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Maia Martcheva · Horst R. Thieme

Progression age enhanced backward bifurcation in an epidemic model with super-infection

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Abstract. We consider a model for a disease with a progressing and a quiescent exposed class and variable susceptibility to super-infection. The model exhibits backward bifurcations under certain conditions, which allow for both stable and unstable endemic states when the basic reproduction number is smaller than one.

1. Introduction and discussion

Conceivably, an infected individual is subject to further contacts with infectious individuals. It depends on the type of the disease whether, in a mathematical model, these can be ignored or whether so-called *super-infection* should be included.

Super-infection in micro- and macro-parasitic diseases
Super-infection is the concurrent or subsequent multiple infection of a host with the same parasite, may it be with identical or different strains. Super-infection does not play a significant role in the class of micro-parasitic infectious diseases known as childhood diseases like measles, chicken pox, rubella etc. where the primary infection progresses very fast (in a time scale of days or weeks) and renders long-lasting immunity so that subsequent infections are either unsuccessful or hardly make a difference. The significance of multiple infections has long been recog-

M. Martcheva: Department of Mathematics, Polytechnic University, Brooklyn, NY 11201, USA. e-mail: mayam@duke.poly.edu

Present address: Department of Biological Statistics and Computational Biology, 434 Warren Hall, Cornell University, Ithaca, NY 14853-7801
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Horst R. Thieme: Department of Mathematics, Arizona State University, Tempe, AZ, 85287-1804, USA. e-mail: h.thieme@asu.edu
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nized in another class of micro-parasitic, namely plasmodial, diseases, in particular in malaria, among other things for sustaining immunity. (See [1], Section 14.4.3 et seq., and [16] for discussions and references.) Super-infection, typically by a different strain, may play an important role in the recurrence of influenza outbreaks [2]. Multiple infections are so common in macro-parasitic diseases that it may be more appropriate to speak about a constant invasion of the host by the (often helminthic) parasites, either directly or transmitted by vectors. It is in schistosomiasis that super-infection has first been linked to the occurrence of multiple endemic equilibria, and concepts like *breakpoint density* and *transmission threshold* have been formulated. Here the multiplicity of endemic equilibria is due to the pairing of male and female worms in the human host and is actually the variant of an *Allee* effect observed in other ecological scenarios (See [1], Section 16.24, for further information and references). An Allee type (or depensating [13]) relation between parasite acquisition and average parasite load can also lead to multiple endemic equilibria [24].

Super-infection conceivably is also important for slowly progressing micro-parasitic diseases like the viral diseases HIV and hepatitis A,B &C and the bacterial diseases cholera, typhoid and tuberculosis. Super-infection manifests itself in Hepatitis A by shortening the latency period (dose-dependent latent period [36,37]). Apart from having an initial phase in which the infectious agent develops rapidly in the human host, the scenarios of progression seem to be somewhat different in these diseases. In HIV the fast initial phase appears to be followed by a long phase with low virus titers which is eventually followed in many or most cases by AIDS ([1], Section 11.3). Hepatitis B &C, cholera and typhoid display a division of the infected individuals into one part that develop symptoms and recover and another that become asymptomatic active carriers of the disease, often for many years ([1], Section 10.3). Something similar happens in tuberculosis except that the asymptomatically infected individuals (approximately 90 % of the infected individuals) are passive carriers for a long time until, possibly, their infectivity is activated. In HIV, super-infection can perhaps speed up the progression to AIDS, while in tuberculosis it could play a part in activating passive carriers. While the first is hypothetical at this point, it is subject to debate to what extent the second happens; super-infection (in this context also called exogenous reinfection) seems to be well-documented for immuno-suppressed individuals; in immuno-competent people the primary infection appears to protect against secondary infections (see [19] for references and discussion). Other factors in reactivation are malnutrition or an otherwise caused weakening of the immune system.

While even today, tuberculosis remains a prominent killer among the infectious diseases with an estimated 3 million deaths per year, there has only been a limited use of mathematical models in its study. After some early modeling efforts (see [4], Section 16.2, for some discussion and references, and [19] for further references), the interest has been renewed by the interference of tuberculosis and AIDS and the development of antibiotic resistance [5–10,19–21,39,40]. Only [19] addresses the possible role of super-infection, in particular in leading to multiple endemic equilibria which occur when the *basic replacement ratio* (*reproduction number*), $\mathcal{R}_0$, is still smaller than one.

Multiple endemic equilibria

The phenomenon of multiple endemic equilibria, in particular in the subcritical (or subthreshold) case where the basic replacement ratio is smaller than one, has recently attracted a lot of attention in mathematical epidemiology. From a control point of view, in order to eradicate a well-established infectious disease, it is then not sufficient to lower $\mathcal{R}_0$ below one, but below another threshold value which is called *transmission threshold* in [1], Section 16.2.4, and *minimal transition value* in [42]. An alternative way of eradication, if one can only lower $\mathcal{R}_0$ below one but not below the transmission threshold, consists in lowering the disease prevalence into the domain of attraction of the disease-free equilibrium. If one orders the multiple endemic equilibria according to the associated disease prevalence (the first having the lowest) one can often show (and we do it in this paper) that the first endemic equilibrium is unstable. Often the first endemic equilibrium is a saddle (we are not able to show this for our model) and its stable manifold forms, or is part of, the boundary of the domain of attraction of the disease-free equilibrium. Roughly speaking, this second type of control then amounts to bringing the disease prevalence under the prevalence of the first endemic equilibrium, the *breakpoint density* in schistosomiasis ([1], Fig. 16.3). If $\mathcal{R}_0$ is between the transmission threshold and 1 and the disease is eradicated, the population is safe against reintroduction of the disease provided that new infectives enter only in small numbers. If the new infectives come with a prevalence higher than the breakpoint density, the disease will be reestablished. That is why the first unstable equilibrium is sometimes called the *watershed equilibrium*.

Mathematically, if the models are sufficiently simple, the existence of multiple equilibria can be shown directly, mostly by solving a quadratic equation; in complex models, bifurcation techniques are used and the existence of multiple equilibria is concluded from a backward (or subcritical) bifurcation of endemic equilibria from the disease-free equilibrium.

Epidemiologically, several mechanisms have been identified to cause the occurrence of multiple endemic equilibria. The mating of male and female schistosomes has already been mentioned, though we should add here that the breakpoint phenomenon is not likely to be of much practical use in the control of schistosomiasis ([1], pp. 482, 483 and 487). In [18,22,23,31,26,33], backward bifurcation of endemic equilibria occurs as a result of the incorporation of several groups of susceptible individuals with different susceptibilities to the disease. Replacing standard or mass action incidence by a power law leads to backward bifurcation as well [17,35] as can the incorporation of certain vaccination regimes [25,26,33,34] or chronological age-structure [11] into the model.

It is one of the aims of this paper to strengthen the case (already made in [19]) for super-infection to cause multiple endemic equilibria, though through a different model.

Modeling super-infection using progression age

In [36,37,19], super-infection is modeled to transfer latent individuals directly into the infectious class. In this paper we propose a different mechanism, namely that super-infection speeds up the progression of a latent individual to active

infectiousness. This idea, though in a different way and without explicitly mentioning a concrete disease, has already been pursued in a series of papers stretching from the late sixties to the early eighties [14,28,29,41] (see [47] for details and more references). In these papers, it is assumed that an infected individual, during the latency period, is subject to constant super-infection (our words) and becomes infectious as soon as the accumulated super-infection reaches a certain threshold. Multiple endemic equilibria are not observed because the models do not include births and deaths. Differently from these papers, we think that super-infection, as the primary infection itself, is a random event and should not be obligatory once the primary infection has occurred. We formalize this concept by splitting the latency stage into two substages, a progressive latent stage and a quiescent latent stage. With a certain rate η_1, the individual passes from the progressive latent stage to the infectious stage or, with a rate ρ, drops to the quiescent stage. Super-infection lifts the individual back into the progressive stage. Note the difference to [36,37] and [19] where there is only one latent stage and super-infection directly transfers latent individuals into the infectious class. In order to give the term disease-progression a meaning, we assign a class age, a, to both progressing and quiescent exposed individuals, namely the time after infection that has been spent in the progressive stage. We model the progression by a linear transport equation, i.e., a first order linear partial differential equation, with a nonlinear boundary condition. Since in the progressive stage, the exposed individuals increase their class age, while it is on hold in the quiescent stage, we call a the progression age. To incorporate an analog of the threshold idea of [14,28,29,41], we let the transition rate to infectiousness, $\eta_1(a)$ depend on the age of progression. In particular we allow $\eta_1(a) = 0$ for small $a > 0$ and introduce a^+ as the largest a such that $\eta_1 = 0$ on $[0, a]$. We call a^+ the *critical progression age for activation*.

The idea of a progression threshold that must be reached before an individual is activated to be infectious, however it is formulated, forces the mathematical modeler to leave the framework of ordinary differential equations in which the models in [19] and [36,37] are cast. In our case, we have to incorporate a semilinear partial differential equation into the model, in [14,28,29,41] it is a functional differential equation with state-dependent delay which can equivalently be recast using a quasilinear PDE. The trade-off consists in capturing a new effect.

Progression age enhanced backward bifurcation

To explain this new effect, we need to consider the per capita rate of infection, k, and the per capita rate of super-infection, $\tilde{k}$. Obviously these two parameters are not independent because they are compound parameters which include common contact rates while the probabilities that a contact actually leads to an infection may be different. So we write $\tilde{k} = \psi k$. The factor ψ describes how an individual's susceptibility at a secondary infection relates to the susceptibility at the primary infection. If $\psi < 1$, the primary infection protects against secondary infections, while it facilitates super-infection if $\psi > 1$. In order to see how progression age enhances backward bifurcation of endemic equilibria, let us look at the case that all parameters are independent of progression age and the model collapses to an ODE model. As it will turn out, $\psi > 1$ is required for multiple endemic equilibria to

occur, i.e., it is necessary that super-infection is facilitated by the primary infection. However, if η_1, the transfer rate of progressive exposed individuals to infectivity, depends on progression age, ψ can be arbitrarily small as long as it is compensated by a sufficiently large critical progression age a^+ or a sufficiently large transition rate ρ from the progressive to the quiescent latent stage. More precisely, if $\psi\rho a^+ > 1$, multiple endemic equilibria exist via a backward bifurcation in k. This means that super-infection can be important even if the protection provided by the primary against secondary infections is high.

In order to better understand how the various mechanisms in our model cooperate in making backward bifurcations possible, let the transition rate η_1 be a step function, $\eta_1 = 0$ on $[0, a^+)$ and $\eta_1 = \eta$ on (a^+, ∞) with a positive constant η. Then there is a backward bifurcation of endemic equilibria in k if $\psi\left(\frac{\rho}{\rho+\mu+\eta} + \rho a^+\right) > 1$. The opposite strict inequality implies forward bifurcation. All parameters have been explained before except μ which is the natural mortality rate. Notice that the left hand side of this inequality is 0 if ψ or ρ are zero. This shows that both super-infection and the transition from the progressive to the quiescent latent stage (at rate ρ) are needed for backward bifurcation to be possible. The two different latent stages are needed because we assume that super-infection does not directly propel latent individuals into the infectious stage, but rather accelerates the progression towards infectivity.

In [19] it is assumed that super-infection directly transfers latent individuals into the infectious stage, and only one latent stage is needed to make backward bifurcation of endemic equilibria possible. Similarly to our analysis, a positive minimum, ψ_0, is found for ψ such that subcritical multiple endemic equilibria exist if and only if $\psi \geq \psi_0$. Depending on the other parameters, $\psi_0 < 1$ can occur, though the model does not include progression age or any other class age for individuals in the latent stage. In our model, parameters that depend on progression age are needed for $\psi_0 < 1$, otherwise $\psi_0 = \frac{\rho+\eta_1+\mu}{\rho} > 1$.

The existence of multiple equilibria can be an indicator for complex dynamical behavior of the disease. Liu [36] observes periodic solutions in his model with dose-dependent latent period, but they are presumably caused by his choosing a Hill function in the super-infection rate rather than taking a standard incidence like term as we do. In our model, if the disease is assumed to be non-fatal as in [36], the endemic equilibria are either stable or unstable with a leading positive eigenvalue of the linearization. This does not rule out periodic solutions completely, but one of the main mathematical tools of finding them. If disease fatalities are included, this issue deserves further attention, though we do not touch it here. Instead we address another issue of disease dynamics and establish the existence of global compact attractor which, if $\mathcal{R}_0 > 1$, has a positive distance from the states in which the disease is eradicated.

Organization of work

In the next section we introduce the model, explain the meaning of the parameters and list the assumptions they satisfy. To keep the model simple, we have not incorporated treatment (differently from [19]), but we do not expect our results to be much different if we had.

In section 3, we consider the equilibria of the model. First we investigate some conditions for nonexistence of endemic equilibria.

Then we identify the basic replacement ratio, $\mathcal{R}_0$, in terms of the model parameters. We show that, if $\mathcal{R}_0 > 1$, there always exist endemic equilibria and that their number is odd. We also give a lower bound for the transmission threshold [1], or minimal transition value in [42]. Finally, we discuss the case $\mathcal{R}_0 < 1$ and conditions for occurrence of backward bifurcation. Backwards bifurcation leads to multiple endemic equilibria the number of which is even.

Section 4 is devoted to the analysis of the stability/instability of equilibria. As usual, the disease-free equilibrium is stable if $\mathcal{R}_0 < 1$ and unstable as $\mathcal{R}_0 > 1$. If there are multiple equilibria and if they are numbered according to the associated disease prevalence (from low to high with the first having the lowest prevalence), then every other endemic equilibrium is unstable. If $\mathcal{R}_0 < 1$, the first endemic equilibrium is unstable, while the second endemic equilibrium is unstable if $\mathcal{R}_0 > 1$. If the disease is non-fatal, we can also show that every other equilibrium is stable, i.e., the stability of the multiple equilibria alternates.

In Appendix A, we discuss an abstract formulation of the problem, and we establish the well-posedness of the model, i.e, existence and uniqueness of solutions and their continuous dependence on initial data.

