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Global stability properties of a renewal epidemic model

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Abstract We investigate the global dynamics of a general Kermack-McKendrick-type epidemic model formulated in terms of a system of renewal equations. Specifically, we consider a renewal model for which both the force of infection and the infected removal rates are arbitrary functions of the infection age, τ, and use the direct Lyapunov method to establish the global asymptotic stability of the equilibrium solutions. In particular, we show that the basic reproduction number, R_0, represents a sharp threshold parameter such that for $R_0 \leq 1$, the infection-free equilibrium is globally asymptotically stable; whereas the endemic equilibrium becomes globally asymptotically stable when $R_0 > 1$, i.e. when it exists.

Keywords global stability, Lyapunov, renewal, Kermack-McKendrick

1 Introduction

The classic Kermack-McKendrick paper (Kermack and McKendrick, 1927) is a seminal contribution to the mathematical theory of epidemic modelling. Within, the authors formulate a general epidemic model in which the infectiousness of infected individuals and the rate at which they recover or are removed is an arbitrary function of the infection age, τ; from this, they derive several fundamental results including the conditions for an epidemic outbreak and the final size equation. As a consequence of their general formulation, the

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analysis and conclusions of the Kermack-McKendrick paper encompass a wide class of epidemic models, including countless incarnations that have since appeared in the infectious diseases modelling literature (e.g. the SIR and SEIR models).

In this article we revisit the classic Kermack-McKendrick model (Kermack and McKendrick, 1927) and further investigate the system properties and global dynamics in the presence of demographic influences. Our main result, which is derived in section 3, is to show that the basic reproduction number R_0 represents a sharp threshold parameter that determines the global stability of the infection-free and endemic equilibria. Specifically, we find that when $R_0 \leq 1$ the infection-free equilibrium point is the unique equilibrium in the nonnegative orthant and is globally asymptotically stable within this region. Conversely, when $R_0 > 1$ an endemic solution emerges in the interior of this region which is globally asymptotically stable away from the invariant S-axis. Both of these results are proved by the direct Lyapunov method, that is, by identifying appropriate Lyapunov functionals.

Lyapunov functions have previously been used to establish the global asymptotic stability properties of SIR, SIS and SIRS models (see e.g. (Korobeinikov, 2004)) for which the population is either constant (Korobeinikov and Wake, 2002; O'Regan et al, 2010) or varying (Li and Muldowney, 1995; Li et al, 1999). These results have also been extended to SEIR and SEIS models in (Fan et al, 2001; Li and Muldowney, 1995; Li et al, 1999; McCluskey, 2008), and epidemic models with multiple parallel infectious stages (Korobeinikov, 2008) or strains (Bichara et al, 2013). However, these results have each been established within the context of compartmental-type epidemic models for which the per-capita flow rates between the stages of infection are assumed to be constant and infectiousness is fixed for the duration of their infectious period.

Only recently, by using an approach that relied on both the direct Lyapunov method and semigroup theory, were (Magal et al, 2010) able to determine the global stability properties of equilibria in infection-age models. This work has since been expanded (McCluskey, 2008, 2009, 2010a) and extended to models with general incidence functions (Chen et al, 2016; Huang and Takeuchi, 2011; McCluskey, 2010b; Soufiane and Touaoula, 2016) and multiple parallel infectious stages (Wang and Liu, 2012) or strains (Martcheva and Li, 2013). Here, we provide an alternative treatment given in terms of the original renewal formulation of the Kermack-McKendrick model.

In the next section we briefly describe the renewal system variables, parameters and their governing equations, and then discuss the system phase-space. Then, in section 3, we derive the main result of this article where we introduce a set of Lyapunov functionals which we use to establish the global asymptotic stability of the infection-free and endemic equilibria.

2 Model description

In the renewal formulation of the Kermack-McKendrick model we need only explicitly consider a class of susceptible (i.e. infection-naïve) individuals, S, who each experience a time-dependent force of infection $F(t)$.[1] By definition, the force of infection is the per-capita rate at which susceptibles become infected. Therefore the incidence at time t, $v(t)$, is given by

$$v(t) = F(t)S(t),$$

where $S(t)$ is the number of susceptibles and $v(t)$ describes the rate at which new infected individuals appear at time t. Assuming then that individuals who have been infected for τ units of time on average contribute an amount $A(\tau)$ to the force of infection, we find that the total force of infection at time t, $F(t)$, can be written in terms of a renewal equation:

$$\begin{aligned} F(t) &= \int_0^\infty A(\tau)v(t-\tau)\,d\tau, \\ &= \int_0^\infty A(\tau)F(t-\tau)S(t-\tau)\,d\tau. \end{aligned}$$

Here $v(t-\tau)$ represents the number of individuals who became infected at time $t-\tau$.

