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Global stability of an SEIS epidemic model with recruitment and a varying total population size

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Abstract

This paper considers an SEIS epidemic model that incorporates constant recruitment, disease-caused death and disease latency. The incidence term is of the bilinear mass-action form. It is shown that the global dynamics is completely determined by the basic reproduction number R_0. If $R_0 \leqslant 1$, the disease-free equilibrium is globally stable and the disease dies out. If $R_0 > 1$, a unique endemic equilibrium is globally stable in the interior of the feasible region and the disease persists at the endemic equilibrium. © 2001 Elsevier Science Inc. All rights reserved.

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1. Introduction

We study a model for the transmission dynamics of an infectious disease that spreads in a population through direct contact of hosts. It is assumed that, after the initial infection, a host stays in a latent period before becoming infectious. An infectious host may die from disease or recover with no acquired immunity to the disease and again become susceptible. Many sexually transmitted diseases (STD) such as gonorrhea and chlamydial infections are known to result in little or no acquired immunity following recovery [1]. For other diseases that cause a very brief

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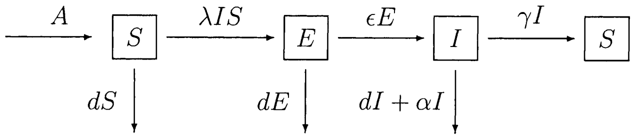
immune reaction in their hosts, the immune period may also be ignored, and the model under study may be a suitable approximation. The host population is partitioned into three classes, the susceptible, exposed (latent), and infectious, with sizes denoted by S, E, and I, respectively. The host total population $N = S + E + I$. The dynamical transfer of hosts is depicted in the following figure.



The influx of susceptibles comes from two sources, a constant recruitment A and recovered hosts γI. The natural death rate is assumed to be the same constant d for all hosts, and infectious hosts suffer an extra disease-related death with constant rate α. The parameters ϵ and γ denote the transfer rates among the corresponding classes. Heuristically, $1/\epsilon$ is the mean latent period and $1/\gamma$ is the mean infectious period. The incidence term is of the bilinear mass-action form λIS.

The transfer diagram leads to the following system of differential equations

$$\begin{aligned} S' &= A - \lambda IS - dS + \gamma I, \\ E' &= \lambda IS - (d+\epsilon)E, \\ I' &= \epsilon E - (d+\gamma+\alpha)I, \end{aligned} \tag{1}$$

which, together with $N = S + E + I$, implies

$$N' = A - dN - \alpha I. \tag{2}$$

Thus the total population size N may vary in time. In the absence of disease, the population size $N(t)$ converges to the equilibrium A/d. It follows from (2) that $\limsup_{t\to\infty} N(t) \leqslant A/d$. We thus study (1) in the following feasible region:

$$T = \{(S, E, I) \in \mathbb{R}^3_+ : S + E + I \leqslant A/d\}, \tag{3}$$

which can be shown to be positively invariant with respect to (1). Denote the boundary and the interior of T by ∂T and $\mathring{T}$, respectively. Direct calculation shows that system (1) has two possible equilibria in the non-negative cone $\mathbb{R}^3_+$: the disease-free equilibrium $P_0 = (A/d, 0, 0) \in \partial T$, and a unique endemic equilibrium $P^* = (S^*, E^*, I^*)$ with

$$S^* = \frac{(d+\epsilon)(d+\gamma+\alpha)}{\lambda\epsilon}, \quad I^* = \frac{A - dS^*}{\lambda S^* - \gamma}, \quad E^* = \frac{d+\alpha+\gamma}{\epsilon} I^*.$$

Let

$$R_0 = \frac{A\lambda\epsilon}{d(d+\epsilon)(d+\gamma+\alpha)}. \tag{4}$$

Then R_0 represents the average number of secondary infections from a single infectious host in a totally susceptible population of size A/d. It is called the basic reproduction number [1] or the contact number [2]. If $R_0 \leqslant 1, P_0$ is the only equilibrium in T. If $R_0 > 1$, the unique endemic equilibrium P^* exists in $\mathring{T}$.