Since our model is an infinite-dimensional system, to use the results in section 4 to establish stability/instability, we actually need to prove the familiar relation between the roots of the characteristic equation and the stability of the equilibrium. This is done in Appendix B using the abstract framework from Appendix A which we also employ to prove uniform strong endemicity (persistence) of the disease if $\mathcal{R}_0 > 1$ (Appendix C). In Appendix C we also show that the semiflow (dynamical system) induced by the solutions of the model has a global compact attractor.

2. The model

We consider a disease spreading in a population with the total population size at time t given by $N(t)$. The presence of the disease divides the population into subclasses. We consider the susceptible individuals who are healthy but can be infected through a contact with an infective individual. We denote the classes of the susceptible and infective individuals by $S(t)$ and $I(t)$. The population in each of these two classes is otherwise considered homogeneous. Upon a contact with an infective individual, the susceptible individual either becomes infectious right away and enters the infective class (with probability p) or becomes exposed and enters an exposed class (with probability $q = 1 - p$) where it is infected but not infectious, i.e. the disease is latent. To model the effect of super-infection we subdivide the latent stage, and accordingly the exposed class, into a latent stage where the disease progresses and a latent stage where the disease development is on hold; we call the first substage the *progressive latent stage* and the second the *quiescent latent stage*. A freshly exposed individual first enters the progressive exposed class from which, at a certain rate ρ, it can drop to the quiescent stage. In the quiescent stage individuals can be re-infected (super-infection) and reenter the progressive exposed

class. Individuals that have stayed in the exposed class long enough become infectious themselves and enter the infective class, I, at a rate η_1. We keep track of the class age of progressing exposed individuals and let a denote the time after infection that an exposed individual has spent in the progressive stage. We call a the *progression age*. We let the transition rates ρ and η_1 as well as the super-infection rate depend on class age a. $E_1(a,t)$, as a function of a, is the class-age density of exposed individuals in the progressive latent stage at time t, while $E_2(a,t)$ is the density of individuals in the quiescent exposed class again stratified over progression age. Since we want to include the effect of disease-related deaths on the disease dynamics, infective individuals die from the disease at a per capita rate γ. In this paper we do not consider the demographic consequences of the disease and therefore choose the simplest demographics consistent with an endemic model, namely a constant influx of susceptible individuals into the population, at rate Λ, and a constant per capita natural death rate, μ. Other, more realistic, demographic structures are reviewed in [27], though in the context of different epidemic models.

Our model takes the form:

$$\begin{aligned}
S'(t) &= \Lambda - k\frac{SI}{N} - \mu S \\
I'(t) &= pk\frac{SI}{N} + \int_0^\infty \eta_1(a)E_1\,da - (\mu+\gamma)I \\
(\partial_t + \partial_a)E_1(a,t) &= -\rho(a)E_1 + \tilde{k}(a)\frac{E_2 I}{N} - \eta_1(a)E_1 - \mu E_1 \qquad (2.1)\\
E_1(0,t) &= qk\frac{SI}{N} \\
\partial_t E_2(a,t) &= \rho(a)E_1 - \tilde{k}(a)\frac{E_2 I}{N} - \mu E_2
\end{aligned}$$

where we have used the following parameters:

- Λ recruitment rate into the population,
- μ per capita natural death rate,
- γ disease-induced mortality rate,
- p probability of a susceptible individual transferring to the infective class after a contact with an infective,
- q probability of an susceptible individual transferring to the progressing exposed class after a contact with an infective,
- k effective per capita infection rate for susceptible individuals,
- $\tilde{k}(a)$ per capita super-infection rate for individuals in the quiescent exposed class with progression age a,
- $\rho(a)$ per capita rate of transition from the progressive exposed to the quiescent exposed stage,
- $\eta_1(a)$ per capita rate of transition from the progressive exposed to the infective stage.

We make the following assumptions for the parameters of the model that will be valid throughout this article:

$$\begin{aligned} &\eta_1(\cdot), \rho(\cdot), \tilde{k}(\cdot) \in L^\infty(0,\infty), \\ &\rho(\cdot), \tilde{k}(\cdot) \text{ are uniformly continuous}, \\ &p+q=1. \end{aligned} \tag{2.2}$$

In addition we assume that all parameters of the model are nonnegative and $\mu > 0$. The equations in the system (2.1) are supplemented with initial conditions: $S(0) = S_0$, $I(0) = I_0$, $E_1(a,0) = E_1^0(a)$, $E_2(a,0) = E_2^0(a)$. Integrating the third and fifth equation with respect to a and adding the resulting system of ODEs, we obtain the equation for the total population size.

$$N'(t) = \Lambda - \mu N - \gamma I$$

with initial condition $N(0) = N_0$. In a disease-free population, the equation of the total population size takes the form $N'(t) = \Lambda - \mu N$. Thus, in a disease-free population the total population size can be explicitly found $N(t) = N_0 e^{-\mu t} + \frac{\Lambda}{\mu}(1 - e^{-\mu t})$ and it follows that $\lim_{t\to\infty} N(t) = \frac{\Lambda}{\mu}$.

We introduce also the following quantities which will be used throughout this article:

$$\begin{aligned} \pi(a) &= e^{-\int_0^a \rho(\sigma)\,d\sigma} \\ \pi_1(a) &= e^{-\int_0^a \eta_1(\sigma)\,d\sigma}. \end{aligned} \tag{2.3}$$

The expression $\pi(a)\pi_1(a)$ gives the probability of remaining in the progressive exposed stage till stage age a, provided the individual has survived to that age.

The model (2.1) is a well-posed system of differential equations. Rigorous justification of this fact in the framework of semigroup theory can be found in Appendix A.

3. Equilibria

To compute the steady states of the system (2.1), we set the derivatives with respect to time in (2.1) equal to zero. This way we obtain a system of three algebraic equations and an ODE. The time-independent steady state for the total population size satisfies the equation $0 = \Lambda - \mu N^* - \gamma I^*$. Next, we normalize with the equilibrium total population size thus obtaining the following system for the proportions $s^* = S^*/N^*$, $i^* = I^*/N^*$, $e_1^*(a) = E_1^*(a)/N^*$, $e_2^*(a) = E_2^*(a)/N^*$:

$$\begin{aligned} 0 &= \mu - ks^*i^* - \mu s^* + \gamma i^* \\ 0 &= pks^*i^* + \int_0^\infty \eta_1(a)e_1^*(a)da - (\mu+\gamma)i^* \\ \tfrac{d}{da}e_1^* &= -\rho(a)e_1^* + \tilde{k}(a)e_2^*i^* - \eta_1(a)e_1^* - \mu e_1^* \\ e_1^*(0) &= qks^*i^* \\ 0 &= \rho(a)e_1^* - \tilde{k}(a)e_2^*i^* - \mu e_2^*. \end{aligned} \tag{3.1}$$

The following algebraic condition is also satisfied:

$$s^* + i^* + \int_0^\infty e_1^*(a)\,da + \int_0^\infty e_2^*(a)\,da = 1. \tag{3.2}$$

Each solution $\mathcal{E}^* = (s^*, i^*, e_1^*, e_2^*)$ of the system (3.1) gives an equilibrium of the system (2.1).

3.1. Nonexistence of endemic equilibria

The system (3.1) always has the solution $\mathcal{E}^0 = (1, 0, 0, 0)$ to which corresponds the disease-free equilibrium of the system (2.1), $S^* = \frac{\Lambda}{\mu}$, $I^* = E_1^* = E_2^* = 0$. We note that equilibrium states with only some of the infected classes being zero do not exist. To find endemic equilibria, that is equilibria where $I^* \neq 0$, we use the last equation to express e_2^* in terms of e_1^* and i^*:

$$e_2^*(a) = \frac{\rho(a)e_1^*(a)}{\tilde{k}(a)i^* + \mu}. \tag{3.3}$$

Next, using the first equation, we express s^* in terms of i^*:

$$s^* = \frac{\mu + \gamma i^*}{ki^* + \mu}. \tag{3.4}$$

We note that $s^* \leq 1$ if and only if $\gamma \leq k$. Thus, if $\gamma > k$, the model (2.1) has only the disease-free equilibrium. In fact, this condition for nonexistence can be made more precise.

We use the expressions above to eliminate s^* and e_2^* from the third equation and its initial condition thus obtaining an ODE for e_1^* in terms of i^*:

$$\begin{aligned} \tfrac{d}{da}e_1^*(a) &= -\rho(a)e_1^* + \tilde{k}(a)i^*\frac{\rho(a)e_1^*(a)}{\tilde{k}(a)i^* + \mu} - \eta_1(a)e_1^* - \mu e_1^* \\ e_1^*(0) &= qks^*i^*. \end{aligned} \tag{3.5}$$

Solving this equation we obtain an expression of e_1^* in terms of i^*:

$$e_1^*(a) = qks^*i^*e^{-\mu a}\pi(a)\pi_1(a)e^{\int_0^a \frac{\rho(\sigma)\tilde{k}(\sigma)i^*}{\tilde{k}(\sigma)i^*+\mu}\,d\sigma} \tag{3.6}$$

where $\pi(a)$ and $\pi_1(a)$ are defined in (2.3).

Equation (3.6) implies an estimate from below on $e_1^*(a)$:

$$e_1^*(a) > qks^*i^*e^{-\mu a}\pi(a)\pi_1(a).$$

Integrating with respect to a we get:

$$\int_0^\infty e_1^*(a)\,da > ks^*i^*\alpha$$

where α is given by

$$\alpha = q \int_0^\infty e^{-\mu a} \pi(a) \pi_1(a)\, da. \tag{3.7}$$

We observe that $\mu\alpha < q \leq 1$. The expression $\mu\alpha$ can be interpreted as the probability of dying from natural courses while being in the progressive latent stage provided that there is no super-infection ([46], Section 2.6). The inequality above, (3.2), and (3.4) lead to the following inequality for i^*:

$$i^* < \frac{k(1-\mu\alpha) - (\gamma+\mu)}{k(1+\gamma\alpha)}.$$

Thus, we have a more accurate result on nonexistence of endemic equilibria:

Theorem 3.1. *If $k \leq \frac{\gamma+\mu}{1-\mu\alpha}$ then the system (2.1) does not have endemic equilibria.*

Consequently, we will assume that $k > \frac{\gamma+\mu}{1-\mu\alpha}$ when we discuss the existence of equilibria. We note that this implies that $k > \gamma + \mu$ and, in particular, guarantees that $s^* < 1$.

3.2. Existence and number of equilibria

Equation (3.6) can be rewritten in the form

$$e_1^*(a) = qks^* i^* e^{-\mu a} \pi_1(a) e^{-\int_0^a \frac{\rho(\sigma)\mu}{\tilde{k}(\sigma) i^* + \mu}\, d\sigma} \tag{3.8}$$

We note that e_1^* is an increasing function of i^* and, therefore, the equilibrium proportion of progressing exposed individuals increases as the proportion of infective individuals increases. Substituting in the second equation of (3.1) and dividing by i^*, we obtain the following equation for i^*:

$$\frac{pks^*}{\mu+\gamma} + \frac{qks^*}{\mu+\gamma} \int_0^\infty \eta_1(a) e^{-\mu a} \pi_1(a) e^{-\int_0^a \frac{\rho(\sigma)\mu}{\tilde{k}(\sigma) i^* + \mu}\, d\sigma}\, da = 1. \tag{3.9}$$

Denote the integral in equation (3.9) by $\varphi(i^*)$:

$$\varphi(i^*) = \int_0^\infty \eta_1(a) e^{-\mu a} \pi_1(a) e^{-\int_0^a \frac{\rho(\sigma)\mu}{\tilde{k}(\sigma) i^* + \mu}\, d\sigma}\, da. \tag{3.10}$$

Integrating by parts one can obtain a different representation which will also be useful:

$$\varphi(i^*) = 1 - \mu \int_0^\infty \left(1 + \frac{\rho(a)}{\tilde{k}(a) i^* + \mu}\right) e^{-\mu a} \pi_1(a) e^{-\int_0^a \frac{\rho(\sigma)\mu}{\tilde{k}(\sigma) i^* + \mu}\, d\sigma}\, da. \tag{3.11}$$

Regarding the properties of this integral from (3.10) and (3.11) we see that:

Proposition 3.1. *For all $0 \leq i^* \leq 1$ we have*

$$\varphi(i^*) < 1.$$

In addition, $\varphi(i^*)$ is an increasing function of i^*.

By (3.4), the i^* component of each equilibrium $\mathcal{E}^* = (s^*, i^*, e_1^*, e_2^*)$ is a solution to the following equation in i obtained from (3.9):

$$\frac{pk}{\mu+\gamma} + \frac{qk}{\mu+\gamma}\varphi(i) = \frac{ki+\mu}{\mu+\gamma i}. \tag{3.12}$$

The remaining components of $\mathcal{E}^*$ are computed correspondingly from (3.4), (3.8), (3.3). Thus, the existence and number of equilibria depends on the number of times the graphs of the functions

$$\begin{aligned} g(i) &= \frac{pk}{\gamma+\mu} + \frac{qk}{\gamma+\mu}\varphi(i) \\ f(i) &= \frac{ki+\mu}{\gamma i+\mu} \end{aligned} \tag{3.13}$$

have a common point.

