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GLOBAL STABILITY FOR AN SEIR EPIDEMIOLOGICAL MODEL WITH VARYING INFECTIVITY AND INFINITE DELAY

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ABSTRACT. A recent paper (Math. Biosci. and Eng. (2008) 5:389-402) presented an SEIR model for an infectious disease that included infection-age structure to allow for varying infectivity. The incidence is of mass action type, but because of the varying infectivity, has the form \( \beta S(t) \int_0^\infty k(a) i(t,a) \, da \). Nevertheless, the authors gave a thorough analysis leaving out only the elusive global stability of the endemic equilibrium.

Here, we show that the endemic equilibrium is globally stable for \( R_0 > 1 \). The proof uses a Lyapunov functional that includes an integral over all previous states.

1. Introduction. A recent paper [16] presented an SEIR model for an infectious disease that included infection-age structure to allow for varying infectivity. The incidence is of mass action type, but because of the varying infectivity, has the form \( \beta S(t) \int_0^\infty k(a) i(t,a) \, da \). Nevertheless, the authors gave a thorough analysis leaving out only the elusive global stability of the endemic equilibrium.

That issue is resolved in this paper using a Lyapunov functional related to the type of Lyapunov function used for ordinary differential equation (ODE) ecological models [3, 4] in the 1980s and used more recently for ODE epidemiological models [6, 10, 11, 12, 13, 14, 15]. In [5], an ODE model of arbitrary dimension that includes varying infectivity is studied using the same type of Lyapunov function. For each of these models, the Lyapunov function is a sum of terms of the form \( f(y) = y - 1 - \ln y \), where \( y \) is a variable of the system. The model studied in this paper has infinite delay, and so it is necessary to include in the Lyapunov functional a term that integrates over all previous states.

We now provide a brief outline of the paper. In Section 2 we describe the equations that are to be studied. Section 3 includes results by Röst and Wu from [16], providing the context in which this paper is to be read. Many of these results are then used in Section 4 where the global stability of the endemic equilibrium is shown — the key result of this paper.

2. Model equations. A population is divided into classes: susceptible, exposed, infectious, and recovered, denoted by \( S, E, I, \) and \( R \), respectively. The infectious class is structured by age of infection (i.e. time since entry into class \( I \)). The density of individuals with infection-age \( a \) at time \( t \) is given by \( i(t,a) \) with \( I(t) = \int_0^\infty i(t,a) \, da \).

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Constant recruitment into $S$ is given by $A$. Incidence is of mass action type with baseline coefficient $\beta$. The relative infectivity of individuals of infection-age $a$ is $k(a)$, where $k$ is an integrable function taking values in the interval $[0, 1]$. The natural death rate is $d$, the disease-related death rate is $r$, the average latency period is $1/\mu$ and the average period of infectivity is $1/r$.

The original model equations [16] are

$$\frac{dS(t)}{dt} = \Lambda - \beta S(t) \int_0^\infty k(a)i(t, a)da - dS(t)$$

$$\frac{dE(t)}{dt} = \beta S(t) \int_0^\infty k(a)i(t, a)da - (\mu + d)E(t)$$

$$\frac{dI(t)}{dt} = \mu E(t) - (d + \delta + r)I(t)$$

$$\frac{dR(t)}{dt} = rI(t) - dR(t)$$

with the boundary condition

$$i(t, 0) = \mu E(t).$$

Solving (2) gives

$$i(t, a) = \mu e^{-(d+\delta+r)a} E(t - a).$$

This allows equation (1) to be rewritten as

$$\frac{dS(t)}{dt} = \Lambda - \mu \beta S(t) \int_0^\infty k(a)e^{-(d+\delta+r)a} E(t - a)da - dS(t)$$

$$\frac{dE(t)}{dt} = \mu \beta S(t) \int_0^\infty k(a)e^{-(d+\delta+r)a} E(t - a)da - (\mu + d)E(t),$$

where the equations for $\frac{dI}{dt}$ and $\frac{dR}{dt}$ are omitted because they decouple.