We prove that the dynamics of (1) are completely determined by the threshold parameter R_0. If $R_0 \leqslant 1$, the disease-free equilibrium is globally asymptotically stable in T, and thus the disease always dies out. If $R_0 > 1$, the unique endemic equilibrium is globally asymptotically stable in $\mathring{T}$, so that the disease, if initially present, will persist at the unique endemic equilibrium level. While the global stability of P_0 when $R_0 \leqslant 1$ can be routinely proved using a well-known Lyapunov function, the global stability of P^* when $R_0 > 1$ has been an open problem in the literature due to the high dimensionality of the model. Our proof uses a theoretical approach developed in [3].

In the special case when $\epsilon \to \infty$ or $\gamma = 0$, model (1) reduces to an SIS model or an SEI model with varying population, respectively. Thus our results generalize earlier global-stability results on SIS and SEI models with recruitment and mass action incidence (see [4,5]). Genik and van den Driessche [6] considered an SEIS model with recruitment-death demographic and varying population. The disease latency is described using a general distribution function $P(t)$. The incidence used in [6] is of the standard form $\lambda IS/N$. When $P(t) = \exp(\epsilon t)$, an ODE model results. The global stability of a unique endemic equilibrium when the basic reproduction number is greater than 1 is conjectured but unresolved. Though we have established the global stability of the unique endemic equilibrium P^* when $R_0 > 1$ for our model, our results do not extend to models considered in [6] because of the different incidence forms. Gao et al. [7] considered four SEI models with density dependent death rates and exponential birth rate. They have shown that periodic solutions can exist when the bilinear mass-action incidence is used. It is also pointed out in [7] that periodic solutions do not exist in SEI models with a constant recruitment. Results in the present paper provide a rigorous proof for their claim.

Our paper is organized as follows. In the following section, we state our main results and prove the global stability of P_0 when $R_0 \leqslant 1$. The mathematical framework that is used in the proof of the global stability of P^* when $R_0 > 1$ (Theorem 2.2) is outlined in Section 3. Proof of Theorem 2.2 is given in Section 4.

2. Main results

We state our main results in this section. Proof of Theorem 2.2 will be given in Section 4.

Theorem 2.1. (a) *If $R_0 \leqslant 1$, then P_0 is the only equilibrium and it is globally asymptotically stable in T.* (b) *If $R_0 > 1$, then P_0 is unstable and there exists an unique endemic equilibrium $P^* \in \mathring{T}$. Furthermore, all solutions starting in $\mathring{T}$ and sufficiently close to P_0 move away from P_0 if $R_0 > 1$.* (c) *If $R_0 > 1$, system* (1) *is uniformly persistent in $\mathring{T}$.*

Proof. Set $L = \epsilon E + (d + \epsilon)I$. Then

$$L' = \lambda\epsilon IS - (d + \epsilon)(d + \alpha + \gamma)I = \frac{\lambda\epsilon I}{R_0}\left(R_0 S - \frac{A}{d}\right) \leqslant 0 \quad \text{if} \quad R_0 \leqslant 1. \tag{5}$$

Furthermore, $L' = 0$ if and only if $I = 0$. Therefore the largest compact invariant set in $\{(S, E, I) \in T : L' = 0\}$, when $R_0 \leqslant 1$, is the singleton $\{P_0\}$. LaSalle's Invariance Principle [8] then implies that P_0 is globally stable in T. This proves the claim (a). The claim (b) follows from the fact that $L' > 0$ if $I > 0$ and $S > A/(dR_0)$. The uniform persistence (see [9,10] for definition) of (1) can be proved by applying a uniform persistence result in [11, Theorem 4.3], and using a similar argument as in the proof of Proposition 3.3 of [12]. □

The uniform persistence of (1) in the bounded set $\mathring{T}$ is equivalent to the existence of a compact $K \subset \mathring{T}$ that is absorbing for (1), namely, each compact set $K_0 \subset \mathring{T}$ satisfies $x(t, K_0) \subset K$ for sufficiently large t, where $x(t, x_0)$ denotes the solution of (1) such that $x(0, x_0) = x_0$, see [9]. The following result completes the determination of the global dynamics of (1) when $R_0 > 1$. Its proof will be given in Section 4.

Theorem 2.2. *Assume that $R_0 > 1$. Then the unique endemic equilibrium P^* is globally asymptotically stable in $\mathring{T}$.*

Theorems 2.1 and 2.2 completely determine the global dynamics of system (1). They establish R_0 as a sharp threshold parameter. If $R_0 \leqslant 1$ the disease always dies out, whereas when $R_0 > 1$ the disease persists at an endemic equilibrium level if it initially exists. Our results contain as special cases the earlier global stability results for SIS ($\epsilon \to \infty$) and SEI ($\gamma = 0$) models. See [4,5] for surveys of these earlier results.