The existence and the number of equilibria depends also on a threshold condition related to the basic reproductive number for the disease:

$$\mathcal{R}_0 = \frac{pk}{\mu+\gamma} + \frac{qk}{\mu+\gamma}\int_0^\infty \eta_1(a)e^{-\mu a}\pi_1(a)\pi(a)da. \tag{3.14}$$

In interpreting this expression notice that $\frac{1}{\mu+\gamma}$ is the average time spent in the infectious stage, so $\frac{k}{\mu+\gamma}$ is the average number of individuals an infectious individual can infect while being infectious, if all the rest of the population is susceptible. Recall that p is the probability of entering the infectious class immediately after being infected, while q is the probability of going through the exposed period first. The integral in (3.14) gives the probability of making it through the exposed period alive and becoming infectious (cf. [46], Section 2.6). So $\mathcal{R}_0$ gives the average number of secondary cases that are produced by an infective individual while everybody else is susceptible. Notice that $\mathcal{R}_0$ does not depend on the super-infection rate $\tilde{k}$ which is a reflection of the fact that super-infection does not lead to additional infections. Typically in simpler models, if $\mathcal{R}_0 < 1$, then the disease-free equilibrium is the only equilibrium which is globally asymptotically stable and the disease will die out from the population. On the other hand if $\mathcal{R}_0 > 1$ there are one or more endemic equilibria which are at least locally stable. In this case it can be shown that the disease persists in the population (see the last section). Let us make a connection to the condition for non-existence of endemic equilibria which we found in Theorem 3.1. Integrating by parts, we can rewrite $\mathcal{R}_0$ as

$$\mathcal{R}_0 = \frac{k}{\mu+\gamma}(1-\mu\alpha-\beta),$$

where α is given by (3.7) and

$$\beta = q\int_0^\infty \rho(a)e^{-\mu a}\pi_1(a)\pi(a)da. \tag{3.15}$$

Note that β can be interpreted as the probability of dropping to the quiescent latent stage ([46], Section 2.6). The condition for non-existence of endemic equilibria in Theorem 3.1 can be reformulated as

$$\mathcal{R}_1 := \frac{k}{\mu+\gamma}(1-\mu\alpha) \leq 1. \tag{3.16}$$

Recalling that $\mu\alpha$ is the probability of dying during the progressive latent stage, $\mathcal{R}_1$ is the average number of individuals infected by an infectious individual in an otherwise susceptible population that do not die during the progressive latent stage. Notice that $\mathcal{R}_0 < \mathcal{R}_1$.

In order to get a handle on the number of endemic equilibria we introduce the following terminology. Let $\mathcal{E}^* = (s^*, i^*, e_1^*, e_2^*)$ and $\mathcal{E}^{**} = (s^{**}, i^{**}, e_1^{**}, e_2^{**})$ be two equilibria of the system (2.1). We say that $\mathcal{E}^* \leq \mathcal{E}^{**}$ if $i^* \leq i^{**}$. Thus, the equilibria are ordered according to the value of the proportions of the infective individuals in them. We call $\mathcal{E}^*$ a *simple* equilibrium if

$$\frac{qk}{\gamma+\mu}\varphi'(i^*) \neq \frac{(k-\gamma)\mu}{(\gamma i^*+\mu)^2}. \tag{3.17}$$

Geometrically that means that the slopes of the functions $g(i)$ and $f(i)$ are different at the equilibrium point $\mathcal{E}^*$ and, therefore, their graphs intersect at $\mathcal{E}^*$. Hence, the difference $g(i) - f(i)$ changes sign. We note that if $\mathcal{E}^*$ and $\mathcal{E}^{**}$ are simple then $\mathcal{E}^* \neq \mathcal{E}^{**}$. We call $\mathcal{E}^*$ a *high multiplicity* equilibrium if

$$\frac{qk}{\gamma+\mu}\varphi'(i^*) = \frac{(k-\gamma)\mu}{(\gamma i^*+\mu)^2}. \tag{3.18}$$

Geometrically this means that the functions $f(i)$ and $g(i)$ have a common tangent at the equilibrium point $\mathcal{E}^*$ and their graphs either intersect or just touch at $\mathcal{E}^*$.

Theorem 3.2. *(a) If $\mathcal{R}_1 \leq 1$, with $\mathcal{R}_1$ from (3.16), then there are no endemic equilibria.*

(b) If $\mathcal{R}_0 < 1$ and the system (2.1) has endemic equilibria which are all simple, then there is an even number of endemic equilibria.

(c) If $\mathcal{R}_0 > 1$, the system (2.1) always has at least one equilibrium. If there are several endemic equilibria which are all simple, then their number is odd.

Proof. Part (a) has been proved above. The function $f(i)$ is increasing and concave down. We have $f(0) = 1$ and $f(1) = \frac{k+\mu}{\gamma+\mu}$. The function $g(i)$ is also increasing but its concavity may be changing. We have $g(0) = \mathcal{R}_0$ and $g(1) < \frac{k}{\gamma+\mu}$. Thus, $g(1) < f(1)$. Consequently, if $\mathcal{R}_0 < 1$ then $g(0) < f(0)$ and there are either zero intersections of the two graphs, or an even number of them. If $\mathcal{R}_0 > 1$ then $g(0) > f(0)$ and there is at least one intersection of the graphs. If there are others, their total number is odd (see Figure 1). □

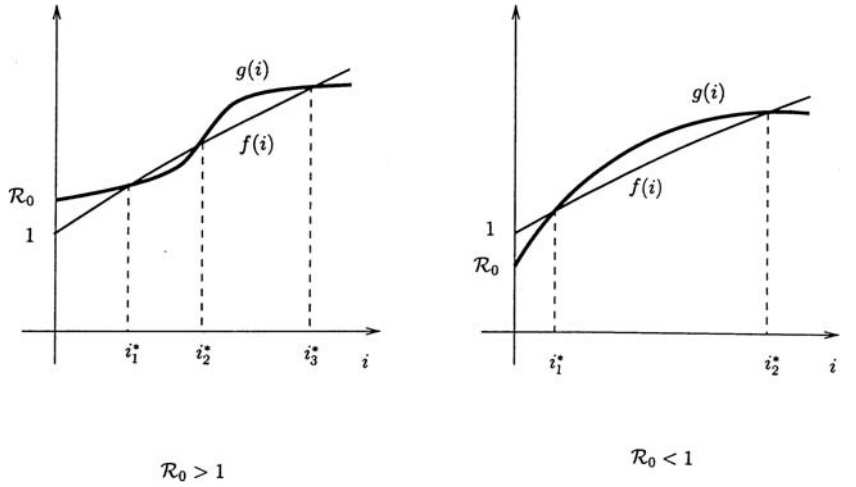

Fig. 1 . To each intersection of the functions $f(i)$ and $g(i)$ corresponds i^* which gives an equilibrium $\mathcal{E}^*$ of the system. In the case when $\mathcal{R}_0 > 1$ the first one and the third one are stable (at least when $\gamma = 0$) while the second one is unstable. In the case $\mathcal{R}_0 < 1$ the first one is unstable and the second one is stable (at least when $\gamma = 0$). Notice that the stability/instability of $\mathcal{E}^*$ is in direct connection to the relation between the slopes of $f(i)$ and $g(i)$ at i^*.

We derive a uniqueness condition for endemic equilibria. To this end we need the derivative of φ in (3.10),

$$\varphi'(i^*) = \int_0^\infty \eta_1(a)e^{-\mu a}\pi_1(a)e^{-\int_0^a \frac{\rho(\sigma)\mu}{\tilde{k}(\sigma)i^*+\mu}d\sigma}\left(\int_0^a \frac{\rho(\sigma)\tilde{k}(\sigma)\mu}{(\tilde{k}(\sigma)i^*+\mu)^2}d\sigma\right)da. \tag{3.19}$$

Assume that there are two endemic equilibria. By Rolle's theorem, there exists some $i \in (0, 1)$ such that

$$g'(i) = f'(i).$$

Then

$$g'(i) < \frac{qk}{(\mu+\gamma)\mu}\int_0^\infty \eta_1(a)e^{-\mu a}\pi_1(a)e^{-\int_0^a \frac{\rho(\sigma)\mu}{\tilde{k}(\sigma)+\mu}d\sigma}\left(\int_0^a \rho(\sigma)\tilde{k}(\sigma)d\sigma\right)da$$

and, recalling that $k > \gamma$ is necessary for existence of equilibria,

$$f'(i) > \frac{(k-\gamma)\mu}{(\gamma+\mu)^2}.$$

So we get the following condition for uniqueness.

Theorem 3.3. *There exists at most one endemic endemic equilibrium if*

$$qk\int_0^\infty \eta_1(a)e^{-\mu a}\pi_1(a)e^{-\int_0^a \frac{\rho(\sigma)\mu}{\tilde{k}(\sigma)+\mu}d\sigma}\left(\int_0^a \rho(\sigma)\tilde{k}(\sigma)d\sigma\right)da \le \frac{(k-\gamma)\mu^2}{\gamma+\mu}.$$

Less precise but perhaps more insightful conditions are the following.

Corollary 3.1. *There exists at most one endemic equilibrium if at least one of the following conditions are satisfied*

$$q\int_0^\infty \pi_1(a)\rho(a)\tilde{k}(a)da \le \frac{(k-\gamma)\mu^2}{k(\gamma+\mu)},$$

or

$$(\sup\eta_1)\frac{q}{\mu}\int_0^\infty e^{-\mu a}\rho(a)\tilde{k}(a)da \le \frac{(k-\gamma)\mu^2}{k(\gamma+\mu)}.$$

Notice that the right hand sides of these inequalities become very simple if the disease is non-fatal; they equal μ, if $\gamma = 0$. The two conditions show that, within the framework of our model, both super-infection and the possibility of dropping from the progressive to a quiescent stage are needed to have more than one endemic equilibrium.

3.3. Existence of endemic equilibria when $\mathcal{R}_0 < 1$. Backward bifurcation

Now we turn our attention to the existence of endemic equilibria when $\mathcal{R}_0 < 1$. We choose the infection rate k as a bifurcation parameter in (3.12). In a first step, we assume that there is no coupling between the infection rate and the super-infection rate $\tilde{k}$. We solve (3.12) with respect to k:

$$k = \frac{\mu(\mu+\gamma)}{p(\mu+\gamma i^*)+q(\mu+\gamma i^*)\varphi(i^*)-(\mu+\gamma)i^*} \tag{3.20}$$

We compute the derivative of $k(i^*)$ with respect to i^*:

$$k'(i^*) = -\mu(\mu+\gamma)\frac{p\gamma+q\gamma\varphi(i^*)+q(\mu+\gamma i^*)\varphi'(i^*)-(\mu+\gamma)}{(p(\mu+\gamma i^*)+q(\mu+\gamma i^*)\varphi(i^*)-(\mu+\gamma)i^*)^2}. \tag{3.21}$$

The bifurcation at the point $i^* = 0$ is subcritical if and only if $k'(0) < 0$. Thus, the bifurcation at the point $i^* = 0$ is subcritical if and only if

$$q\gamma\varphi(0)+q\mu\varphi'(0) > \mu+q\gamma. \tag{3.22}$$

(3.11) leads to the following criterion for subcritical bifurcation:

Proposition 3.2. *The system exhibits backward bifurcation if and only if*

$$q\varphi'(0) - q\gamma\int_0^\infty \left(1+\frac{\rho(a)}{\mu}\right)e^{-\mu a}\pi_1(a)\pi(a)\,da > 1. \tag{3.23}$$

The following two forms of $\varphi'(0)$ corresponding to the two forms of $\varphi(i^*)$ in (3.10) and (3.11) will be useful:

$$\varphi'(0) = \frac{1}{\mu}\int_0^\infty \eta_1(a)e^{-\mu a}\pi_1(a)\pi(a)\int_0^a \rho(\sigma)\tilde{k}(\sigma)\,d\sigma\,da, \tag{3.24}$$

$$\varphi'(0) = \frac{1}{\mu}\int_0^\infty \left[\rho(a)\tilde{k}(a) - \left(\mu^2+\rho(a)\right)\int_0^a \rho(\sigma)\tilde{k}(\sigma)\,d\sigma\right] \times e^{-\mu a}\pi_1(a)\pi(a)\,da. \tag{3.25}$$

The model (2.1) exhibits backward bifurcation if there is a set of parameters such that inequality (3.23) is satisfied. To give an example we assume that all parameters of the model are constant except possibly $\eta_1(a)$. It is sufficient to show that it is possible to choose the remaining parameters so that $\mu q\varphi'(0) > \mu + q\gamma$. Indeed, using representation (3.24) we get

$$q\mu\varphi'(0) = q\tilde{k}\rho \int_0^\infty a\,\eta_1(a)e^{-\mu a}\pi_1(a)\pi(a)\,da.$$

Clearly, since the integral is positive we can choose $\tilde{k}$ large enough so that the inequality holds. Furthermore, the reproductive number $\mathcal{R}_0$ does not depend on $\tilde{k}$ and therefore its value will remain below one.

We note that the backward bifurcation inequality holds true even if all coefficients are constant. This, in particular, implies that the ODE model obtained from (2.1) through assuming all coefficients constant also exhibits backward bifurcation. It follows from Proposition 3.2 that there is no backward bifurcation if $q = 0$ or $\tilde{k}(a)\rho(a) = 0$ for all $a \geq 0$, but Corollary 3.1 actually gives us a more general condition because backward bifurcation leads to multiple equilibria in our situation.

As we already pointed out in the introduction, k and $\tilde{k}$ are related, while we have used k as an independent bifurcation parameter. We show that this does not make any difference. Assume that $\tilde{k}$ depends on k in a continuously differentiable way. Then φ in (3.20) is not only a function of i^*, but also of k, $\varphi = \varphi(i^*, k)$. So (3.20) becomes a fixed point equation in k parameterized over i^*. However, $\varphi(0, k)$ is independent of k and $\frac{\partial}{\partial k}\varphi(i^*, k) \to 0$ as $i^* \to 0$ uniformly for k in compact subintervals of $[0, \infty)$. See (3.10). This shows that the right hand side of (3.20) is a uniform strict contraction in k and solutions $k(i^*)$ of (3.20) exist for small $i^* > 0$ with k being differentiable at 0 ([12], Theorem 2.2). Since $\frac{\partial}{\partial k}\varphi(0, k) = 0$, the chain rule implies that $k(0)$ and $k'(0)$ are the same as given by (3.20) and (3.21).