In order to specify the initial conditions for (3), we introduce the following notation. Given a non-negative function $E$ defined on the interval $[-\infty, T]$, for any $t \leq T$ we define the function $E_t : \mathbb{R}_{\leq 0} \rightarrow \mathbb{R}_{\geq 0}$ by $E_t(\theta) = E(t + \theta)$ for $\theta \leq 0$.

For equation (1), the initial condition would specify $S(0), E(0), R(0) \geq 0$ and $i(0, \cdot) : \mathbb{R}_{\geq 0} \rightarrow \mathbb{R}_{\geq 0}$. For equation (3), an equation with infinite delay, the initial condition must specify $S(0) \geq 0$ and $E_0 : \mathbb{R}_{\leq 0} \rightarrow \mathbb{R}_{\geq 0}$.

Due to the infinite delay, it is necessary to determine an appropriate phase space. For any $\Delta \in (0, d + \delta + r)$, let

$$C_\Delta = \{ \varphi : \mathbb{R}_{\leq 0} \rightarrow \mathbb{R} \text{ such that } \varphi(\theta)e^{\Delta \theta} \text{ is bounded and uniformly continuous} \}$$

and

$$Y_\Delta = \{ \varphi \in C_\Delta : \varphi(\theta) \geq 0 \text{ for all } \theta \leq 0 \}.$$

Define the norm on $C_\Delta$ and $Y_\Delta$ by

$$||\varphi|| = \sup_{\theta \leq 0} |\varphi(\theta)e^{\Delta \theta}|.$$

It follows immediately that $\varphi(0) \leq ||\varphi||$.

Fixing $\Delta \in (0, d + \delta + r)$, we take the phase space for equation (3) to be $\mathbb{R}_{\geq 0} \times Y_\Delta$. Any initial condition $(S(0), E_0) \in \mathbb{R}_{\geq 0} \times Y_\Delta$ gives a solution $(S(t), E_t)$ that remains
in the phase space for all time. Furthermore, if \((S(t), E(t))\) is bounded for \(t \geq 0\), then the positive orbit \(\Gamma_+ = \{(S(t), E_t) : t \geq 0\}\) has compact closure in \(\mathbb{R}_{\geq 0} \times Y_\Delta\).

Relevant developments of infinite delay equations, including determining the phase space, can be found in [1, 8, 9] and references found therein.

3. Previous results. In their paper, the authors of [16] give a thorough analysis of equation (3). They find the equilibria, calculate the basic reproduction number \(R_0\) and show that the system is point dissipative. The disease-free equilibrium is shown to be globally stable for \(R_0 < 1\). For \(R_0 > 1\) the disease-free equilibrium is unstable, there is a unique endemic equilibrium, which is locally asymptotically stable, and the system is permanent. They also do a final size calculation.

All that remains to complete the analysis is to determine the global behaviour for \(R_0 > 1\). This is done in Section 4 of this paper, where it is shown that the endemic equilibrium is globally stable for \(R_0 > 1\). In preparation for that, we now give results from [16].

**Theorem 3.1.** Equation (3) is point dissipative. That is, there exists \(M > 0\) such that for each solution of (3) there is a \(T > 0\) such that \(S(t) \leq M\) and \(\|E_t\| \leq M\) for all \(t \geq T\).

Note that \(\|E_t\| \leq M\) implies \(E(t) \leq M\).

The basic reproduction number [2] for the model is

\[
R_0 = \frac{\beta\Lambda}{d(\mu + d)} \int_0^\infty k(a)e^{-(d+\delta+r)a}da.
\]

For all values of the parameters, there is a disease-free equilibrium \(P_0 = (S_0,0)\) where \(S_0 = \Lambda/d\). For \(R_0 \leq 1\), \(P_0\) is the only equilibrium. For \(R_0 > 1\), there is a unique endemic equilibrium \(P^* = (S^*,E^*)\) where

\[
S^* = \frac{S_0}{R_0} = \frac{\Lambda}{dR_0} \quad \text{and} \quad E^* = \frac{\Lambda}{\mu + d} \left(1 - \frac{1}{R_0}\right).
\]