In general, the infectivity kernel $A \geq 0$ is an arbitrary function of the infection age τ whose definition motivates us, in analogy with (Magal et al, 2010), to define

$$\bar{\tau} = \sup\left\{\tau \geq 0 \,:\, A(\tau) > 0\right\}, \tag{1}$$

the maximum infection age at which an individual can contribute to the force of infection. In this case we need only look back to this maximum infection age to calculate $F(t)$:

$$\begin{aligned} F(t) &= \int_0^{\bar{\tau}} A(\tau)v(t-\tau)\,d\tau, \\ &= \int_0^{\bar{\tau}} A(\tau)F(t-\tau)S(t-\tau)\,d\tau. \end{aligned} \tag{2}$$

To complete the model description we assume that in addition to removal by infection, individuals are recruited into the susceptible class at a constant rate λ and die naturally at a constant per-capita rate μ. Combining these rates, we find that

$$\frac{dS(t)}{dt} = \lambda - \mu S(t) - F(t)S(t), \tag{3}$$

assuming that infection leads to permanent immunity. Given (3), it is straightforward to show that $S(t) > 0$ for $t > 0$ provided it is nonnegative initially.

[1] The dynamics of the class of infected individuals, I, is implicitly captured through the force of infection, $F(t)$.

An important parameter that governs the system trajectory is the basic reproduction number R_0, defined as the expected number of secondary cases caused by a single (typical) infectious individual in a fully susceptible population. Given the definition of $A(\tau)$ and the expression for $F(t)$ (equation (2)), the functional form of R_0 is naturally given by

$$R_0 = S^0 \int_0^{\bar{\tau}} A(\tau)\, d\tau \tag{4}$$

where

$$S^0 = \lambda/\mu$$

is the steady-state susceptible population in the absence of infection (see below).

Before introducing suitable initial conditions for the system, we emphasize that in order to solve (2) and (3) we must have knowledge of the entire past history of F and S over the interval $\tau \in [-\bar{\tau}, 0]$. Therefore, the state of our system $P = (\mathcal{S}, \mathcal{F})$ belongs to an infinite-dimensional phase-space Ω, which can appropriately be chosen as

$$\Omega = C^0_+([-\bar{\tau}, 0]) \times L^1_+(-\bar{\tau}, 0).$$

With this choice of state-space, standard arguments show that the model (2)-(3) is well defined.

Given Ω, a suitable choice of initial conditions is given by

$$\mathcal{S}_0 \in C^0_+([-\bar{\tau}, 0]) \qquad \text{and} \qquad \mathcal{F}_0 \in L^1_+(-\bar{\tau}, 0).$$

The system equations (2)-(3) induce a continuous semiflow $\Phi_t : \Omega \to \Omega$ where the trajectory is given by $(\mathcal{S}_t(\cdot), \mathcal{F}_t(\cdot)) \in \Omega$ with

$$\mathcal{S}_t(s) = S(t+s), \quad \mathcal{F}_t(s) = F(t+s), \qquad s \in [-\bar{\tau}, 0].$$

We point out that in this notation, the pair $(\mathcal{S}_t(0), \mathcal{F}_t(0)) = (S(t), F(t))$ represents the most recent value in the history of a state along the system trajectory at time t, namely $(\mathcal{S}_t(\cdot), \mathcal{F}_t(\cdot)) \in \Omega$. In this case the model equations (2)-(3) can be understood as rules for updating the most recent values of the histories of F and S respectively.