3.4. Progression age enhanced backward bifurcation

In particular let us assume that $\tilde{k}(a) = k\psi(a)$ as we did in the introduction. We restrict our consideration to a non-fatal disease, $\gamma = 0$, and also assume that all infected individuals enter the latent stage, $q = 1$ and $p = 0$. The condition for backward bifurcation is $\varphi'(0) > 1$. By (3.24), this condition becomes

$$\frac{1}{\mu}\int_0^\infty \eta_1(a)e^{-\mu a}\pi_1(a)\pi(a)\left(\int_0^a \rho(\sigma)k\psi(\sigma)d\sigma\right)da > 1,$$

where k is given by (3.20) evaluated at $i^* = 0$, that is, $k = \frac{\mu}{\varphi(0)}$. This leads to the following criterion for backwards bifurcation in k.

$$\int_0^\infty \eta_1(a)e^{-\mu a}\pi_1(a)\pi(a)\left(\int_0^a \rho(\sigma)\psi(\sigma)\,d\sigma - 1\right)da > 0. \tag{3.26}$$

It is reasonable to expect that individuals in the latent stage do not become infectious immediately after infection, i.e., $\eta_1(a) = 0$ for small $a > 0$. Let a^+ be the largest a such that $\eta_1 = 0$ a.e. on $[0, a)$. The value of a^+ is finite unless

$\eta_1 = 0$ a.e. on $[0, \infty)$, i.e., exposed individuals remain in the latent stage until they die. We call a^+ the *threshold progression age for activation* at which progressing exposed individuals start entering the infectious class. If $a^+ \in (0, \infty)$, η_1 depends on class-age in a crucial way. We have the following result from (3.26).

Theorem 3.4. *The endemic equilibria exhibit backward bifurcation in k if $p = 0$, $\gamma = 0$, $a^+ \in (0, \infty)$ and*

$$\int_0^{a^+} \rho(\sigma)\psi(\sigma)d\sigma > 1.$$

In order to obtain additional insight we assume that ψ and all other parameters of the model are constant with exception of the rate η_1 at which individuals in the progressive latent stage become infective. For the transition rate η_1 we assume an extreme threshold behavior, namely that $\eta_1 = 0$ on $[0, a^+)$ and $\eta_1 = \eta$ on (a^+, ∞) with a positive constant η. For this special case, the criterion (3.26) for backwards bifurcation in k takes the form

$$\psi\left(\frac{\rho}{\rho + \mu + \eta} + \rho a^+\right) > 1.$$

The boundary value $a^+ = 0$ corresponds to the special case that all parameters are constant, $\eta_1 = \eta$. In this special case, there is a backward bifurcation if $\psi > \frac{\rho+\eta_1+\mu}{\rho}$. Moreover, this condition is necessary for backward bifurcation in k requiring that ψ is larger than 1, perhaps substantially so. If, however, this condition is violated, that does not rule out the presence of backward bifurcation with respect to another parameter. In order to show that this condition is necessary for the existence of multiple endemic equilibria we return to equation (3.12) with (3.10) which takes the following form in this special case,

$$\eta_1 k = (ki^* + \mu)\left(\mu + \eta_1 + \frac{\rho\mu}{\psi k i^* + \mu}\right).$$

There is at most one endemic equilibrium if the derivative of the right hand side has no positive zeros. The derivative is

$$k(\mu + \eta_1) + \rho\frac{k\mu^2(1 - \psi)}{(k\psi i^* + \mu)^2}.$$

This is positive if $\psi \leq 1$. If $\psi > 1$, the derivative can be strictly estimated from below by

$$k(\mu + \eta_1) + \rho k(1 - \psi).$$

So there is at most one endemic equilibrium if this expression is non-negative.

We summarize our findings emphasizing how the stage age structure facilitates backward bifurcation and the occurrence of multiple endemic equilibria for $\mathcal{R}_0 < 1$.

Corollary 3.2. *Let $\tilde{k} = k\psi$ with constant ψ and $\rho(a) = \rho$ be constant as well, $p = 0$, $\gamma = 0$. Then the endemic equilibria exhibit a backward bifurcation in k for any choice of ρ and ψ provided the threshold stage age for activation, a^+, is chosen large enough, $\rho\psi a^+ > 1$.*

In the corresponding ODE model where η_1 is also constant, there is a backward bifurcation in k if and only if $\psi > \frac{\mu+\eta_1+\rho}{\rho} > 1$. In fact this condition is necessary for the existence of multiple endemic equilibria, if all parameter functions are constant.

If η_1 is a step function, $\eta_1 = 0$ on $[0, a^+)$ and $\eta_1 = \eta$ on (a^+, ∞), then the endemic equilibria exhibit a backward bifurcation in k if

$$\psi\left(\frac{\rho}{\rho+\mu+\eta} + \rho a^+\right) > 1.$$

4. Local stability of equilibria

Linearizing (2.1) around an equilibrium we obtain a linear system for the perturbations x, y, $z(\cdot)$, $w(\cdot)$ of S, I, E_1, E_2 respectively. We consider the eigenvalue problem for the linear system. For simplicity, we denote the time-independent perturbations corresponding to an eigenvalue λ again with the same letters. Thus, we have to solve the following linear eigenvalue problem

$$\begin{aligned}
\lambda x &= -ks^*y - ki^*x + ks^*i^*n - \mu x \\
\lambda y &= pks^*y + pki^*x - pks^*i^*n + \int_0^\infty \eta_1(a)z(a)\,da - (\mu+\gamma)y \\
z_a &= -(\lambda+\rho+\eta_1+\mu)z + \tilde{k}e_2^*y + \tilde{k}i^*w - \tilde{k}e_2^*i^*n \\
z(0) &= qks^*y + qki^*x - qks^*i^*n \\
\lambda w &= \rho(a)z - \tilde{k}e_2^*y - \tilde{k}i^*w + \tilde{k}e_2^*i^*n - \mu w \\
\lambda n &= -\mu n - \gamma y
\end{aligned} \tag{4.1}$$

where

$$n = x + y + \int_0^\infty z(a)\,da + \int_0^\infty w(a)\,da.$$

Actually we can omit this equation because it follows from the others, at least if $\lambda \neq 0$.

In the next subsection we derive the characteristic equation for the disease-free equilibrium and discuss its solutions.

4.1. The characteristic equation of the disease-free equilibrium and its roots

First we consider conditions for local stability of the disease-free equilibrium. In the case of the disease-free equilibrium we have $i^* = e_1^* = e_2^* = 0$.

The equations for the eigenvalues of the linear operator simplify significantly and take the form:

$$\begin{aligned} \lambda x &= -ky - \mu x \\ \lambda y &= pky + \int_0^\infty \eta_1(a) z(a)\, da - (\mu + \gamma) y \\ z_a &= -(\lambda + \rho + \eta_1 + \mu) z \\ z(0) &= qky \\ \lambda w &= \rho(a) z - \mu w. \end{aligned} \tag{4.2}$$

Solving the differential equation with the corresponding initial condition we obtain:

$$z(a) = qkye^{-\lambda a} e^{-\mu a} \pi_1(a) \pi(a).$$

Solving the last equation for w in terms of z

$$w = \frac{\rho z}{\lambda + \mu}.$$

Substituting in the second equation and canceling y we obtain the following equation for the eigenvalues λ of the linear operator. This equation is often referred to as the *characteristic equation*:

$$\frac{pk}{\lambda + \mu + \gamma} + \frac{qk}{\lambda + \mu + \gamma} \int_0^\infty \eta_1(a) e^{-\lambda a} e^{-\mu a} \pi_1(a) \pi(a)\, da = 1. \tag{4.3}$$

The left hand side of that equality can be viewed as a function of λ. We denote that function by $\mathcal{G}(\lambda)$. If $\lambda \geq -(\mu + \gamma)$ is real, then $\mathcal{G}(\lambda)$ is a decreasing function of λ which approaches zero as λ approaches infinity. From formula (3.14) it follows that $\mathcal{G}(0) = \mathcal{R}_0$. In addition, for any λ with $\Re\lambda \geq 0$ we have $|\mathcal{G}(\lambda)| \leq \mathcal{G}(\Re\lambda)$. Consider the case $\mathcal{R}_0 < 1$ and assume λ is a solution to the equation $\mathcal{G}(\lambda) = 1$ with $\Re\lambda \geq 0$. Then we have:

$$1 = |\mathcal{G}(\lambda)| \leq \mathcal{G}(\Re\lambda) \leq \mathcal{G}(0) = \mathcal{R}_0 < 1$$

which is a contradiction stemming from the assumption that equation (4.3) has a solution with nonnegative real part. Thus, all solutions to the equation (4.3) have negative real part and, therefore, the disease-free equilibrium is stable (see Appendix B for rigorous justification of this conclusion). In the case $\mathcal{R}_0 > 1$ we have that $\mathcal{G}(0) > 1$ and, since $\mathcal{G}(\lambda) \to 0$ as $\lambda \to \infty$, the equation (4.3) has a real solution which is positive. This implies that the disease-free equilibrium is unstable (see Appendix B). We summarize these results in the following theorem.

Theorem 4.1. *If $\mathcal{R}_0 < 1$ then the disease-free equilibrium is locally asymptotically stable. If $\mathcal{R}_0 > 1$ the disease-free equilibrium is unstable.*

4.2. The characteristic equation of an endemic equilibrium

Now we turn to the general system (4.1) and we compose the characteristic equation corresponding to an arbitrary endemic equilibrium. Expressing n from the last equation in terms of y and successively eliminating x and w we obtain a differential equation for z. In particular,

$$n = -\frac{\gamma}{\lambda+\mu} y$$

we can eliminate n from the remaining equations. Next, from the first equation above we can express x in terms of y:

$$x = -ks^* y \frac{\lambda+\mu+\gamma i^*}{(\lambda+\mu)(\lambda+ki^*+\mu)}.$$

From the second to last equation we express w in terms of z and y:

$$w = \frac{\rho(a)z}{\lambda+\tilde{k}i^*+\mu} - \tilde{k}e_2^* y \frac{\lambda+\mu+\gamma i^*}{(\lambda+\mu)(\lambda+\tilde{k}i^*+\mu)}.$$

We use the expressions for n, x and w to eliminate them from the equations for z. We obtain:

$$\begin{aligned} z_a &= -\left(\lambda+\eta_1+\mu+\rho\frac{\lambda+\mu}{\lambda+\tilde{k}i^*+\mu}\right) z + \tilde{k}e_2^* y \frac{\lambda+\mu+\gamma i^*}{\lambda+\tilde{k}i^*+\mu}, \\ z(0) &= qks^* y \frac{\lambda+\mu+\gamma i^*}{\lambda+ki^*+\mu}. \end{aligned} \tag{4.4}$$

This equation can be solved to express z in terms of y. Integrating we obtain:

$$\begin{aligned} z(a) = {} & qks^* y \frac{\lambda+\mu+\gamma i^*}{\lambda+ki^*+\mu} e^{-(\lambda+\mu)a}\pi_1(a) e^{-\int_0^a \rho(\sigma)\frac{\lambda+\mu}{\lambda+\tilde{k}(\sigma)i^*+\mu}\,d\sigma} \\ & + y\int_0^a \tilde{k}(\sigma)e_2^*(\sigma)\frac{(\lambda+\mu+\gamma i^*)\pi_1(a)}{(\lambda+\tilde{k}(\sigma)i^*+\mu)\pi_1(\sigma)} \\ & e^{-(\lambda+\mu)(a-\sigma)} e^{-\int_\sigma^a \rho(\tau)\frac{\lambda+\mu}{\lambda+\tilde{k}(\tau)i^*+\mu}\,d\tau}\,d\sigma. \end{aligned}$$

Using the expressions for e_2^* and e_1^* in (3.3) and (3.8) we have:

$$\begin{aligned} z(a) = {} & qks^* y \frac{\lambda+\mu+\gamma i^*}{\lambda+ki^*+\mu} e^{-(\lambda+\mu)a}\pi_1(a)\Gamma(0,a;\lambda) \\ & + qks^* i^* y e^{-\mu a}\pi_1(a)\int_0^a \frac{\tilde{k}(\sigma)\rho(\sigma)(\lambda+\mu+\gamma i^*)}{(\tilde{k}(\sigma)i^*+\mu)(\lambda+\tilde{k}(\sigma)i^*+\mu)} \\ & \times e^{-\lambda(a-\sigma)}\Gamma(0,\sigma;0)\Gamma(\sigma,a;\lambda)d\sigma. \end{aligned}$$

where we have used the following notation:

$$\Gamma(\sigma,a;\lambda) = e^{-\int_\sigma^a \frac{\rho(\lambda+\mu)}{\lambda+\tilde{k}(\tau)i^*+\mu}\,d\tau}$$

Substituting these expressions for x, z and w in the equation for y, and canceling y we obtain the *characteristic equation* for the λ:

$$s^*H(\lambda; i^*) + s^*i^*D(\lambda; i^*) = 1 \tag{4.5}$$

where we have used the notation:

$$\begin{aligned} H(\lambda; i^*) &= \frac{(\lambda + \mu + \gamma i^*)}{(\lambda + \mu + \gamma)(\lambda + ki^* + \mu)} \\ &\quad \times \left(pk + qk \int_0^\infty \eta_1(a) e^{-\lambda a} e^{-\mu a} \pi_1(a) \Gamma(0, a; \lambda)\, da \right) \\ D(\lambda; i^*) &= qk \frac{\lambda + \mu + \gamma i^*}{\lambda + \mu + \gamma} \int_0^\infty \eta_1(a) e^{-\mu a} \pi_1(a) \mathcal{I}(a; \lambda, i^*)\, da \end{aligned} \tag{4.6}$$

$$\mathcal{I}(a; \lambda, i^*) = \int_0^a \frac{\tilde{k}(\sigma)\rho(\sigma)}{(\tilde{k}(\sigma)i^* + \mu)(\lambda + \tilde{k}(\sigma)i^* + \mu)} e^{-\lambda(a-\sigma)} \Gamma(0, \sigma; 0) \Gamma(\sigma, a; \lambda) d\sigma$$

Let $\mathcal{Q}(\lambda; i^*)$ denote the left-hand side of the characteristic equation. Thus,

$$\mathcal{Q}(\lambda; i^*) = s^*H(\lambda; i^*) + s^*i^*D(\lambda; i^*).$$

Let $\mathcal{E}^* = (s^*, i^*, e_1^*, e_2^*)$ be an equilibrium. The functions $H(\lambda; i^*)$, $D(\lambda; i^*)$, $\mathcal{Q}(\lambda; i^*)$ have the following properties:

1. The function $H(\lambda; i^*)$ is an eventually decreasing function of $\lambda > 0$ and $\lim_{\lambda \to \infty} H(\lambda; i^*) = 0$. We also have $H(0; i^*) = 1$.
   See (3.9) and (3.4).
2. The function $D(\lambda; i^*)$ satisfies the equality

$$D(0; i^*) = qk \frac{\mu + \gamma i^*}{\mu(\mu + \gamma)} \varphi'(i^*).$$

   Recall (3.19).
3. The function $\mathcal{Q}(\lambda; i^*)$ satisfies:

$$\mathcal{Q}(0; i^*) = s^* + qks^*i^* \frac{\mu + \gamma i^*}{\mu(\mu + \gamma)} \varphi'(i^*). \tag{4.7}$$

4. It is not hard to see that for λ real we have $\mathcal{Q}(\lambda; i^*) \to 0$ as $\lambda \to \infty$ for each i^* fixed.