Note that while we write an equilibrium of (3) as a point \((\tilde{S}, \tilde{E})\) in \(\mathbb{R}^2\), more formally, an equilibrium point is a point \((\tilde{S}, \tilde{E}) \in \mathbb{R}_{\geq 0} \times Y_\Delta\) satisfying \(\tilde{S} = S\) and \(\tilde{E}(\theta) = E\) for all \(\theta \leq 0\). The equilibrium solution is given by \((S(t), E_t) = (\tilde{S}, \tilde{E}) \in \mathbb{R}_{\geq 0} \times Y_\Delta\) for each \(t\). Related to this is an equilibrium of (1) for which \(S(t), E(t), I(t)\) and \(R(t)\) are constant functions and for which \(i(t,a) = \hat{i}(a) = \mu\hat{E}e^{-(d+\delta+r)a}\) is independent of time \(t\).

**Theorem 3.2.** If \(R_0 < 1\), then all solutions converge to the disease-free equilibrium, which is locally asymptotically stable.

As with many finite dimensional models, if \(R_0\) is larger than one, then the disease-free equilibrium attracts disease-free states and repels states for which disease is present. Let \(a = \inf \{a : \int_0^\infty k(\sigma)d\sigma = 0\}\). For a system with a truly infinite delay, we have \(\tilde{a} = \infty\), whereas, for a system with a bounded distributed delay, we have \(0 < \tilde{a} < \infty\).

For a state \((\tilde{S}, \tilde{E}) \in \mathbb{R}_{\geq 0} \times Y_\Delta\), we say that disease is present if \(\tilde{E}(-a) > 0\) for some \(a \in [0, \tilde{a}]\). Recall that elements of \(Y_\Delta\) are continuous. Thus, if \(\tilde{E}\) is positive at some point, then \(\tilde{E}\) is positive on an interval about that point. If disease is present for \((\tilde{S}, \tilde{E})\), then the solution of (3) with initial condition \((\tilde{S}, \tilde{E})\) will satisfy \(E(t) > 0\) for some \(t > 0\). If \(\tilde{E}\) does not satisfy the given condition (i.e. \(\tilde{E}(-a) = 0\) for all...
\(a \in [0, \bar{a})\), then the solution of (3) will have \(E(t)\) identically zero for \(t \geq 0\), and will converge to \(I_0\). For a solution for which disease is present for the initial condition, we say the disease is initially present.

**Theorem 3.3.** Suppose \(R_0 > 1\). Then the disease-free equilibrium is unstable and the endemic equilibrium is locally asymptotically stable. Furthermore, the system is persistent; that is, there exists \(\eta > 0\) such that for any solution for which the disease is initially present, we have

\[
\liminf_{t \to \infty} S(t) \geq \eta \quad \text{and} \quad \liminf_{t \to \infty} E(t) \geq \eta.
\]

**Remark 1.** In [16], it is implicitly understood that \(\bar{a} = \infty\) meaning that the system has a true infinite delay. However, for a bounded distributed delay, which gives \(\bar{a} < \infty\), the proofs in [16] still hold, as do the new results of this paper.

### 4. Global stability for \(R_0 > 1\)

Let \(X(t) = (S(t), E_t)\) be a solution of equation (3) for which disease is initially present. It is shown in the proof of Theorem 6.1 of [16] that the semi-flow induced by equation (3) has properties that imply the existence of a global compact attractor (see Theorem 3.4.6 of [7]). Combined with Theorem 3.1 and Theorem 3.3, it follows that the \(\omega\)-limit set \(\Omega\) of \(X\) is non-empty, compact, and invariant. It follows that \(\Omega\) is the union of orbits of equation (3). That is, if \((\tilde{S}, \tilde{E}) \in \mathbb{R}_{\geq 0} \times Y_\Delta\) is an omega limit point of \(X\), then there is a solution through \((\tilde{S}, \tilde{E})\) such that every point on the solution is in \(\Omega\).