Lemma 1 *If the infectivity kernel A is of bounded variation, that is $A \in BV([0, \bar{\tau}])$, system trajectories $(\mathcal{S}_t(\cdot), \mathcal{F}_t(\cdot))$ generated by model equations (2)-(3) that originate in Ω are eventually compact. That is, $\Phi_{t'} : \Omega \to \Omega^c$ where $\Omega^c \subset \Omega$ is some compact set and t' is sufficiently large.*

Proof of Lemma 1. First, we rewrite equation (2) using our updated notation:

$$F(t) = \int_0^{\bar{\tau}} A(\tau)\mathcal{F}_t(-\tau)\mathcal{S}_t(-\tau)\, d\tau.$$

By corollary 1 of theorem 2 in (Mikusiński and Ryll-Nardzewski, 1951) — which states that the convolution of a function of bounded variation with a

bounded function is continuous — we have that $F(t>0) \in C^0_+$ for $\mathcal{F}_0 \in L^1_+$ and $\mathcal{S}_0 \in C^0_+$. Substituting this result into (3) we find that $S(t>0) \in C^1_+$. Therefore, it follows that $\Phi_{t>\bar{\tau}} : \Omega \to C^1_+([-\bar{\tau},0]) \times C^0_+([-\bar{\tau},0])$.

Consider now the interval $t > \bar{\tau}$. By theorem 5 of (Mikusiński and Ryll-Nardzewski, 1951) — which states that the convolution of a function of bounded variation with a continuous function is absolutely continuous — we have that $F(t>\bar{\tau}) \in AC_+$. Therefore, $\Phi_{t>2\bar{\tau}} : \Omega \to \Omega^c$ where

$$\Omega^c = C^1_+([-\bar{\tau},0]) \times AC_+([-\bar{\tau},0]). \tag{5}$$

□

Henceforth we assume that $A \in BV_+([0,\bar{\tau}])$ such that the system trajectory is eventually compact and the ω-limit set of (2)-(3) is non-empty.

Continuing, of particular interest within the larger, forward invariant phase-space Ω, is the interior region $\widehat{\Omega} \subset \Omega$ for which new infections will arise either at the present time or at some time in the future. That is,

$$\widehat{\Omega} = \left\{ (\mathcal{S},\mathcal{F}) \in \Omega \,:\, \exists\, a \in [0,\bar{\tau}] \text{ s.t. } \int_0^{\bar{\tau}} A(\tau+a)\mathcal{F}(-\tau)\mathcal{S}(-\tau)\,d\tau > 0 \right\}.$$

Conversely, we can also segregate the boundary, $\partial\Omega$, of the phase-space, for which no new infections can arise and for which the infection will be eradicated

$$\partial\Omega = \Omega \setminus \widehat{\Omega}.$$

Finally, it is easy to verify that the fixed states of the system (2)-(3) are given by

$$\begin{aligned} P_0 &= (\mathcal{S}^0,\mathcal{F}^0) = (S^0,F^0) = \left(\frac{\lambda}{\mu},0\right), \\ \bar{P} &= (\bar{\mathcal{S}},\bar{\mathcal{F}}) = (\bar{S},\bar{F}) = \left(\frac{\lambda}{\mu R_0},\mu(R_0-1)\right). \end{aligned} \tag{6}$$

Importantly, we see that the endemic equilibrium point, $\bar{P}$, only exists in the interior region $\widehat{\Omega}$ for $R_0 > 1$; for the limiting case $R_0 = 1$, the endemic and infection-free equilibria coincide.

Ultimately, our goal will be to establish that i) when $R_0 \leq 1$ all system trajectories of (2)-(3) within Ω asymptotically approach the infection-free equilibrium point $P_0 \in \partial\Omega$ and ii) when $R_0 > 1$ trajectories that originate in Ω asymptotically approach the endemic equilibrium $\bar{P} \in \widehat{\Omega}$, except those that originate in $\partial\Omega$ which approach P_0.

3 Global stability analysis

3.1 Infection-free equilibrium

Theorem 1 *The infection-free equilibrium point P_0 of the system (2)-(3) is globally asymptotically stable in Ω for $R_0 \leq 1$. However, if $R_0 > 1$, solutions of (2)-(3) starting sufficiently close to P_0 in Ω leave a neighbourhood of P_0, except those starting within the boundary region $\partial\Omega$ which approach P_0.*

Proof of Theorem 1. To verify theorem 1 we define $D = \Phi_{\bar{\tau}}(\Omega)$ where, from (3), we have $\mathcal{S}(0) > 0$ for $(\mathcal{S}, \mathcal{F}) \in D$. Note, D is closed and forward invariant, and any trajectory originating in Ω enters D either at, or before $t = \bar{\tau}$.