The following theorem characterizes the value of $\mathcal{Q}(0; i^*)$ with respect to whether the equilibrium is obtained from $g(i)$ crossing $f(i)$ and becoming from larger to smaller or from $g(i)$ crossing $f(i)$ and becoming from smaller to larger. The functions f and g have been introduced in (3.13).

Theorem 4.2. *Let $\mathcal{E}^* = (s^*, i^*, e_1^*, e_2^*)$ be an equilibrium. The following are valid:*

1. *$\mathcal{Q}(0; i^*) < 1$ if and only if $g'(i^*) < f'(i^*)$.*
2. *$\mathcal{Q}(0; i^*) = 1$ if and only if $g'(i^*) = f'(i^*)$.*
3. *$\mathcal{Q}(0; i^*) > 1$ if and only if $g'(i^*) > f'(i^*)$.*

Proof. We prove only the first point. The rest can be shown similarly. The following is a sequence of equivalent transformations.

$$\begin{aligned} \mathcal{Q}(0; i^*) &< 1 \\ s^* + qks^*i^* \frac{\mu + \gamma i^*}{(\mu + \gamma)\mu} \varphi'(i^*) &< 1 \\ qks^*i^* \frac{\mu + \gamma i^*}{(\mu + \gamma)\mu} \varphi'(i^*) &< \frac{(k - \gamma)i^*}{ki^* + \mu} \\ \frac{qk}{\gamma + \mu} \varphi'(i^*) &< \frac{(k - \gamma)\mu}{(\gamma i^* + \mu)^2} \\ g'(i^*) &< f'(i^*) \end{aligned} \tag{4.8}$$

This completes the proof. □

4.3. Examining the signs of the roots of the characteristic equation

Theorem 4.2 through the results in Appendix B is the main tool in showing stability or instability of the equilibria. Its condition 3. leads directly to instability as Proposition 4.3 below asserts. Again we will assume that all possible endemic equilibria are simple. If $\mathcal{E}^*$ is an equilibrium that is not simple, then we have $g'(i^*) = f'(i^*)$ and Theorem 4.2 implies that $\mathcal{Q}(0; i^*) = 1$. Therefore, the characteristic equation $\mathcal{Q}(\lambda; i^*) = 1$ has $\lambda = 0$ as a solution, and the stability of the endemic equilibrium cannot be determined by a linear stability analysis. Fortunately, endemic equilibria almost always are simple in the following sense.

Remark. Let either k be independent of $\tilde{k}$ or $\tilde{k}(a) = k\psi(a)$. Then, for a.a. $k > 0$, all endemic equilibria are simple.

Proof. We use the terminology and the results in [12], Section 2.10. Define

$$\xi(k, i^*) = \frac{ks^*}{\mu + \gamma}[p + q\varphi(i^*)],$$

where $s^* = \frac{\mu + \gamma i^*}{ki^* + \mu}$ is also a function of i^* and $\varphi(i^*)$, given by (3.10), possibly a function of k via $\tilde{k}$. We have an endemic equilibrium if and only if $i^* > 0$ and $\xi(k, i^*) = 1$. Notice that $\partial_k \xi(k, i^*) > 0$ for the partial derivatives of ξ with respect to k. So 1 is a regular value of ξ. By Theorem 10.3 in [12], 1 is a regular value of $\xi(k, \cdot)$ for a.a. k. It is easy to see that this is equivalent to every endemic equilibrium being simple for a.a. k.

Proposition 4.3 *Let $\mathcal{R}_0 < 1$ and assume the system (2.1) has endemic equilibria $\mathcal{E}^m$ for $m = 1, \ldots, M$ and all of them are simple. Assume they are numbered in increasing order, that is, $\mathcal{E}^1 < \mathcal{E}^2 < \cdots < \mathcal{E}^M$. Then, every other one is unstable, with $\mathcal{E}^1$ unstable.*

Proof. Let f, g be the functions defined in (3.13). At an odd numbered equilibrium $\mathcal{E}^*$ the function $g(i)$ increases to become from smaller than the function $f(i)$ to larger than the function $f(i)$ (this is, in particular, the case with $\mathcal{E}^1$ since $g(0) = \mathcal{R}_0$, $f(0) = 1$ and $\mathcal{R}_0 < 1$, (see Figure 1)) and we have

$$g'(i^*) > f'(i^*).$$

Therefore,

$$\frac{qk}{\gamma + \mu}\varphi'(i^*) > \frac{(k-\gamma)\mu}{(\gamma i^* + \mu)^2}.$$

Consequently, from Theorem 4.2 it follows

$$\mathcal{Q}(0; i^*) = s^* + qks^*i^*\frac{\mu + \gamma i^*}{(\mu + \gamma)\mu}\varphi'(i^*) > 1.$$

Thus, the equation $\mathcal{Q}(\lambda; i^*) = 1$ has a positive real solution and therefore $\mathcal{E}^*$ is unstable. □

A similar line of reasoning leads to the following proposition. Again, the instability of the endemic equilibria which we detect is associated with a positive real root of the characteristic equation (or eigenvalue of (4.1)), i.e., it is not associated with a Hopf bifurcation of periodic solutions.

Proposition 4.4 *Let $\mathcal{R}_0 > 1$ and assume the system (2.1) has endemic equilibria $\mathcal{E}^m$ for $m = 1, \ldots, L$ and all of them are simple. Assume they are numbered in increasing order, that is, $\mathcal{E}^1 < \mathcal{E}^2 < \cdots < \mathcal{E}^L$. Then, every other one is unstable, with $\mathcal{E}^2$ unstable.*

Proof. In this case we have $g(0) = \mathcal{R}_0$, $f(0) = 1$ and $\mathcal{R}_0 > 1$. Thus, $g(0) > f(0)$. Furthermore, at $\mathcal{E}^1$ the function $g(i)$ becomes from larger than $f(i)$ smaller than $f(i)$ (see Figure 1). Therefore, at $\mathcal{E}^2$ $g(i)$ increases to become larger than $f(i)$ and $g'(i^*) > f'(i^*)$ where i^* is the proportion of infective individuals in $\mathcal{E}^2$. Thus, Theorem 4.2 implies that $\mathcal{E}^2$ is unstable as well as every even numbered equilibrium. □

Concerning the remaining simple equilibria we have that $g'(i^*) < f'(i^*)$ and, by Theorem 4.2, $\mathcal{Q}(\lambda; i^*) < 1$. Unfortunately, $\mathcal{Q}(\lambda; i^*) < 1$ does not automatically imply local stability of an equilibrium, unless $\gamma = 0$. We have the following general criterion:

Proposition 4.5 *An endemic equilibrium $\mathcal{E}^* = (s^*, i^*, e_1^*, e_2^*)$ is stable if $\tilde{k} \cdot \rho \equiv 0$ or if*

$$\gamma + qki^*\frac{\mu + \gamma i^*}{\mu}\varphi'(i^*) < ki^*. \tag{4.9}$$

Proof. Let λ be a nonnegative real number or a complex number with nonnegative real part. By (3.9),

$$s^*|H(\lambda, i^*)| \leq \frac{|\lambda + \mu + \gamma i^*|}{|\lambda + \mu + \gamma||\lambda + \mu + ki^*|}(\mu + \gamma).$$

So

$$s^*|H(\lambda, i^*)| < 1, \qquad s^*|H(\lambda, i^*)| \leq \frac{\mu + \gamma}{\mu + ki^*}.$$

From the derivative of equation (3.10) we see that

$$|D(\lambda, i^*)| \leq qk\frac{|\lambda + \mu + \gamma i^*|}{\mu|\lambda + \mu + \gamma|}\varphi'(i^*) \leq \frac{qk}{\mu}\varphi'(i^*).$$

If $\tilde{k} \cdot \rho \equiv 0$, then $\varphi'(i^*) = 0$ and $|\mathcal{Q}(\lambda, i^*)| < 1$, and the characteristic equation is not satisfied. By (3.4),

$$|\mathcal{Q}(\lambda, i^*)| \leq \frac{\mu + \gamma}{\mu + ki^*} + \frac{qk}{\mu}\frac{\mu + \gamma i^*}{\mu + ki^*}i^*\varphi'(i^*). \tag{4.10}$$

So $|\mathcal{Q}(\lambda, i^*)| < 1$ as well if the second condition holds. □

We notice that if $\gamma = 0$ inequality (4.10) becomes

$$|\mathcal{Q}(\lambda, i^*)| \leq s^* + \frac{qk}{\mu}s^*i^*\varphi'(i^*) = \mathcal{Q}(0, i^*).$$

Thus an endemic equilibrium with $\mathcal{Q}(0; i^*) < 1$ is locally asymptotically stable. In particular we have the following result.

Corollary 4.1 *If $\gamma = 0$ and all endemic equilibria are simple, the endemic equilibria alternate in stability such that the first one is unstable if $\mathcal{R}_0 < 1$ and locally asymptotically stable if $\mathcal{R}_0 > 1$, respectively.*

Without super-infection, there is at most one endemic equilibrium and it is locally asymptotically stable if it exists.

4.4. Stability of the bifurcating solution for small values of i^*.

In this subsection we show that the bifurcating backward solution is unstable for small i^* and the bifurcating forward solution is stable for small i^*. While the result for the bifurcating backward solution follows from Proposition 4.3, the result on the stability of the bifurcating forward solution adds to our knowledge on the dynamical behavior of the system.

Proposition 4.6 *Let k be either independent of $\tilde{k}$ or $\tilde{k}(a) = k\psi(a)$. As long as $i^* > 0$ is sufficiently small, the corresponding endemic equilibrium is locally asymptotically stable in case of a forward bifurcation in k from the disease-free equilibrium, and unstable in case of a backward bifurcation.*

Proof. We rewrite the characteristic equation $\mathcal{Q}(\lambda; i^*) = 1$ as $\mathcal{F}(\lambda; i^*) = 0$ where $\mathcal{F}(\lambda; i^*) = \mathcal{Q}(\lambda; i^*) - 1$. This equation defines locally λ as a function of i^*, provided $\frac{\partial \mathcal{F}}{\partial \lambda} \neq 0$ near the point $(\lambda(i^*); i^*)$. First we compute $\lambda(0)$, that is the value of λ when $i^* = 0$ from the equation $\mathcal{F}(\lambda(0); 0) = 0$. This equation is exactly equation (4.3) which has one real solution and all complex solutions have real part smaller than the real solution. We consider the branch corresponding to the real solution. Since at the bifurcation point $\mathcal{R}_0 = 1$ we have that $\lambda(0) = 0$. We note that all complex solutions of the equation $\mathcal{F}(\lambda(0); 0) = 0$ can be bounded away from the imaginary axis so that there is some positive interval of values of i^* for which none of the other solutions crosses the imaginary axis. Indeed, consider the strip $-\epsilon < \Re\lambda < \epsilon$ where $0 < \epsilon < \mu + \gamma$. The function $\mathcal{F}(\lambda; 0)$ is analytic there. We have that $|\mathcal{Q}(\lambda; 0)| \to 0$ as $|\lambda| \to \infty$ and therefore all the solutions in the strip lie in a bounded set. The uniqueness theorem for analytic functions then implies that $\mathcal{F}(\lambda; 0)$ can have only finitely many zeroes in that strip (or else be identically zero). Thus, there is a strip neighborhood of $\lambda = 0$ in which zero is the only solution of (4.3). We note that our model shares this property with the McKendrick-von Foerster chronological age-structured model [32].

The Implicit Function Theorem gives us

$$\left.\frac{d\lambda}{di^*}\right|_{i^*=0,\lambda=0} = -\left.\frac{\frac{\partial \mathcal{F}}{\partial i^*}}{\frac{\partial \mathcal{F}}{\partial \lambda}}\right|_{i^*=0,\lambda=0}.$$

We have

$$\begin{aligned}\frac{\partial \mathcal{F}}{\partial \lambda}(0,0) = -\frac{pk}{(\mu+\gamma)^2} - \frac{qk}{(\mu+\gamma)^2}\int_0^\infty \eta_1(a)e^{-\mu a}\pi_1(a)\pi(a)da \\ -\frac{qk}{\mu+\gamma}\int_0^\infty \eta_1(a)ae^{-\mu a}\pi_1(a)\pi(a)da < 0.\end{aligned} \tag{4.11}$$

At the bifurcation point we have also k as a function of i^* given by equation (3.20) and therefore

$$k_0 = k(0) = \frac{\mu+\gamma}{p+q\varphi(0)}.$$

Differentiating the function

$$\mathcal{F}(0, i^*) = s^* + qks^*i^*\frac{\mu+\gamma i^*}{\mu(\mu+\gamma)}\varphi'(i^*) - 1$$

we obtain

$$\begin{aligned}\left.\frac{\partial \mathcal{F}}{\partial i^*}\right|_{i^*=0,\lambda=0} &= \frac{\gamma - k_0}{\mu} + \frac{qk_0}{\mu+\gamma}\varphi'(0) \\ &= \frac{1}{\mu(p+q\varphi(0))}[\gamma(p+q\varphi(0)) - (\mu+\gamma) + q\mu\varphi'(0)].\end{aligned} \tag{4.12}$$

The bifurcation is subcritical if and only if

$$\left.\frac{\partial \mathcal{F}}{\partial i^*}\right|_{i^*=0,\lambda=0} > 0.$$

Thus, if the bifurcation is subcritical, we have that

$$\frac{\partial \lambda}{\partial i^*} > 0$$

and the leading eigenvalue becomes positive. Therefore, for small i^*, $\mathcal{E}^*$-unstable. If the bifurcation is supercritical, then

$$\left.\frac{\partial \mathcal{F}}{\partial i^*}\right|_{i^*=0,\lambda=0} < 0$$

and therefore,

$$\frac{\partial \lambda}{\partial i^*} < 0.$$

Thus, for small i^*, the bifurcating forward equilibrium solution is stable.