**Lemma 4.1.** Suppose \(R_0 > 1\) and \(Z(t) = (\phi(t), \varphi_t)\) is a solution to equation (3) that lies in \(\Omega\). Then \(\eta \leq \phi(t) \leq M\) and \(\eta \leq \varphi(t) \leq M\) for all \(t \in \mathbb{R}\).

**Proof.** Fix \(\epsilon > 0\) and \(T \in \mathbb{R}\), and let \(\tilde{Z} = Z(T) = (\phi(T), \varphi_T)\). Then \(\tilde{Z} \in \Omega\) is an omega limit point of \(X\). Thus, there exists a sequence \(\{t_n\}\) that increases to infinity such that \(X(t_n) \to \tilde{Z}\).

Then \(S(t_n) \to \phi(T)\). By Theorem 3.1 and Theorem 3.3, we have \(\eta - \epsilon \leq S(t_n) \leq M\) for large \(n\), and so the same inequalities apply to \(\phi(T)\). Also, \(0 \leq |E(t_n) - \varphi(T)| \leq \|E(t_n) - \varphi_T\|\), which goes to 0 as \(n \to \infty\). Thus, since \(\eta - \epsilon \leq E(t_n) \leq M\) for large enough \(n\), the same is true for \(\varphi(T)\).

Because the choice of \(T\) was arbitrary, as was the choice of \(\epsilon > 0\), the desired result follows for all \(t \in \mathbb{R}\). \(\square\)

**Theorem 4.2.** Suppose \(R_0 > 1\) and \(Z(t) = (\phi(t), \varphi_t)\) is a solution to equation (3) that lies in \(\Omega\). Then \(Z\) converges to the endemic equilibrium; that is,

\[
\lim_{t \to \infty} (\phi(t), \varphi(t)) = (S^*, E^*)
\]

**Proof.** We begin by normalizing. Let \(s(t) = \phi(t)/S^*, x(t) = \varphi(t)/E^*\) and \(x_t = \varphi_t/E^*\). Then

\[
\frac{ds(t)}{dt} = \frac{\Lambda}{S^*} - \mu \beta E^* s(t) \int_0^\infty k(a)e^{-(d+\delta+r)a}x(t-a)da - ds(t)
\]

\[
\frac{dx(t)}{dt} = \mu \beta S^* s(t) \int_0^\infty k(a)e^{-(d+\delta+r)a}x(t-a)da - (\mu + d)x(t).
\]
The endemic equilibrium for (4) is \( p^* = (s^*, x^*) = (1, 1) \). Thus, by evaluating both sides of (4) at \( p^* \), we have
\[
0 = \frac{\Lambda}{S^*} - \mu \beta S^* \int_0^\infty k(a)e^{-(d+\delta+r)a} da - d
\]
\[
0 = \mu \beta S^* \int_0^\infty k(a)e^{-(d+\delta+r)a} da - (\mu + d).
\]
Let
\[
f(y) = y - 1 - \ln y,
\]
and let
\[
U_s(t) = f(s(t)),
\]
\[
U_x(t) = \alpha_x f(x(t)),
\]
\[
U_+(t) = \int_0^\infty \alpha(a)f(x(t-a)) da,
\]
where
\[
\alpha_x = \frac{E^*}{S^*} \quad \text{and} \quad \alpha(a) = \mu \beta E^* \int_a^\infty k(\sigma)e^{-(d+\delta+r)\sigma} d\sigma.
\]
We will study the behaviour of the Lyapunov functional
\[
U(t) = U_s + U_x + U_+.
\]
We note that \( \alpha_x \) is positive, as is \( \alpha(a) \) for each \( a \in [0, \bar{a}) \). The function \( f \) has domain \( \mathbb{R}_{\geq 0} \) and range \( \mathbb{R}_{\geq 0} \). We also note that \( f \) has only one extreme value, which is the global minimum: \( f(1) = 0 \). Thus, \( U(t) \geq 0 \) with equality if and only if \( s(t) = x(t) = 1 \) and \( x(t-a) = 1 \) for almost all \( a \in [0, \bar{a}) \). Lemma 4.1 implies \( U \) is well-defined; that is, \( U_+ \) is finite for all \( t \).