3. A geometric approach to global-stability problems

In this section we briefly outline a general mathematical framework for proving global stability, which will be used in Section 4 to prove Theorem 2.2. The framework is developed in the papers of Smith [13], Li and Muldowney [3,14]. The presentation here follows that in [3].

Let $x \mapsto f(x) \in \mathbb{R}^n$ be a C^1 function for x in an open set $D \subset \mathbb{R}^n$. Consider the differential equation

$$x' = f(x). \tag{6}$$

Denote by $x(t, x_0)$ the solution to (6) such that $x(0, x_0) = x_0$. We make the following two assumptions:

(H_1) There exists a compact absorbing set $K \subset D$.

(H_2) Eq. (6) has a unique equilibrium $\bar{x}$ in D.

The equilibrium $\bar{x}$ is said to be *globally stable* in D if it is locally stable and all trajectories in D converge to $\bar{x}$. The following global-stability problem is formulated in [3].

Theorem 3.1 (Global-stability problem). *Under the assumptions* (H_1) *and* (H_2), *find conditions on* (6) *such that the local stability of $\bar{x}$ implies its global stability in D.*

Assumptions (H_1) and (H_2) are satisfied if $\bar{x}$ is globally stable in D. For $n \geqslant 2$, a *Bendixson criterion* is a condition satisfied by f which precludes the existence of non-constant periodic solutions of (6). A Bendixson criterion is said to be *robust under C^1 local perturbations of f at $x_1 \in D$* if, for sufficiently small $\epsilon > 0$ and neighborhood U of x_1, it is also satisfied by $g \in C^1(D \to \mathbb{R}^n)$ such that the support $\mathrm{supp}(f - g) \subset U$ and $|f - g|_{C^1} < \epsilon$, where

$$|f-g|_{C^1} = \sup\left\{|f(x)-g(x)| + \left|\frac{\partial f}{\partial x}(x) - \frac{\partial g}{\partial x}(x)\right| : x \in D\right\}.$$

Such g will be called *local ϵ-perturbations of f at x_1*. It is easy to see that the classical Bendixson's condition $\operatorname{div} f(x) < 0$ for $n = 2$ is robust under C^1 local perturbations of f at each $x_1 \in \mathbb{R}^2$. Bendixson criterion for higher dimensional systems that are C^1 robust are discussed in [3,14,15].

A point $x_0 \in D$ is *wandering* for (6) if there exists a neighborhood U of x_0 and $T > 0$ such that $U \cap x(t, U)$ is empty for all $t > T$. Thus, for example, all equilibria and limit points are non-wandering. The following is a version of the local C^1 Closing lemma of Pugh (see [16–18]).

Lemma 3.1. *Let $f \in C^1(D \to \mathbb{R}^n)$. Assume that all positive semi-trajectories of* (6) *are bounded. Suppose that x_0 is a non-wandering point of* (6) *and that $f(x_0) \neq 0$. Then, for each neighborhood U of x_0 and $\epsilon > 0$, there exists a C^1 local-ϵ perturbation g of f at x_0 such that*

(a) $\operatorname{supp}(f-g) \subset U$ *and*

(b) *the perturbed system $x' = g(x)$ has a non-constant periodic solution whose trajectory passes through x_0.*

The following general global-stability principle is established in [3].

Theorem 3.2. *Suppose that assumptions* (H_1) *and* (H_2) *hold. Assume that* (6) *satisfies a Bendixson criterion that is robust under C^1 local perturbations of f at all non-equilibrium non-wandering points for* (6). *Then $\bar{x}$ is globally stable in D provided it is stable.*

The main idea of the proof in [3] for Theorem 3.2 is as follows: suppose that system (6) satisfies a Bendixson criterion. Then it does not have any non-constant periodic solutions. Moreover, the robustness of the Bendixson criterion implies that all nearby differential equations have no non-constant periodic solutions. Thus by Lemma 3.1, all non-wandering points of (6) in D must be equilibria. In particular, each omega limit point in D must be an equilibrium. Therefore $\omega(x_0) = \{\bar{x}\}$ for all $x_0 \in D$ since $\bar{x}$ is the only equilibrium in D.