5. Disease persistence

When a disease is present in a population we would like to know under what circumstances the disease will remain endemic for large time. Consequently, we identify conditions which lead to the persistence of the prevalence (endemicity), that is, conditions that result in the prevalence being bounded away from zero.

We call the disease *uniformly weakly endemic* if there exists some $\epsilon > 0$ independent of the initial conditions such that

$$\limsup_{t\to\infty} I(t) > \epsilon \qquad \text{whenever } I(0) > 0, \tag{5.1}$$

for all solutions of model (2.1).

One of the important implications of uniform weak endemicity of the disease is that the disease-free equilibrium is unstable.

We call the disease *uniformly strongly endemic* if there exists some $\epsilon > 0$ independent of the initial conditions such that

$$\liminf_{t\to\infty} I(t) > \epsilon \qquad \text{whenever } I(0) > 0, \tag{5.2}$$

for all solutions of model (2.1).

It is evident from the definitions that, if the disease is uniformly strongly endemic, it is also uniformly weakly endemic.

Before we show endemicity of the disease, let us demonstrate that uniform weak or strong persistence of the prevalence imply uniform weak or strong persistence of the other disease classes, respectively. We note that from the equation for the susceptibles in (2.1) we have

$$S'(t) > \Lambda - kS - \mu S$$

and, therefore, $\limsup_{t\to\infty} S(t) \geq \liminf_{t\to\infty} S(t) \geq \frac{\Lambda}{k+\mu}$. We also have from the equation for the total population size $N' < \Lambda - \mu N$ and, therefore,

$\liminf_{t\to\infty} N(t) \le \limsup_{t\to\infty} N(t) < \frac{\Lambda}{\mu}$. Given persistence of the prevalence, these inequalities imply persistence of the incidence. Assume (5.1). Then

$$\limsup_{t\to\infty} \frac{S(t)I(t)}{N(t)} > \frac{\mu\epsilon}{k+\mu}. \tag{5.3}$$

Analogously, assuming (5.2) we have

$$\liminf_{t\to\infty} \frac{S(t)I(t)}{N(t)} > \frac{\mu\epsilon}{k+\mu}. \tag{5.4}$$

Inequalities (5.3) and (5.4) lead to the persistence of the remaining epidemiological classes. Integrating along characteristic lines (see Remark A.4), we have

$$E_1(a,t) \ge qk\frac{S(t-a)I(t-a)}{N(t-a)}\pi(a)\pi_1(a)e^{-\mu a}, \qquad t > a.$$

Then, for any fixed a, we respectively have

$$\limsup_{t\to\infty} E_1(a,t) > qk\frac{\mu\epsilon}{k+\mu}\pi(a)\pi_1(a)e^{-\mu a},$$
$$\liminf_{t\to\infty} E_1(a,t) > qk\frac{\mu\epsilon}{k+\mu}\pi(a)\pi_1(a)e^{-\mu a}.$$

We establish uniform weak endemicity first.

Proposition 5.1 *If $\mathcal{R}_0 > 1$, the disease is uniformly weakly endemic.*

Proof. We argue by contradiction. Assume that

$$\limsup_{t\to\infty} I(t) \le \epsilon_0$$

with $0 < \epsilon_0 \le \frac{\Lambda}{2\gamma}$. The total population size satisfies the inequality $N' > \Lambda - \mu N - \epsilon_0\gamma \ge \frac{\Lambda}{2} - \mu N$. Hence,

$$\liminf_{t\to\infty} N(t) \ge \frac{\Lambda}{2\mu}.$$

Consequently,

$$\limsup_{t\to\infty} \frac{I(t)}{N(t)} \le \frac{2\epsilon_0\mu}{\Lambda} =: \frac{\epsilon}{2}.$$

The above inequality implies that for $t > t_1$ we have

$$\frac{I(t)}{N(t)} \le \epsilon.$$

For these values of the proportion of infectives we have $S' \ge \Lambda - k\epsilon S - \mu S$. Reasoning as before, we obtain

$$\limsup_{t\to\infty} \frac{S(t)}{N(t)} \ge \frac{\mu}{k\epsilon+\mu}.$$

Thus, for $t > t_2$ we have

$$\frac{S(t)}{N(t)} \geq \frac{\mu}{2k\epsilon + \mu}.$$

Since $I(s) > 0$ leads to $I(t) > 0$ for all $t \geq s$ we may assume that $I(0) \neq 0$. Consequently, the semiflow properties of the solution (Theorem A.3) imply that without loss of generality we have the above inequalities valid for all $t \geq 0$. Integrating along characteristics (see Remark A.4), the density of the active exposed class can be estimated from below as

$$E_1(a,t) \geq \begin{cases} E_1^0(a-t)\frac{\pi(a)}{\pi(a-t)}\frac{\pi_1(a)}{\pi_1(a-t)}e^{-\mu t}, & a \geq t, \\ qk\frac{\mu}{2k\epsilon+\mu} I(t-a)\pi(a)\pi_1(a)e^{-\mu a}, & a < t. \end{cases}$$

Consequently, the number of infected individuals satisfies the following integro-differential inequality:

$$I' \geq pk\frac{\mu}{2k\epsilon+\mu} I + qk\frac{\mu}{2k\epsilon+\mu}\int_0^t \eta_1(a)\pi(a)\pi_1(a)e^{-\mu a} I(t-a)da - (\mu+\gamma)I$$

where we have omitted the term which corresponds to the initial condition in the right-hand side of the inequality for E_1. Applying Laplace transform to both sides of the above inequality we obtain:

$$\lambda\hat{I} - I(0) \geq pk\frac{\mu}{2k\epsilon+\mu}\hat{I} + qk\frac{\mu}{2k\epsilon+\mu}\hat{I} \times \int_0^\infty e^{-\lambda a}\eta_1(a)\pi(a)\pi_1(a)e^{-\mu a}da - (\mu+\gamma)\hat{I}.$$

We can rewrite the above expression as

$$-I(0) \geq \Bigg[pk\frac{\mu}{(2k\epsilon+\mu)(\mu+\gamma)} \tag{5.5}$$

$$+ qk\frac{\mu}{(2k\epsilon+\mu)(\mu+\gamma)}\int_0^\infty e^{-\lambda a}\eta_1(a)\pi(a)\pi_1(a)e^{-\mu a}da \tag{5.6}$$

$$- \frac{\lambda}{\mu+\gamma} - 1\Bigg](\mu+\gamma)\hat{I}.$$

Since $\mathcal{R}_0 > 1$ the expression in the bracket is positive for $\lambda > 0$ and $\epsilon > 0$ but both sufficiently small. Therefore the right-hand side of this inequality is positive, while the left-hand side is negative which is a contradiction. This completes the proof. □

The proof of uniform strong endemicity is post-poned, because we first need to establish the existence of a global compact attractor for the semiflow that is induced by the solutions of system (2.1) (see Appendix C), but we give a preview of the result.

Theorem 5.1 *If $\mathcal{R}_0 > 1$, the disease is uniformly strongly endemic.*

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Appendix

A. Abstract formulation and well-posedness

The system (2.1) cannot be directly written as an abstract Cauchy problem since the boundary term of E_1 is nonlinear. To cope with the problem we remove the nonlinearity from the boundary condition and incorporate it into the nonlinear operator. As a consequence we obtain a semilinear abstract Cauchy problem of the form

$$\begin{aligned} v'(t) &= \mathcal{A}v + F(v), \\ v(0) &= v^0 \end{aligned} \tag{A.1}$$

in which the operator $\mathcal{A}$ is a linear closed operator but is not densely defined. In general, the differential equation may not have a strong solution. Thus, we solve it in integrated form:

$$v(t) = v^0 + \mathcal{A}\int_0^t v(s)\,ds + \int_0^t F(v(s))\,ds. \tag{A.2}$$

A continuous solution to (A.2) is called an *integral solution* to (A.1).

Let $u = (S, I, E_1, E_2)^T$ with superscript T denoting the transpose of the vector. Throughout this work, $\mathcal{X}$ denotes the space $\mathcal{X} = \mathbf{R} \times \mathbf{R} \times L^1(0,\infty) \times L^1(0,\infty)$ with the following norm:

$$\|u\| = |S| + |I| + \int_0^\infty |E_1(a)|da + \int_0^\infty |E_2(a)|da.$$

To incorporate the boundary condition, we enlarge the state space by setting $X = \mathcal{X} \times \mathbf{R}$. We also set $X^\circ = \mathcal{X} \times \{0\}$. The positive cone in the corresponding space is denoted by subscript $_+$. For any vector $u = (u_1, u_2, u_3, u_4)^T \in \mathcal{X}$, let $v = (u, 0)^T \in X^\circ$. We introduce a linear functional $\mathcal{N}(v) : X^\circ \to \mathbf{R}$ as follows $\mathcal{N}(v) = u_1 + u_2 + \int_0^\infty u_3(a)\,da + \int_0^\infty u_4(a)\,da$. Now we are prepared to define the linear operator $\mathcal{A} : \mathcal{D}(\mathcal{A}) \to X$:

$$\mathcal{A}v = \begin{pmatrix} -\mu u_1 \\ -(\mu+\gamma)u_2 \\ -(\frac{\partial}{\partial a} + \rho(a) + \eta_1(a) + \mu)u_3 \\ -\mu u_4 \\ -u_3(0) \end{pmatrix}$$

with domain

$$\mathcal{D}(\mathcal{A}) = \{v \in X_+^\circ : u_3(\cdot) \in W_1^1[0,\infty)\}.$$

It can be seen that $\overline{\mathcal{D}(\mathcal{A})} = X^\circ$, but the operator $\mathcal{A}$ is not densely defined in X and therefore it cannot be the generator of a C_0-semigroup. We also introduce a

nonlinear operator $F : X^\circ \to X$:

$$F(v)(a) = \begin{pmatrix} \Lambda - k\dfrac{u_1 u_2}{\mathcal{N}(v)} \\ pk\dfrac{u_1 u_2}{\mathcal{N}(v)} + \displaystyle\int_0^\infty \eta_1(a)u_3(a)\,da \\ \tilde{k}(a)\dfrac{u_4 u_2}{\mathcal{N}(v)} \\ \rho(a)u_3(a) - \tilde{k}(a)\dfrac{u_4 u_2}{\mathcal{N}(v)} \\ qk\dfrac{u_1 u_2}{\mathcal{N}(v)} \end{pmatrix} \tag{A.3}$$

The operator F above is not defined when $v = 0$. We assign values to the fractions $\frac{u_1 u_2}{\mathcal{N}(v)}$ and $\frac{u_4 u_2}{\mathcal{N}(v)}$ as follows: $\frac{u_1 u_2}{\mathcal{N}(v)} = 0$ and $\frac{u_4 u_2}{\mathcal{N}(v)} = 0$ when $v = 0$. This extends the domain of F to include $v = 0$.

The following proposition asserts that F is Lipschitz continuous.

Proposition A.1 *There exists a constant L such that*

$$\|F(v) - F(\bar{v})\| \le L\|v - \bar{v}\|$$

for every two elements $v, \bar{v} \in X^\circ$.

The resolvents of the operator $\mathcal{A}$ satisfy the estimates of the Hille-Yosida theorem:

Proposition A.2 *The operator $\mathcal{A}$ is a closed linear operator such that $\lambda - \mathcal{A}$ has a bounded inverse for $\lambda > -\mu$ and*

$$\|(\lambda - \mathcal{A})^{-n}\| \le \frac{1}{(\lambda + \mu)^n} \tag{A.4}$$

for all positive integers n.

Proof. For an element $f \in X$ with coordinates $f = (f_1, f_2, f_3, f_4, \xi)$ consider the equation $(\lambda - \mathcal{A})v = f$. Solving the system we obtain:

$$\begin{aligned} v &= (\lambda - \mathcal{A})^{-1} f \\ &= \begin{pmatrix} \dfrac{f_1}{(\lambda + \mu)} \\ \dfrac{f_2}{(\lambda + \mu + \gamma)} \\ \xi\pi(a)\pi_1(a)e^{-(\lambda+\mu)a} + \displaystyle\int_0^a \frac{\pi(a)}{\pi(s)}\frac{\pi_1(a)}{\pi_1(s)}e^{-(\mu+\lambda)(a-s)} f_3(s)\,ds \\ \dfrac{f_4}{(\lambda + \mu)} \\ 0 \end{pmatrix} \end{aligned} \tag{A.5}$$

Integrating the third and fourth terms with respect to a (assuming that $\lambda > -\mu$) and adding the absolute values of the remaining terms leads to estimate (A.4). □

Now, we are ready to show the main result of this section – the well-posedness of the system (2.1). Notice that the state space X_+° can be identified with $\mathcal{X}_+$.

Theorem A.3 *The system of equations (2.1) represented by the integral equation (A.2) has a unique continuous solution with values in X_+°. Moreover the map $\Psi : [0, \infty) \times X_+ \to X_+$ defined by $\Psi(t, v^0) = v(t)$ is a continuous semiflow, i.e., the map Ψ is continuous and $\Psi(t, \Psi(s, \cdot)) = \Psi(t + s, \cdot)$ and $\Psi(0, \cdot)$ is the identity map. Finally Ψ satisfies an exponential Lipschitz condition: There exist $M \geq 1$ and $\omega \in \mathbf{R}$ such that*

$$\|\Psi(t, v^0) - \Psi(t, w^0)\| \leq Me^{\omega t}\|v^0 - w^0\| \qquad \forall t \geq 0, v^0, w^0 \in X_+.$$

Proof. This result is a direct consequence of Theorem 2.3 and Theorem 3.2 in [43]. Propositions A.1 and A.2 guarantee that the Assumptions 2.1 and 3.1 in [43] are satisfied. To use Theorem 2.3 in [43] we have to establish the following two conditions

(a) $\lambda(\lambda - \mathcal{A})^{-1}$ maps X_+ into itself for sufficiently large λ.