For clarity, we calculate the derivatives of each of \( U_s, U_x \) and \( U_+ \) separately and then combine them to get \( \frac{dU}{dt} \). Also, instances of \( s(t) \) and \( x(t) \) will be written as \( s \) and \( x \), respectively.
\[
\frac{dU_s}{dt} = \left(1 - \frac{1}{s}\right) \frac{ds}{dt}
\]
\[
= s - 1 \left(\frac{\Lambda}{S^*} - \mu \beta E^* s \int_0^\infty k(a)e^{-(d+\delta+r)a}x(t-a) da - d s\right).
\]
Subtracting the right-hand side of the first equation of (5) gives
\[
\frac{dU_s}{dt} = \frac{s-1}{s} \left(\mu \beta E^* \int_0^\infty k(a)e^{-(d+\delta+r)a} \left(1 - sx(t-a)\right) da + d (1 - s)\right)
\]
\[
= -d(s-1)^2 + \mu \beta E^* \int_0^\infty k(a)e^{-(d+\delta+r)a} \left(1 - sx(t-a) - \frac{1}{s} + x(t-a)\right) da.
\]
In calculating \( \frac{dU_x}{dt} \), we use the second equation of (5) to replace \( (\mu + d) \) with the integral, obtaining
\[
\frac{dU_x}{dt} = \alpha_x \left(1 - \frac{1}{x}\right) \left(\mu \beta S^* \int_0^\infty k(a)e^{-(d+\delta+r)a}x(t-a) da - (\mu + d)x\right)
\]
\[
= \frac{E^*}{S^*} \left(1 - \frac{1}{x}\right) \mu \beta S^* \int_0^\infty k(a)e^{-(d+\delta+r)a} \left(sx(t-a) - x\right) da
\]
\[
= \mu \beta E^* \int_0^\infty k(a)e^{-(d+\delta+r)a} \left(sx(t-a) - x - \frac{sx(t-a)}{x} + 1\right) da.
\]
We now calculate the derivative of \( U_+(t) \).
\[
\frac{dU_+}{dt} = \frac{d}{dt} \int_0^\infty \alpha(a)f(x(t - a))da
\]
\[
= \int_0^\infty \alpha(a) \frac{d}{dt}f(x(t - a))da
\]
\[
= -\int_0^\infty \alpha(a) \frac{d}{da}f(x(t - a))da.
\]
Using integration by parts, we get
\[
\frac{dU_+}{dt} = -\alpha(a)f(x(t - a))|_{a=0}^\infty + \int_0^\infty \frac{d}{da} (\alpha(a)) f(x(t - a))da.
\]
By Lemma 4.1, since the solution \( Z(t) \) is in the omega limit set \( \Omega \), we have \( \frac{dx}{dt} \leq x(t) \leq \frac{dx}{dt} \) for all \( t \in \mathbb{R} \). Thus, \( f(x(t - a)) \) is bounded above and below. Then, noting that \( 0 \leq \alpha(a) = \mu \beta E^* \int_a^\infty k(\sigma)e^{-(d+\delta+r)\sigma}d\sigma \leq \mu \beta E^* \int_0^\infty e^{-(d+\delta+r)\sigma}d\sigma = \frac{\mu \beta E^*}{(d+\delta+r)}e^{-(d+\delta+r)a} \rightarrow 0 \), it follows that \( \lim_{a \rightarrow \infty} \alpha(a)f(x(t - a)) = 0 \). Also, at \( a = 0 \) we get \( \alpha(a)f(x(t - a)) = \alpha(0)f(x(t)) \), and so
\[
\frac{dU_+}{dt} = (\alpha(0)f(x(t)) + \int_0^\infty \frac{d}{da} (\alpha(a)) f(x(t - a))da.
\]
Filling in for \( \alpha(0) \), evaluating the derivative \( \frac{d}{da} \alpha(a) = -\mu \beta E^* k(a)e^{-(d+\delta+r)a} \), and then combining the two resulting integrals gives
\[
\frac{dU_+}{dt} = \mu \beta E^* \int_0^\infty k(a)e^{-(d+\delta+r)a}(f(x(t)) - f(x(t - a)))da
\]
\[
= \mu \beta E^* \int_0^\infty k(a)e^{-(d+\delta+r)a}(x - \ln x - x(t - a) + \ln x(t - a))da.
\]
Adding equations (6), (7), and (8), we obtain
\[
\frac{dU}{dt} = -d\frac{(s - 1)^2}{s} - \mu \beta E^* \int_0^\infty k(a)e^{-(d+\delta+r)a}C(a)da,
\]
where
\[
C(a) = -2 + \frac{1}{s} + \frac{sx(t - a)}{x} + \ln x - \ln x(t - a)
\]
\[
= \left( \frac{1}{s} - 1 + \ln s \right) + \left( \frac{sx(t - a)}{x} - 1 - (\ln s + \ln x(t - a) - \ln x) \right)
\]
\[
= f \left( \frac{1}{s} \right) + f \left( \frac{sx(t - a)}{x} \right)
\]
\[
\geq 0.
\]
Thus, \( \frac{dU}{dt} \leq 0 \) with equality if and only if \( s(t) = 1 \) and \( x(t - a)/x(t) = 1 \) for almost all \( a \in [0, \bar{a}) \). It follows that \( U(t) \) is a non-increasing function that is bounded below by zero, and therefore \( \lim_{t \rightarrow \infty} U(t) \) exists.

