \infty} a_1(m)a_2(m) - a_3(m) > ((\lambda_1 - \mu_1) + (r + v) + \mu_2)((\lambda_1 - \mu_1)\mu_2) - (\lambda_1 - \mu_1)(r + v)\mu_2
\]
\[
> (r + v)(\lambda_1 - \mu_1)\mu_2 - (\lambda_1 - \mu_1)(r + v)\mu_2 = 0.
\]
Thus, for \( r > v \), for all \( m > m^* \) sufficiently large, \((n_{1a}, n_{1l}, n_2)\) is asymptotically stable, as claimed. \( \square \)

Next, we prove Proposition 3.5.

**Proof of Proposition 3.5.** In order to verify the proposition, we have to show that for \( m > m^* \) sufficiently close to \( m \), all eigenvalues of \( A(n_{1a}, n_{1d}, n_{1l}, n_2) \) have a strictly negative real part. To this aim, let us first study the extreme case when \( m = m^* \), in other words, \((\bar{n}_{1a},0,0,0) = (n_{1a}, n_{1d}, n_{1l}, n_2)\). Then, the Jacobi matrix \( A(n_{1a}, n_{1d}, n_{1l}, n_2) = A(\bar{n}_{1a}, 0, 0, 0) \) is given according to (4.7). Again, \((\lambda_1 - \mu)\) is a strictly negative eigenvalue of this matrix thanks to our assumptions. Using Laplace’s expansion theorem, it follows that the remaining three eigenvalues of the matrix are \( -\kappa \mu_1 - \sigma < 0 \) and the two eigenvalues of the last \( 2 \times 2 \) block of the matrix. This block has a zero eigenvalue because \( m = m^* \) is equivalent to the assertion that (2.2) holds with an equality instead of ‘>’, in other words, the determinant of the \( 2 \times 2 \) block is zero. However, even in this case, the trace of the \( 2 \times 2 \) block is negative, and hence 0 is only a single eigenvalue of the block and hence also of the Jacobi matrix. The other eigenvalue equals the trace \(-(r + v) - (1 - q)D\bar{n}_{1a} - \mu_2 \) of the block, and hence all eigenvalues are real.

Now, in the limit \( m \downarrow m^* \) the trace of the Jacobi matrix \( A(n_{1a}, n_{1d}, n_{1l}, n_2) \) remains negative and bounded away from zero, and the determinant tends to zero from above (since \( n_2 \) tends to 0 and \( n_{1a} \) to \( \bar{n}_{1a} \); cf. (4.5)) by continuity. In this limit, each eigenvalue of \( A(n_{1a}, n_{1d}, n_{1l}, n_2) \) converges to the corresponding one of \( A(\bar{n}_{1a}, 0, 0, 0) \) corresponding to \( m = m^* \). In particular, precisely one eigenvalue tends to 0, and hence this eigenvalue must be real. Hence, one eigenvalue tends to zero and three remain bounded away from zero, while the imaginary part of any of the eigenvalues has to tend to zero. This implies that for \( m > m^* \) sufficiently close to \( m^* \), there can be at most one eigenvalue with positive real part, namely the real one that converges to zero. But if there was precisely one such eigenvalue, this would contradict the assertion of the lemma that for all \( m > m^* \), there are either 2 or 4 eigenvalues with positive real parts. Hence, we conclude that for all \( m > m^* \) sufficiently small, all eigenvalues of \( A(n_{1a}, n_{1d}, n_{1l}, n_2) \) have negative real parts. \( \square \)

**Appendix B. Code**

(* Wolfram Mathematica® code.
Save the content of this section in .nb format and open it in Mathematica.*)

(* Kesten-Stigum left eigenvector for given parameters \( q, r, m, v \).
Its dormant coordinate is 0 for \( q=0 \). *)
KestenStigumEV[q_, r_, m_, v_] := Eigenvectors[{-3, 0, q*0.5}, {0, -r - v, (1 - q)*0.5}, {0, m*v, -(1 - q)*0.5}][[3]]*(-1)

(* Numerical solution of our 4-dimensional system of ODEs, started from equilibrium for type 1a and in a small number (here 0.1) times the Kesten-Stigum left eigenvector for the dormant, infected, and virus coordinates. Variable parameters: $q,r,m,v$, and the time horizon $t_{\text{max}}$ written as $t_{\text{max}}$ here.
$\lambda_1$ is fixed as 5, $\mu_1$ as 4, $C$ as 1, $D$ as 0.5, $\kappa$ as 1, $\sigma$ as 2, and $\mu_2$ as 0.3.
For the dormancy-free 3-dimensional system of ODEs put $q=0$ and do not plot the dormant coordinate. *)

a[q_, r_, m_, v_, tmax_]:= NDSolve[{n1a'[t] == n1a[t]*(5 - 4 - (n1a[t] + n1d[t] + n1i[t]) - 0.5*n2[t]) + r*n1i[t] + 2*n1d[t],
n1d'[t] == 0.5*q*n1a[t]*n2[t] - 3*n1d[t],
n1i'[t] == 0.5*(1 - q)*n1a[t]*n2[t] - (r + v)*n1i[t],
n2'[t] == -0.5*(1 - q)*n1a[t]*n2[t] - 0.3*n2[t] + m*v*n1i[t],
n1a[0] == 1, n1d[0] == KestenStigumEV[q, r, m, v][[1]]*0.1,
n1i[0] == KestenStigumEV[q, r, m, v][[2]]*0.1,
n2[0] == KestenStigumEV[q, r, m, v][[3]]*0.1}, {n1a, n1d, n1i, n2}, {t, 0, tmax}],
PlotRange -> All, PlotLegends -> {n1a[t], n1d[t], n1i[t], n2[t]},
PlotStyle -> {ColorData[97, "ColorList"][[1]],
ColorData[97, "ColorList"][[2]], ColorData[97, "ColorList"][[3]]}

Acknowledgements. The authors thank F. Gillich for interesting comments that inspired Section 2.6.3. JB was supported by DFG Priority Programme 1590 “Probabilistic Structures in Evolution” and Berlin Mathematics Research Center MATH+.

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