(b) $\frac{1}{h}\operatorname{dist}(v + hF(v), X_+) \to 0$ as $h \searrow 0, t \geq 0, v \in X_+^\circ$.

For any $f \in X_+$, with $f = (f_1, f_2, f_3, f_4, \xi)$ and $\lambda > -\mu$ we have that $(\lambda - \mathcal{A})^{-1} f$ is given by the expression (A.5). Therefore, $(\lambda - \mathcal{A})^{-1}$ maps X_+ in itself and condition (a) is satisfied for any $\lambda > 0$. To see condition (b) consider the nonlinear operator

$$\hat{F}(v) = F(v) + \alpha v$$

where the real positive number α is chosen so that $\alpha > \max\{k, \sup_{a\in[0,\infty)} \tilde{k}(a)\}$. We note that the operator $\hat{F}$ maps the positive cone of X° into the positive cone of X, that is, $\hat{F} : X_+^\circ \to X_+$. Thus, for any positive and sufficiently small h and any $v \in X_+^\circ$, we have

$$\frac{1}{h}\operatorname{dist}(v + hF(v); X_+) = \frac{1}{h}\operatorname{dist}(v - \alpha hv + h\hat{F}(v); X_+) = 0.$$

The last equality is valid since for h sufficiently small $v - \alpha hv \in X_+$ and $h\hat{F}(v) \in X_+$. □

Though (2.1) is not satisfied in a strict sense, but only in the integral sense of (A.2), we would like to use integration along characteristics for the PDE and also be able to integrate the PDE in time. We show that this is still possible.

Remark A.4. The equation for the active exposed class, E_1, in (2.1) is of the form

$$\begin{aligned} (\partial_t + \partial_a)E_1 &= -\nu(a)E_1 + F(a, t), \\ E_1(0, t) &= B(t), \\ E_1(a, 0) &= f(a), \end{aligned} \tag{A.6}$$

where f and $F(\cdot, t)$ are in $L_1[0, \infty)$. The result that the vector-valued function v is a solution of (A.2) means for E_1 that it solves this equation after integrating over

both t and a,

$$\begin{aligned}\int_0^a (E_1(r,t) - f(r))dr + \int_0^t (E_1(a,s) - B(s))ds \\ = -\int_0^t \int_0^a \nu(r)E_1(r,s)drds + \int_0^t \int_0^a F(r,s)drds, \qquad t,a \geq 0.\end{aligned} \tag{A.7}$$

(A.7) has at most one solution. Set $\pi_2(a) = e^{-\int_0^a \nu(r)dr}$. Integrating along characteristics, the partial differential equation (A.6) has the formal solution

$$E_1(a,t) = \begin{cases} f(a-t)\frac{\pi_2(a)}{\pi_2(a-t)} + \int_0^t F(a-s,t-s)\frac{\pi_2(a)}{\pi_2(a-s)}ds, & a > t, \\ B(t-a)\pi_2(a) + \int_0^a F(a-s,t-s)\frac{\pi_2(a)}{\pi_2(a-s)}ds, & a < t. \end{cases} \tag{A.8}$$

This solution only satisfies the partial differential equation (A.6) under smoothness and compatibility assumptions; however, it always solves the integral equation (A.2) as one can see by an elementary, though lengthy computation.

We take the limit in (A.7) for $a \to \infty$. As $\int_0^t E_1(\cdot,s)ds \in W_1^1[0,\infty)$, it tends to 0 as $a \to \infty$ and we obtain

$$\begin{aligned}\int_0^\infty (E_1(r,t) - f(r))dr - \int_0^t B(s)ds \\ = -\int_0^t \int_0^\infty \nu(r)E_1(r,s)drds + \int_0^t \int_0^\infty F(r,s)drds, \qquad t \geq 0.\end{aligned}$$

Hence we can differentiate in time and obtain

$$\frac{d}{dt}\int_0^\infty E_1(a,t)da = B(t) + \int_0^\infty F(a,t)da - \int_0^\infty \nu(a)E_1(a,t)da. \tag{A.9}$$

B. Connection between the roots of the characteristic equation and the stability of equilibria

For models in ODEs establishing that the characteristic equation has only roots with negative real part directly leads to the conclusion that the the corresponding equilibrium point is locally stable. This is not the case with PDEs where the roots of the characteristic equation only give information about the eigenvalues of the generator of the solution semigroup connected to the linear system of perturbations but not about the spectrum of the semigroup itself. Semigroups for which there is a relation between the eigenvalues of the generator and the long-time behavior of the semigroup include compact, eventually compact, quasi-compact and eventually uniformly continuous semigroups.

Let $v^* = (u^*, 0)^T$ be an equilibrium of (A.1). To establish the local stability we use the following theorem which is a special case of Theorem 2.10 in [3], Chapter B-IV.

Theorem B.1 *Let $T(t)$ be a quasi-compact C_0-semigroup and A its infinitesimal generator. Then $e^{\epsilon t}\|T(t)\| \to 0$ as $t \to \infty$ for some $\epsilon > 0$ if and only if all eigenvalues of A have strictly negative real part.*

We note that $T(t)$ is called *quasi-compact* if $T(t) = T_1(t) + T_2(t)$ with operator families $T_1(t)$ and $T_2(t)$ such that $\|T_1(t)\| \to 0$ as $t \to \infty$, and $T_2(t)$ is eventually compact, that is, there exists $t_0 > 0$ such that $T_2(t)$ is a compact operator for all $t > t_0$.

We write the solution of (A.1) in the form $v(t) = v^* + \chi(t)$ where the vector of the perturbations $\chi(t) \in X^\circ$ for every t and has components $(x, y, z, w, 0)$. Furthermore, we note that the operator F given by (A.3) is Frèchet differentiable for every v^* (except $v^* = 0$). Thus, the linearized problem for the perturbations reads

$$\begin{aligned} \chi'(t) &= \mathcal{A}\chi(t) + F'(v^*)\chi(t), \\ \chi(0) &= \chi^0 \end{aligned} \tag{B.1}$$

We rewrite the linearized problem (B.1) in the following form:

$$\begin{aligned} \chi'(t) &= \mathcal{B}\chi(t) + \mathcal{K}\chi(t), \\ \chi(0) &= \chi^0 \end{aligned} \tag{B.2}$$

where $\mathcal{B} : X^\circ \to X$ is defined as follows

$$\mathcal{B}\chi = \begin{pmatrix} -\mu x \\ -(\mu+\gamma)y \\ -(\frac{\partial}{\partial a} + \rho(a) + \eta_1(a) + \mu)z + \tilde{k}(a)i^*w \\ \rho(a)z - (\tilde{k}(a)i^* + \mu)w \\ -z(0) \end{pmatrix}$$

with $\mathcal{D}(\mathcal{B}) = \mathcal{D}(\mathcal{A})$. The operator $\mathcal{K} : X^\circ \to X$ is defined as follows

$$\mathcal{K}\chi = \begin{pmatrix} -ks^*y - ki^*x + ks^*i^*\mathcal{N}(\chi) \\ pks^*y + pki^*x - pks^*i^*\mathcal{N}(\chi) + \int_0^\infty \eta_1(a)z(a)\,da \\ \tilde{k}(a)e_2^*(a)y - \tilde{k}(a)e_2^*(a)i^*\mathcal{N}(\chi) \\ -\tilde{k}(a)e_2^*(a)y + \tilde{k}(a)e_2^*(a)i^*\mathcal{N}(\chi) \\ qks^*y + qki^*x - qks^*i^*\mathcal{N}(\chi) \end{pmatrix}. \tag{B.3}$$

Clearly, $\mathcal{K}$ is a bounded perturbation $\mathcal{B}$. Moreover, $\mathcal{K}$ is compact. We note that $\mathcal{A} + F'(v^*) = \mathcal{B} + \mathcal{K}$.

Next, we observe that the powers of the resolvents of $\mathcal{B}$ satisfy the Hille-Yosida estimate.

Theorem B.2 *The operator $\mathcal{B}$ is a closed linear operator such that $\lambda - \mathcal{B}$ has a bounded inverse for $\lambda > -\mu$ and*

$$\|(\lambda - \mathcal{B})^{-n}\| \leq \frac{1}{(\lambda+\mu)^n} \tag{B.4}$$

for all positive integers n.

Proof. For an element $f \in X_+$ with coordinates $f = (f_1, f_2, f_3, f_4, \xi)$ consider the equation $(\lambda - \mathcal{B})v = f$ with $\lambda > -\mu$. This results in the system:

$$\begin{aligned}
&(\lambda + \mu)x = f_1\\
&(\lambda + \gamma + \mu)y = f_2\\
&z' = -(\lambda + \rho(a) + \eta_1(a) + \mu)z + \tilde{k}(a)i^* w + f_3\\
&z(0) = \xi\\
&(\lambda + \tilde{k}(a)i^* + \mu)w = \rho(a)z + f_4.
\end{aligned} \tag{B.5}$$

Clearly, $x \geq 0$ and $y \geq 0$. The system for $z(a)$ and $w(a)$ can be explicitly solved. We have

$$\begin{aligned}
z(a) \;&= \xi\pi_1(a)e^{-(\lambda+\mu)a}e^{-\int_0^a \frac{\rho(\sigma)(\lambda+\mu)}{(\lambda+\tilde{k}(\sigma)i^*+\mu)}\,d\sigma}\\
&\quad + \int_0^a \frac{\pi_1(a)}{\pi_1(s)}e^{-(\mu+\lambda)(a-s)}e^{-\int_s^a \frac{\rho(\sigma)(\lambda+\mu)}{(\lambda+\tilde{k}(\sigma)i^*+\mu)}\,d\sigma}\,\breve{f}(s)\,ds,
\end{aligned}$$

where

$$\breve{f}(a) = \frac{f_4}{(\lambda + \tilde{k}(a)i^* + \mu)} + f_3(a).$$

We have $z(a) \geq 0$, and therefore, $w(a) \geq 0$. In addition, $z(a), w(a) \in L^1[0, \infty)$. Thus, the solution of the system (B.5) is nonnegative. Next, we note that $z(a) \to 0$ as $a \to \infty$. Indeed, this is certainly true for the first term. The second term is dominated by

$$\int_0^\infty e^{-(\mu+\lambda)(a-s)}\,\breve{f}(s)\,ds.$$

Thus the functions $e^{-(\mu+\lambda)(a-s)}\breve{f}(s) \to 0$ pointwise for every s. These functions are also dominated by $\breve{f}(s)$ which is integrable. Consequently, the Lebesgue dominated convergence theorem implies the result.

Integrating the equations for z and w in the age variable and adding all equations we obtain for $\lambda > -\mu$:

$$|x| + |y| + \|z\| + \|w\| \leq \frac{1}{\lambda + \mu}(|\xi| + |f_1| + |f_2| + \|f_3\| + \|f_4\|).$$

Hence, for $f \in X_+$ we have

$$\|(\lambda - \mathcal{B})^{-1} f\| \leq \frac{1}{(\lambda + \mu)}\|f\|.$$

To conclude the proof it remains to notice that if $f \in X$ we have $\|(\lambda - \mathcal{B})^{-1} f\| \leq \|(\lambda - \mathcal{B})^{-1}|f|\|$. Consequently, the claim follows. □

The part of $\mathcal{B}$ in X° is a densely defined operator whose resolvents satisfy the Hille-Yosida estimates and is, therefore ([38]), the generator of a C_0-semigroup on X°, $S(t)$. The Hille-Yosida estimate in addition implies that

$$\|S(t)\| \leq e^{-\mu t}.$$

Moreover, since $\mathcal{K}$ is a bounded perturbation, the part of $\mathcal{B}+\mathcal{K}$ in X° also generates a C_0-semigroup on X°, $T(t)$. Furthermore, $\mathcal{K}S(t) : X^\circ \to X$ is compact for every $t > 0$. Consequently, all conditions of part (b), Theorem 3 in [45] are satisfied and $T(t)$ is quasi-compact. By Theorem B.1 we have $e^{\epsilon t}\|T(t)\| \to 0$ as $t \to \infty$ whenever the eigenvalues of $\mathcal{B} + \mathcal{K}$ have negative real part. This, in particular, implies that the growth bound of $T(t)$ does not exceed $-\epsilon$ and is clearly negative. In addition, since the essential type of $T(t)$ is smaller or equal to the growth bound of $T(t)$ then it is also negative.

Proposition A.1, Proposition A.2 and the proof of Theorem A.3 imply that Assumptions 3.1 in [43] are satisfied. The operator F is continuously Frèchet differentiable in $X_+^\circ \setminus \{0\}$. Thus, the nonlinear semiflow $\Psi(t, v^0)$ of the solutions of (2.1) satisfies the following properties which follow from Corollary 4.3 in [43]:

i) If all eigenvalues of $\mathcal{A} + F'(v^*)$ have strictly negative real part, then there exists $\omega < 0$ and constants $c > 0$ and $\delta > 0$ such that

$$\|\Psi(t, v^0) - v^*\| \leq ce^{\omega t}\|v^0 - v^*\| \tag{B.6}$$

for all $v^0 \in X_+^\circ \setminus \{0\}$ with $\|v^0 - v^*\| \leq \delta$.

Inequality (B.6) implies that if v^* is an equilibrium such that all eigenvalues of $\mathcal{A} + F'(v^*)$ have negative real part then v^* is locally asymptotically stable, that is, trajectories which start sufficiently close to the steady state v^* remain close and return to the steady state when time tends to infinity.

ii) If at least one eigenvalue of $\mathcal{A} + F'(v^*)$ has strictly positive part, then v^* is unstable steady state, that is, there exists a constant $\varepsilon > 0$ and a sequence of initial conditions $v_j^0 \to v^*$ in $X_+^\circ \setminus \{0\}$ and $t_j \to \infty$ such that

$$\|\Psi(t_j, v_j^0) - v^*\| \geq \varepsilon$$

for all integer j.