A method of deriving a Bendixson criterion in $\mathbb{R}^n$ is developed in [15]. The idea is to show that the second compound equation

$$z'(t) = \frac{\partial f^{[2]}}{\partial x}(x(t, x_0))z(t), \tag{7}$$

with respect to a solution $x(t, x_0) \subset D$ to (6), is uniformly asymptotically stable, and the exponential decay rate of all solutions to (7) is uniform for x_0 in each compact subset of D. Here $\partial f^{[2]}/\partial x$ is the second additive compound matrix of the Jacobian matrix $\partial f/\partial x$, see Appendix A. It is an $\binom{n}{2} \times \binom{n}{2}$ matrix, and thus (7) is a linear system of dimension $\binom{n}{2}$. If D is simply connected, the above mentioned stability property of (7) implies the exponential decay of the surface area of any compact 2d surface in D, which in turn precludes the existence of any invariant simple closed rectifiable curve in D, including periodic orbits. The required uniform asymptotic stability of the linear system (7) can be proved by constructing a suitable Lyapunov function.

Let $x \mapsto P(x)$ $\binom{n}{2} \times \binom{n}{2}$ matrix-valued function that is C^1 for $x \in D$. Assume that $P^{-1}(x)$ exists and is continuous for $x \in K$, the compact absorbing set. A quantity $\bar{q}_2$ is defined as

$$\bar{q}_2 = \lim_{t\to\infty} \sup \sup_{x_0 \in K} \frac{1}{t} \int_0^t \mu(B(x(s, x_0)))\, \mathrm{d}s, \tag{8}$$

where

$$B = P_f P^{-1} + P \frac{\partial f^{[2]}}{\partial x} P^{-1}, \tag{9}$$

the matrix P_f is obtained by replacing each entry p_{ij} of P by its derivative in the direction of f, p_{ijf}. The quantity $\mu(B)$ is the *Lozinskiĭ measure* of B with respect to a vector norm $|\cdot|$ in $\mathbb{R}^N$, $N = \binom{n}{2}$, defined by

$$\mu(B) = \lim_{h\to 0^+} \frac{|I + hB| - 1}{h},$$

see [19, p. 41]. It is shown in [3] that, if D is simply connected, the condition $\bar{q}_2 < 0$ rules out the presence of any orbit that gives rise to a simple closed rectifiable curve that is invariant for (6), such as periodic orbits, homoclinic orbits, and heteroclinic cycles. Moreover, it is robust under C^1 local perturbations of f near any non-equilibrium point that is non-wandering. In particular, the following global stability result is proved in Theorem 3.5 of [3].

Theorem 3.3. *Assume that D is simply connected and that assumptions* (H_1), (H_2) *hold. Then the unique equilibrium $\bar{x}$ of* (6) *is globally stable in D if $\bar{q}_2 < 0$.*

It is remarked in [3] that, under the assumptions of Theorem 3.3, the condition $\bar{q}_2 < 0$ also implies the local stability of $\bar{x}$, since, assuming the contrary, $\bar{x}$ is both the alpha and omega limit point of a homoclinic orbit which is ruled out by the condition $\bar{q}_2 < 0$.

4. Proof of Theorem 2.2.

We now apply the theory outlined in the preceding section, in particular Theorem 3.3, to prove that the endemic equilibrium P^* is globally asymptotically stable in $\mathring{T}$ as stated in Theorem 2.2. The following lemma will be used later in the proof.

Lemma 4.1. *Assume $R_0 > 1$. Then there exists $\bar{t} > 0$ such that, each solution $(S(t), E(t), I(t))$ to* (1) *with $(S(0), E(0), I(0)) \in K$, the compact absorbing set in $\mathring{T}$, satisfies $\lambda S(t) > \gamma$ for $t > \bar{t}$.*

Proof. From (1) we have $S'(t) = A - dS(t) - (\lambda S(t) - \gamma)I(t)$. If $\lambda S(t) \leqslant \gamma$, then $S'(t) \geqslant A - dS(t) \geqslant A - d\gamma/\lambda$. Note $R_0 > 1$ implies $A - d\gamma/\lambda > 0$. It follows that each solution to (1) crosses the line $\lambda S = \gamma$ in finite time and remains above the line afterwards, and thus $\lambda S(t) > \gamma$, for $t > \bar{t}$. The continuous dependence of solutions on the initial data implies that $\bar{t}$ can be chosen uniformly for $(S(0), E(0), I(0)) \in K$. $\square$