Consider the Lyapunov functional $U : D \to \mathbb{R}_+$ defined by

$$U(\mathcal{S}, \mathcal{F}) = g\left(\frac{\mathcal{S}(0)}{S^0}\right) + \int_0^{\bar{\tau}} \eta(\tau)\mathcal{F}(-\tau)\mathcal{S}(-\tau)\, d\tau$$

where

$$g(x) = x - 1 - \log x \qquad \text{and} \qquad \eta(\tau) = \int_\tau^{\bar{\tau}} A(s)\, ds. \tag{7}$$

In particular we have $\eta(\bar{\tau}) = 0$,

$$\eta(0) = \frac{R_0}{S^0} \qquad \text{and} \qquad \eta'(\tau) = -A(\tau) \tag{8}$$

where a $'$ denotes differentiation with respect to τ. Importantly, the functional $U(\mathcal{S}, \mathcal{F}) \geq 0$ is well defined since $\mathcal{S}(0) > 0$, and has a global minimum at the infection-free equilibrium P_0.

Next, let $(\mathcal{S}_t(\cdot), \mathcal{F}_t(\cdot))$ be a trajectory of the model (2)-(3) with initial condition in D. With $\mathcal{S}_t(s) = S(t+s)$ and $\mathcal{F}_t(s) = F(t+s)$ we may write

$$\begin{aligned} U(\mathcal{S}_t(\cdot), \mathcal{F}_t(\cdot)) &= g\left(\frac{\mathcal{S}_t(0)}{S^0}\right) + \int_0^{\bar{\tau}} \eta(\tau)\mathcal{F}_t(-\tau)\mathcal{S}_t(-\tau)\, d\tau, \\ &= g\left(\frac{S(t)}{S^0}\right) + \int_0^{\bar{\tau}} \eta(\tau)F(t-\tau)S(t-\tau)\, d\tau. \end{aligned}$$

In order to compute the time derivative of $U(\mathcal{S}_t, \mathcal{F}_t)$ we rewrite this as

$$U(\mathcal{S}_t(\cdot), \mathcal{F}_t(\cdot)) = g\left(\frac{S(t)}{S^0}\right) + \int_{t-\bar{\tau}}^{t} \eta(t-s)F(s)S(s)\, ds. \tag{9}$$

Differentiating each term in (9) along system trajectories separately, we first have

$$\begin{aligned}\frac{d}{dt}\left[g\left(\frac{S(t)}{S^0}\right)\right] &= \left(\frac{1}{S^0}-\frac{1}{S(t)}\right)\frac{dS(t)}{dt},\\ &= \frac{\lambda}{S^0}-\mu\,\frac{S(t)}{S^0}-F(t)\,\frac{S(t)}{S^0}-\frac{\lambda}{S(t)}+\mu+F(t),\\ &= \mu\left(2-\frac{S(t)}{S^0}-\frac{S^0}{S(t)}\right)-F(t)\,\frac{S(t)}{S^0}+F(t),\\ &= -\mu\,\frac{S(t)}{S^0}\left(1-\frac{S^0}{S(t)}\right)^2-F(t)\left(\frac{S(t)}{S^0}-1\right) \qquad (10)\end{aligned}$$

where in the second line we have substituted in the identity $\lambda = \mu S^0$.

Next we differentiate the second term in (9) to obtain

$$\begin{aligned}\frac{d}{dt}\left(\int_{t-\bar\tau}^{t}\eta(t-s)F(s)S(s)\,ds\right) &= \eta(0)F(t)S(t)-\eta(\bar\tau)F(t-\tau)S(t-\tau)\\ &\quad+\int_{t-\bar\tau}^{t}\frac{d\eta(t-s)}{dt}F(s)S(s)\,ds,\\ &= R_0F(t)\,\frac{S(t)}{S^0}-\int_{t-\bar\tau}^{t}A(t-s)F(s)S(s)\,ds,\\ &= R_0F(t)\,\frac{S(t)}{S^0}-F(t) \qquad (11)\end{aligned}$$

where in the second line we have substituted in (8) and in the last line we have used the definition of $F(t)$, equation (2).