We note that Corollary 4.3 in [43] remains valid with this relaxed condition on the differentiability of F since its proof is along the lines of [15] where the results are established with weaker assumptions.

C. Uniform strong persistence

The semiflow Ψ defined by the solution of (2.1) as follows

$$\Psi(t, S^0, I^0, E_1^0, E_2^0) = (S(t), I(t), E_1(\cdot, t), E_2(\cdot, t))$$

is a mapping $\Psi : [0, \infty) \times \mathcal{X}_+ \to \mathcal{X}_+$ with $\Psi(t, \Psi(s, \cdot)) = \Psi(t + s, \cdot)$ for all $t, s \geq 0$ and $\Psi(0, \cdot)$ being the identity map. A set K in $\mathcal{X}_+$ is called a *global compact attractor* for Ψ, if K is a maximal compact invariant set and if for all open sets U containing K and all bounded sets B of $\mathcal{X}_+$ there exists some $r > 0$ such that $\Psi(t, B) \subseteq U$ for all $t \geq r$. See [30], Section 3.4.

Proposition C.1 *The semiflow Ψ has a global compact attractor.*

Proof. We show that Ψ satisfies the assumptions of Lemma 3.2.3 and Theorem 3.4.6 in [30]. To this end we additively split the solution semiflow Ψ into two components $\Psi(t, u^0) = \hat{\Psi}(t, u^0) + \tilde{\Psi}(t, u^0)$ such that $\hat{\Psi}(t, u^0) \to 0$ as $t \to \infty$ for every $u^0 \in \mathcal{X}$, and for a fixed t and any bounded set B in $\mathcal{X}_+$, the set $\{\tilde{\Psi}(t, u^0) : u^0 \in B\}$ is precompact. The two summands are defined as follows:

$$\hat{\Psi}(t, S^0, I^0, E_1^0, E_2^0) = (0, 0, \hat{E}_1(\cdot, t), \hat{E}_2(\cdot, t));$$
$$\tilde{\Psi}(t, S^0, I^0, E_1^0, E_2^0) = (S(t), I(t), \tilde{E}_1(\cdot, t), \tilde{E}_2(\cdot, t)).$$

We note that $S(t)$ and $I(t)$ satisfy the system (2.1) with $E_1 = \hat{E}_1 + \tilde{E}_1$ and $E_2 = \hat{E}_2 + \tilde{E}_2$. The functions $\hat{E}_1(\cdot, t)$, $\hat{E}_2(\cdot, t)$ satisfy the system:

$$\begin{aligned}
&(\partial_t + \partial_a)\hat{E}_1 = -\rho(a)\hat{E}_1 + \tilde{k}(a)\frac{\hat{E}_2 I}{N} - \eta_1(a)\hat{E}_1 - \mu\hat{E}_1\\
&\hat{E}_1(0, t) = 0\\
&\hat{E}_1(a, 0) = E_1^0(a)\\
&\partial_t \hat{E}_2 = \rho(a)\hat{E}_1 - \tilde{k}(a)\frac{\hat{E}_2 I}{N} - \mu\hat{E}_2\\
&\hat{E}_2(a, 0) = E_2^0(a).
\end{aligned} \tag{C.1}$$

The system for $\hat{E}_1$ and $\hat{E}_2$ together with the first two equations of the system (2.1) forms a system which is a special case of (2.1) obtained for $q = 0$. This, in particular implies that the functions $\hat{E}_1$ and $\hat{E}_2$ are nonnegative. The functions $\tilde{E}_1$ and $\tilde{E}_2$ are solutions to the system

$$\begin{aligned}
&(\partial_t + \partial_a)\tilde{E}_1 = -\rho(a)\tilde{E}_1 + \tilde{k}(a)\frac{\tilde{E}_2 I}{N} - \eta_1(a)\tilde{E}_1 - \mu\tilde{E}_1\\
&\tilde{E}_1(0, t) = qk\frac{SI}{N}\\
&\tilde{E}_1(a, 0) = 0\\
&\partial_t \tilde{E}_2 = \rho(a)\tilde{E}_1 - \tilde{k}(a)\frac{\tilde{E}_2 I}{N} - \mu\tilde{E}_2\\
&\tilde{E}_2(a, 0) = 0.
\end{aligned} \tag{C.2}$$

The partial differential equations are not satisfied in a strict, but an integral sense. See Remark A.4. Moreover, the functions $\tilde{E}_1$ and $\tilde{E}_2$ are nonnegative. First we show that $\hat{\Psi} \to 0$ as $t \to \infty$. Denote by $\nu(t) = \int_0^\infty \hat{E}_1(a, t)\, da + \int_0^\infty \hat{E}_2(a, t)\, da$. Integrating the equations for $\hat{E}_1$ and $\hat{E}_2$ over $a \in [0, \infty)$ (see Remark A.4 for justification) and adding them, we obtain the inequality $\nu'(t) \le -\mu\nu(t)$. Thus, $\nu(t) \le \nu(0)e^{-\mu t}$. Consequently, $\|\hat{\Psi}(t, u)\| \le e^{-\mu t}\|u\|$, i.e., the function $k(t, r)$ in Lemma 3.2.3 [30] can be chosen as $k(t, r) = e^{-\mu t}r$.

Since $\hat{E}_j$ and $\tilde{E}_j$ are non-negative, $\hat{\Psi} \le \Psi$ and $\tilde{\Psi} \le \Psi$.

Notice that $\|\Psi(t, u_0)\| = N(t)$ where

$$N' \le \Lambda - \mu N,$$

and

$$N(t) \le \left(\|u_0\| + \frac{\Lambda}{\mu}\right)e^{-\mu t} + \frac{\Lambda}{\mu}.$$

Several things can be learned from these two inequalities. First, every ball with radius $r > \Lambda/\mu$ is invariant and attracts all bounded sets. In other words, Ψ is bounded dissipative ([30], Section 3.4). Secondly the orbits of all bounded sets are bounded, i.e., for every $c_1 > 0$ there exists some $c_2 > 0$ such that $\|\Psi(t, u_0)\| \leq c_2$ for all $t \geq 0$ whenever $\|u_0\| \leq c_1$. $\hat{\Psi}$ and $\tilde{\Psi}$ also have this property.

Next, suppose the initial data are in a bounded set, e.g. a ball, that is

$$\|u_0\| = |S^0| + |I^0| + \|E_1^0\| + \|E_2^0\| \leq K \tag{C.3}$$

where K is some constant. We show that for a fixed time t the family of functions

$$(S(t), I(t), \tilde{E}_1(\cdot, t), \tilde{E}_2(\cdot, t)) = \tilde{\Psi}(t, u_0)$$

obtained from taking different initial conditions in the set (C.3) is a compact family of functions. Then Ψ will be asymptotically smooth by Lemma 3.2.3 and have a global compact attractor by Theorem 3.4.6 in [30].

By our previous observations, the set $\{\Psi(t, u_0); t \geq 0, \|u_0\| \leq K\}$ is bounded. Furthermore, we observe that $\tilde{E}_1(a, t) = 0$ for $a > t$. Indeed, integrating (C.2) along the characteristic lines (see Remark A.4 for justification), we obtain

$$\tilde{E}_1(a, t) \leq \tilde{k}_{\max} \int_0^t \tilde{E}_2(a - t + \sigma, \sigma)\, d\sigma.$$

Integrating the equation for $\tilde{E}_2(a, t)$ we obtain the following estimate for $\tilde{E}_2(a, t)$:

$$\tilde{E}_2(a, t) \leq \bar{\rho} \int_0^t \tilde{E}_1(a, s)\, ds.$$

Substituting in the inequality for $\tilde{E}_1$ we obtain

$$\tilde{E}_1(a, t) \leq \bar{\rho}\tilde{k}_{\max} \int_0^t \int_0^\sigma \tilde{E}_1(a - t + \sigma, s)\, ds\, d\sigma.$$

Choose a positive number ξ such that $\frac{\bar{\rho}\tilde{k}_{\max}}{\xi^2} < 1$. Consequently,

$$\sup_{0 \leq t \leq a \leq A} e^{-\xi t} \tilde{E}_1(a, t) \leq \int_0^t \int_0^\sigma e^{-\xi(t-s)} \sup_{0 \leq s \leq a-t+\sigma \leq A} \tilde{E}_1(a - t + \sigma, s) e^{-\xi s}\, ds\, d\sigma$$

for any positive constant A. Denote by z the left hand side of this inequality. Then we have

$$z \leq \bar{\rho}\tilde{k}_{\max} z \int_0^t \int_0^\sigma e^{-\xi(t-s)}\, ds\, d\sigma.$$

Therefore, $z \leq \frac{\bar{\rho}\tilde{k}_{\max}}{\xi^2} z$ which can only be satisfied if $z = 0$.

To show compactness we use the Frèchet-Kolmogorov theorem for compactness in L^1 (see e.g. [48]). We have already established the boundedness of the set. The third condition is trivially satisfied since $\tilde{E}_1(a, t) = 0$ for $a > t$. To see the

second condition of that criterion we integrate $\tilde{E}_1$ along the characteristic lines. See Remark A.4. For $a \leq t$ we have:

$$\tilde{E}_1(a,t) = qk\frac{SI}{N}(t)\pi(a)\pi_1(a)e^{-\mu a} + \int_0^a \frac{\pi(a)}{\pi(\sigma)}\frac{\pi_1(a)}{\pi_1(\sigma)}e^{-\mu(a-\sigma)}\tilde{k}(\sigma)\tilde{E}_2(\sigma, t-a+\sigma)\frac{I}{N}(t-a+\sigma)\,d\sigma \tag{C.4}$$

Next, we integrate $\tilde{E}_2$:

$$\tilde{E}_2(a,t) = \rho(a)\int_0^t e^{-\mu(t-s)}e^{-\tilde{k}(a)\int_s^t \frac{I}{N}(\sigma)\,d\sigma}\tilde{E}_1(a,s)\,ds \tag{C.5}$$

Differentiating $\tilde{E}_1(a,t)$ with respect to a and using the expressions for I', N' from (2.1) and $\partial_t \tilde{E}_2$ from (C.2) we obtain the follow estimate for the L^1-norm of that derivative:

$$\|\partial_a \tilde{E}_1(t)\| \leq K_1 + K_2 t$$

where K_1 and K_2 are constants which depend on the parameters of the model and the constant K from (C.3) but do not depend on t. Next, we consider $\tilde{E}_2$. We use directly the second condition in the Frèchet-Kolmogorov theorem. Given ϵ, let h be small and consider

$$\begin{aligned}
&\int_0^\infty |\tilde{E}_2(a+h,t) - \tilde{E}_2(a,t)|\,da \\
&\quad\leq \int_0^\infty \rho(a+h) \\
&\qquad\times \left(\int_0^t e^{-\mu(t-s)}e^{-\tilde{k}(a+h)\int_s^t \frac{I}{N}(\sigma)\,d\sigma}|\tilde{E}_1(a+h,s) - \tilde{E}_1(a,s)|\,ds\right)da \\
&\qquad+ \int_0^\infty \rho(a+h) \\
&\qquad\times \left(\int_0^t e^{-\mu(t-s)}|e^{-\tilde{k}(a+h)\int_s^t \frac{I}{N}(\sigma)\,d\sigma} - e^{-\tilde{k}(a)\int_s^t \frac{I}{N}(\sigma)\,d\sigma}|\tilde{E}_1(a,s)\,ds\right)da \\
&\qquad+ \int_0^\infty |\rho(a+h) - \rho(a)|\left(\int_0^t e^{-\mu(t-s)}e^{-\tilde{k}(a+h)\int_s^t \frac{I}{N}(\sigma)\,d\sigma}\tilde{E}_1(a,s)\,ds\right)da
\end{aligned} \tag{C.6}$$

To estimate the first integral uniformly in the family of functions we observe that

$$\int_0^\infty |\tilde{E}_1(a+h,s) - \tilde{E}_1(a,s)|\,da \leq \|\partial_a \tilde{E}_1\||h|$$

Thus, the first integral can be made arbitrary small uniformly in the family of functions $S, I, \tilde{E}_1, \tilde{E}_2$ since the L^1-norms of the age-derivative of $\tilde{E}_1$ are uniformly

bounded. Next, to estimate the second integral we use the following inequality for the exponent: let $0 \leq x, y \leq M$, then

$$|e^{-x} - e^{-y}| \leq \frac{e^{2M}}{2M}|x - y|.$$

Furthermore, the uniform continuity of $\tilde{k}$ implies that the second integral can be made arbitrary small independently of the family of functions. The last integral can be made arbitrary small uniformly in the family since ρ is uniformly continuous. This completes the proof of the compactness of $\tilde{\Psi}$. □

We use this result to show uniform strong endemicity.

Proof of Theorem 5.1. We apply Theorem 2.6 in [44]. We consider the solution semiflow Ψ on $\mathcal{X}$ with $\mathcal{X}$ as defined in Appendix A. We define a functional $\phi : \mathcal{X} \to \mathbf{R}_+$ as follows

$$\phi(\Psi(t, S^0, I^0, E_1^0, E_2^0)) = I(t).$$

By Proposition 5.1, the semiflow is uniformly weakly ϕ-persistent. By Proposition C.1, the solution semiflow has a compact attracting set. Total orbits are solutions to the system (2.1) defined for all times both positive and negative. Since the solution semiflow is nonnegative we have that for any s and any $t > s$

$$I(t) \geq I(s)e^{-(\mu+\gamma)(t-s)}.$$

Therefore, $I(t) > 0$ for all $t > s$, provided $I(s) > 0$. Thus Theorem 2.6 in [44] implies that the semiflow is uniformly strongly ϕ-persistent. Consequently, there exists ϵ so that $\liminf_{t\to\infty} I(t) > \epsilon$. □

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