Next, we show that \( \lim_{t \rightarrow \infty} s(t) = 1 \). To do this, we first note that \( \frac{dU}{dt} \leq -g(t) \leq 0 \) where \( g(t) = d\frac{(s - 1)^2}{s} \). Suppose that \( s(t) \) does not converge to 1. Then there exist \( \epsilon > 0 \) and a sequence \( \{t_n\} \) that increases to infinity such that \( g(t_n) \geq \epsilon \) for each \( n \). Note that the bounds on \( Z \) given by Lemma 4.1 imply that the derivative \( \frac{dU}{dt} \) is bounded, and so there exists \( \tau > 0 \) such that \( g(t) \geq \frac{\epsilon}{2} \) for \( t \in I_n = (t_n - \tau, t_n + \tau) \). Then, we have \( \frac{dU}{dt} \leq -\frac{\epsilon}{2} \) for all \( t \in \cup I_n \), which is a set of infinite measure. Hence,
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$U$ decreases to $-\infty$, which contradicts the fact that $U$ is bounded below. Thus, $s(t)$ must converge to 1.

Finally, we show that $\lim_{t \to \infty} x(t) = 1$. To do this, let $y(t) = s(t) + \alpha x(t)$. Then
\[
\frac{dy}{dt} = \frac{ds}{dt} + \alpha \frac{dx}{dt}
\]
\[
= \frac{\Lambda S^*}{s} - ds - \alpha(\mu + d)x
\]
\[
= \frac{\Lambda S^*}{s} + \mu s - (\mu + d)y
\]

Since $s(t)$ converges to 1, this is an asymptotically autonomous ordinary differential equation for which solutions of the limiting equation go to a hyperbolic equilibrium. Thus, $\lim_{t \to \infty} y(t) = 1$.

Since $\lim_{t \to \infty} (s(t), x(t)) = (1, 1)$, it follows that $\lim_{t \to \infty} \left( \phi(t), \varphi(t) \right) = (S^*, E^*)$, completing the proof.

**Theorem 4.3.** If $R_0 > 1$, then all solutions of equation (3) for which the disease is initially present converge to the endemic equilibrium; that is,
\[
\lim_{t \to \infty} (S(t), E(t)) = (S^*, E^*).
\]

**Proof.** Let $Z(t)$ be a solution in $\Omega$, the omega limit set of $X$. By Theorem 4.2, $Z(t)$ converges to the endemic equilibrium $P^*$. Since $\Omega$ is closed, we have $P^* \in \Omega$ and so $X$ gets arbitrarily close to $P^*$. By Theorem 3.3, $P^*$ is locally asymptotically stable and therefore $X$ converges to $P^*$.

We note that the results here include systems with bounded distributed delay.

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