Finally, combining (10) and (11) yields

$$\frac{d}{dt}U(\mathcal{S}_t,\mathcal{F}_t) = -\mu\,\frac{\mathcal{S}_t(0)}{S^0}\left(1-\frac{S^0}{\mathcal{S}_t(0)}\right)^2-(1-R_0)\,\mathcal{F}_t(0)\,\frac{\mathcal{S}_t(0)}{S^0}. \qquad (12)$$

We emphasize that we know for a trajectory $(\mathcal{S}_t,\mathcal{F}_t)\in D\subset\Omega$, that for $t>0$ we already have $\mathcal{F}_t\in C^0([-\bar\tau,0])$, such that this expression is well defined and U is a proper Lyapunov functional on the closed domain D.

Importantly, for $R_0\le 1$ we have $dU/dt\le 0$. The derivative $\dot U(t)=0$ if and only if $\mathcal{S}_t(0)=S^0$ and either (a) $R_0=1$ or (b) $\mathcal{F}_t(0)=0$. Therefore, the largest invariant subset in Ω for which $\dot U=0$ is the singleton $\{P_0\}$. By Lemma 1 the orbit is eventually precompact hence, by the infinite-dimensional form of LaSalle's extension of Lyapunov's global asymptotic stability theorem (Smith, 2010, Theorem 5.17), the infection-free equilibrium point P_0 is globally asymptotically stable in Ω for $R_0\le 1$.

Conversely, if $R_0>1$ and $\mathcal{F}_t(0)>0$, the derivative $\dot U>0$ if $S(t)$ is sufficiently close to S^0. Therefore, solutions starting sufficiently close to the infection-free equilibrium point P_0 leave a neighbourhood of P_0, except those starting in $\partial\Omega$. Since $\dot U\le 0$ for solutions starting in $\partial\Omega$ these solutions approach P_0 through this subspace.

□

3.2 Endemic equilibrium

Theorem 2 *If $R_0 > 1$ the endemic equilibrium point $\bar{P}$ is globally asymptotically stable in $\widehat{\Omega}$ (i.e. away from the boundary region $\partial\Omega$).*

Proof of Theorem 2. First, in theorem 1 we observed that $F(t)$ for $t > 0$ is bounded away from zero when $R_0 > 1$, such that for $R_0 > 1$ the semiflow $\Phi_t : \widehat{\Omega} \to \widehat{\Omega}$. Therefore, in analogy with theorem 1 we define $\widehat{D} = \Phi_{\bar{\tau}}(\widehat{\Omega})$ which is a closed, forward-invariant set for $R_0 > 1$. Moreover $\mathcal{S}, \mathcal{F} > 0$ for $(\mathcal{S}, \mathcal{F}) \in \widehat{D}$ and any trajectory originating in $\widehat{\Omega}$ enters $\widehat{D}$ at the latest at time $t = \bar{\tau}$, provided $R_0 > 1$.

In this case we define $W : \widehat{D} \to \mathbb{R}_+$

$$W(\mathcal{S}, \mathcal{F}) = g\left(\frac{\mathcal{S}(0)}{\bar{S}}\right) + \int_0^{\bar{\tau}} \chi(\tau) g\left(\frac{\mathcal{F}(-\tau)\mathcal{S}(-\tau)}{\bar{F}\bar{S}}\right) d\tau$$

where $g(x)$ has been defined previously in (7) and

$$\chi(\tau) = \bar{F}\bar{S} \int_\tau^{\bar{\tau}} A(s)\, ds.$$

Immediately we have that $\chi(\bar{\tau}) = 0$,

$$\chi(0) = \bar{F} \qquad \text{and} \qquad \chi'(\tau) = -\bar{F}\bar{S}A(\tau).$$

Once again, note that $W(\mathcal{S}, \mathcal{F})$ is well defined on $\widehat{D}$.

Similar to before, we let $(\mathcal{S}_t(\cdot), \mathcal{F}_t(\cdot))$ be a trajectory of the model with initial condition in $\widehat{D}$ and adopt the notation $\mathcal{S}_t(s) = S(t+s)$ and $\mathcal{F}_t(s) = F(t+s)$. We may then write

$$W(\mathcal{S}_t(\cdot), \mathcal{F}_t(\cdot)) = g\left(\frac{S(t)}{\bar{S}}\right) + \int_0^{\bar{\tau}} \chi(\tau)\, g\left(\frac{F(t-\tau)S(t-\tau)}{\bar{F}\bar{S}}\right) d\tau$$

which we at once rewrite as

$$W(\mathcal{S}_t(\cdot), \mathcal{F}_t(\cdot)) = g\left(\frac{S(t)}{\bar{S}}\right) + \int_{t-\bar{\tau}}^{t} \chi(t-s)\, g\left(\frac{F(s)S(s)}{\bar{F}\bar{S}}\right) ds. \tag{13}$$

Once again we differentiate each term separately. Beginning with the first term in (13) we have

$$\begin{aligned}
\frac{d}{dt}\left[g\left(\frac{S(t)}{\bar{S}}\right)\right] &= \left(\frac{1}{\bar{S}} - \frac{1}{S(t)}\right)\frac{dS(t)}{dt}, \\
&= \frac{\lambda}{\bar{S}} - \mu\,\frac{S(t)}{\bar{S}} - F(t)\,\frac{S(t)}{\bar{S}} - \frac{\lambda}{S(t)} + \mu + F(t), \\
&= \mu\left(2 - \frac{S(t)}{\bar{S}} - \frac{\bar{S}}{S(t)}\right) + \bar{F}\left(1 - \frac{\bar{S}}{S(t)}\right) + F(t)\left(1 - \frac{S(t)}{\bar{S}}\right), \\
&= -\mu\,\frac{S(t)}{\bar{S}}\left(1 - \frac{\bar{S}}{S(t)}\right)^2 + \bar{F}\left(1 - \frac{\bar{S}}{S(t)}\right) + F(t)\left(1 - \frac{S(t)}{\bar{S}}\right)
\end{aligned} \tag{14}$$

where in the third line we have substituted in the identity $\lambda = \mu\bar{S} + \bar{F}\bar{S}$.

Turning to the second term we find

$$\begin{aligned}\frac{d}{dt}\left[\int_{t-\bar{\tau}}^{t}\chi(t-s)\,g\left(\frac{F(s)S(s)}{\bar{F}\bar{S}}\right)\,d\tau\right] &= \chi(0)\,g\left(\frac{F(t)S(t)}{\bar{F}\bar{S}}\right) - \chi(\bar{\tau})\,g\left(\frac{F(t-\bar{\tau})S(t-\bar{\tau})}{\bar{F}\bar{S}}\right)\\ &\quad + \int_{t-\bar{\tau}}^{t}\frac{d\chi(t-s)}{dt}g\left(\frac{F(s)S(s)}{\bar{F}\bar{S}}\right)\,ds,\\ &= \bar{F}\,g\left(\frac{F(t)S(t)}{\bar{F}\bar{S}}\right) - \bar{F}\bar{S}\int_{t-\bar{\tau}}^{t}A(t-s)g\left(\frac{F(s)S(s)}{\bar{F}\bar{S}}\right)\,ds.\end{aligned}$$

Substituting in the definition $g(x) = x - 1 - \log x$ and equation (2) this expression becomes

$$\begin{aligned}&\frac{d}{dt}\left[\int_{t-\bar{\tau}}^{t}\chi(t-s)\,g\left(\frac{F(s)S(s)}{\bar{F}\bar{S}}\right)\,ds\right]\\ &\qquad = F(t)\left(\frac{S(t)}{\bar{S}} - 1\right) - \bar{F}\left[\log\left(\frac{F(t)S(t)}{\bar{F}\bar{S}}\right) - \bar{S}\int_{t-\bar{\tau}}^{t}A(t-s)\log\left(\frac{F(s)S(s)}{\bar{F}\bar{S}}\right)\,ds\right].\end{aligned} \tag{15}$$

The final term in the square brackets can be bounded using Jensen's inequality[2]:

$$\begin{aligned}\bar{S}\int_{t-\bar{\tau}}^{t}A(t-s)\log\left(\frac{F(s)S(s)}{\bar{F}\bar{S}}\right)\,ds &\leq \log\left[\bar{S}\int_{t-\bar{\tau}}^{t}A(t-s)\frac{F(s)S(s)}{\bar{F}\bar{S}}\,ds\right],\\ &= \log\left(\frac{F(t)}{\bar{F}}\right).\end{aligned}$$

Importantly, we note that equality between the left- and right-hand sides occurs if and only if $F(t)S(t) = \bar{F}\bar{S}$. Substituting this result back into the expression above we find

$$\begin{aligned}&\log\left(\frac{F(t)S(t)}{\bar{F}\bar{S}}\right) - \bar{S}\int_{t-\bar{\tau}}^{t}A(t-s)\log\left(\frac{F(s)S(s)}{\bar{F}\bar{S}}\right)\,ds\\ &\geq \log\left(\frac{F(t)S(t)}{\bar{F}\bar{S}}\right) - \log\left(\frac{F(t)}{\bar{F}}\right),\\ &= \log\left(\frac{S(t)}{\bar{S}}\right),\\ &\geq 1 - \frac{\bar{S}}{S(t)}\end{aligned}$$

[2] For a concave function $\varphi(\cdot)$ the following inequality holds (Jensen, 1906):

$$\varphi\left(\int_0^\infty h(t)f(t)\,dt\right) \geq \int_0^\infty h(t)\varphi\left(f(t)\right)\,dt$$

where $h(t)$ is a normalized probability distribution.

where in the last line we have used $\log x \geq 1 - \frac{1}{x}$, where equality requires $S(t) = \bar{S}$.

This condition implies that

$$\frac{d}{dt}\left[\int_{t-\bar{\tau}}^{t} \chi(t-s)\, g\left(\frac{F(s)S(s)}{\bar{F}\bar{S}}\right) ds\right] \leq F(t)\left(\frac{S(t)}{\bar{S}} - 1\right) - \bar{F}\left(1 - \frac{\bar{S}}{S(t)}\right). \tag{16}$$

Finally, combining (14) and (16) yields

$$\begin{aligned} \frac{d}{dt}W(\mathcal{S}_t, \mathcal{F}_t) &\leq -\mu\, \frac{\mathcal{S}_t(0)}{\bar{S}}\left(1 - \frac{\bar{S}}{\mathcal{S}_t(0)}\right)^2, \\ &\leq 0. \end{aligned} \tag{17}$$

From equation (17) we see that the largest invariant subset in $\widehat{\Omega}$ for which $\dot{W} = 0$ consists only of the endemic equilibrium point $\bar{P}$. By Lemma 1 the orbit is eventually precompact hence, by LaSalle's extension of Lyapunov's asymptotic stability theorem, the endemic equilibrium point $\bar{P}$ is globally asymptotically stable in $\widehat{\Omega}$.

□

4 Conclusions

In this article we investigated the global dynamics of the general Kermack-McKendrick model which we formulated in terms of a set of renewal equations. Firstly, we discussed how when the basic reproduction number $R_0 \leq 1$ the infection-free equilibrium point P_0 is the unique equilibrium in $\Omega = C^0_+([-\bar{\tau}, 0]) \times L^1_+(-\bar{\tau}, 0)$. In contrast, when $R_0 > 1$, an endemic equilibrium solution emerges in in the interior region $\widehat{\Omega} \subset \Omega$ for which a positive fraction of the population remains infected. By introducing appropriate Lyapunov functionals we established that the infection-free and endemic equilibria are globally asymptotically stable within Ω and $\widehat{\Omega}$ when $R_0 \leq 1$ and $R_0 > 1$, respectively. These results generalize a number of previous investigations into the global stability of epidemic models.

One of the goals of this article was to promote the use of more general epidemic model formulations beyond ordinary differential equation (compartmental) descriptions — that are ubiquitous in the infectious diseases modelling literature — by providing additional tools and theory relevant to the renewal formulation. However, whilst the infected removal and transmission rates in the model we investigated in this article are left as arbitrary functions of the infection age τ, the assumptions regarding the demographic properties of the population are more restrictive. In particular, the model that we have analyzed (eqns. (2) and (3)) assumes that the age distribution of our population is exponential, i.e. that the natural mortality rate μ is constant. For many settings, particularly developed countries, this assumption may be unrealistic. Therefore, it would be interesting to investigate whether the analysis

presented here could be extended to epidemic models for which the natural mortality rate $\mu \to \mu(a)$ is an arbitrary function of an individual's chronological age, a. Research in this direction dates back to at least (Thieme, 1991) (see also (Müller and Kuttler, 2015; Thieme, 2011)) who found that Hopf bifurcations arise when an individual's infectivity is dependent on their chronological age a. Whether this applies to age-structured models in general is a promising avenue of future research.

References

Bichara D, Iggidr A, Sallet G (2013) Global analysis of multi-strains SIS, SIR and MSIR epidemic models. Journal of Applied Mathematics and Computing 44(1):273–292

Chen Y, Zou S, Yang J (2016) Global analysis of an SIR epidemic model with infection age and saturated incidence. Nonlinear Analysis: Real World Applications 30:16 – 31

Fan M, Li MY, Wang K (2001) Global stability of an SEIS epidemic model with recruitment and a varying total population size. Mathematical Biosciences 170(2):199–208

Huang G, Takeuchi Y (2011) Global analysis on delay epidemiological dynamic models with nonlinear incidence. Journal of Mathematical Biology 63(1):125–139

Jensen JLWV (1906) Sur les fonctions convexes et les inégalités entre les valeurs moyennes. Acta Mathematica 30(1):175–193

Kermack WO, McKendrick AG (1927) A contribution to the mathematical theory of epidemics. In: Proceedings of the Royal Society of London A: mathematical, physical and engineering sciences, The Royal Society, vol 115, pp 700–721

Korobeinikov A (2004) Global properties of basic virus dynamics models. Bulletin of Mathematical Biology 66(4):879–883

Korobeinikov A (2008) Global properties of SIR and SEIR epidemic models with multiple parallel infectious stages. Bulletin of Mathematical Biology 71(1):75–83

Korobeinikov A, Wake G (2002) Lyapunov functions and global stability for SIR, SIRS, and SIS epidemiological models. Applied Mathematics Letters 15(8):955–960

Li MY, Muldowney JS (1995) Global stability for the SEIR model in epidemiology. Mathematical biosciences 125(2):155–164

Li MY, Graef JR, Wang L, Karsai J (1999) Global dynamics of a SEIR model with varying total population size. Mathematical Biosciences 160(2):191–213

Magal P, McCluskey C, Webb G (2010) Lyapunov functional and global asymptotic stability for an infection-age model. Applicable Analysis 89(7):1109–1140

Martcheva M, Li XZ (2013) Competitive exclusion in an infection-age structured model with environmental transmission. Journal of Mathematical Analysis and Applications 408(1):225 – 246

McCluskey CC (2008) Global stability for a class of mass action systems allowing for latency in tuberculosis. Journal of Mathematical Analysis and Applications 338(1):518–535

McCluskey CC (2009) Global stability for an SEIR epidemiological model with varying infectivity and infinite delay. Mathematical Biosciences and Engineering 6(3):603–610

McCluskey CC (2010a) Complete global stability for an SIR epidemic model with delay: distributed or discrete. Nonlinear Analysis: Real World Applications 11(1):55–59

McCluskey CC (2010b) Global stability for an SIR epidemic model with delay and nonlinear incidence. Nonlinear Analysis: Real World Applications 11(4):3106 – 3109

Mikusiński J, Ryll-Nardzewski C (1951) Sur le produit de composition. Studia Mathematica 12:51–57

Müller J, Kuttler C (2015) Methods and models in mathematical biology. Springer

O'Regan SM, Kelly TC, Korobeinikov A, O'Callaghan MJ, Pokrovskii AV (2010) Lyapunov functions for SIR and SIRS epidemic models. Applied Mathematics Letters 23(4):446–448

Smith H (2010) An introduction to delay differential equations with applications to the life sciences. Springer

Soufiane B, Touaoula TM (2016) Global analysis of an infection age model with a class of nonlinear incidence rates. Journal of Mathematical Analysis and Applications 434(2):1211 – 1239

Thieme HR (1991) Stability Change of the Endemic Equilibrium in Age-Structured Models for the Spread of S—I—R Type Infectious Diseases, Springer Berlin Heidelberg, Berlin, Heidelberg, pp 139–158

Thieme HR (2011) Global stability of the endemic equilibrium in infinite dimension: Lyapunov functions and positive operators. Journal of Differential Equations 250(9):3772–3801

Wang X, Liu S (2012) Global properties of a delayed SIR epidemic model with multiple parallel infectious stages. Mathematical Biosciences and Engineering 9(3):685–695