From the discussion in Section 2, we know that system (1) satisfies the assumptions $(\mathrm{H}_1), (\mathrm{H}_2)$ in the interior of its feasible region T. Let $x = (S, E, I)$ and let $f(x)$ denote the vector field of (1). The Jacobian matrix $J = \partial f/\partial x$ associated with a general solution $x(t)$ of (1) is

$$J = \begin{bmatrix} -\lambda I - d & 0 & -\lambda S + \gamma \\ \lambda I & -d - \epsilon & \lambda S \\ 0 & \epsilon & -d - \gamma - \alpha \end{bmatrix},$$

and its second additive compound matrix $J^{[2]}$ is, from Appendix A,

$$J^{[2]} = \begin{bmatrix} -\lambda I - \epsilon - 2d & \lambda S & \lambda S - \gamma \\ \epsilon & -\lambda I - \gamma - \alpha - 2d & 0 \\ 0 & \lambda I & -\epsilon - \gamma - \alpha - 2d \end{bmatrix}. \tag{10}$$

Set the function $P(x) = P(S, E, I) = \mathrm{diag}\{1, E/I, E/I\}$, Then

$$P_f P^{-1} = \mathrm{diag}\left\{0, \frac{E'}{E} - \frac{I'}{I}, \frac{E'}{E} - \frac{I'}{I}\right\}$$

and the matrix $B = P_f P^{-1} + PJ^{[2]}P^{-1}$ in (9) can be written in block form

$$B = \begin{bmatrix} B_{11} & B_{12} \\ B_{21} & B_{22} \end{bmatrix}$$

where $B_{11} = -\lambda I - \epsilon - 2d$,

$$B_{12} = \left[\lambda S \frac{I}{E}, \quad (\lambda S - \gamma)\frac{I}{E}\right], \quad B_{21} = \begin{bmatrix} \frac{\epsilon E}{I} \\ 0 \end{bmatrix},$$

$$B_{22} = \begin{bmatrix} \frac{E'}{E} - \frac{I'}{I} - \lambda I - \gamma - \alpha - 2d & 0 \\ \lambda I & \frac{E'}{E} - \frac{I'}{I} - \epsilon - \gamma - \alpha - 2d \end{bmatrix}.$$

Let (u, v, w) denote the vectors in $\mathbb{R}^3 \cong \mathbb{R}^{\binom{3}{2}}$, we select a norm in $\mathbb{R}^3$ as

$$|(u, v, w)| = \max\{|u|, |v| + |w|\},$$

and let μ denote the Lozinskiĭ measure with respect to this norm. Using the method of estimating μ in [20], we have

$$\mu(B) \leqslant \sup\{g_1, g_2\}, \tag{11}$$

where

$$g_1 = \mu_1(B_{11}) + |B_{12}|,$$
$$g_2 = |B_{21}| + \mu_1(B_{22}),$$

$|B_{12}|, |B_{21}|$ are matrix norms with respect to the l_1 vector norm, and μ_1 denotes the Lozinskiĭ measure with respect to the l_1 norm. More specifically, $\mu_1(B_{11}) = -\lambda I - \epsilon - 2d$, $|B_{21}| = \epsilon E/I$, and $|B_{12}| = \max\{\lambda IS/E, |\lambda IS - \gamma I|/E\} = \lambda IS/E$ for $t > \bar{t}$, because of Lemma 4.1. To calculate $\mu_1(B_{22})$, we add the absolute value of the off-diagonal elements to the diagonal one in each column of B_{22}, and then take the maximum of two sums, see [19, p. 41]. This leads to

$$\mu_1(B_{22}) = \frac{E'}{E} - \frac{I'}{I} - \gamma - \alpha - 2d.$$

Therefore, for $t > \bar{t}$,

$$g_1 = -\lambda I - \epsilon - 2d + \frac{\lambda SI}{E}, \tag{12}$$

$$g_2 \leqslant \frac{E'}{E} - \frac{I'}{I} - \gamma - \alpha - 2d + \frac{\epsilon E}{I}. \tag{13}$$

Rewriting (1), we have

$$\frac{E'}{E} + d + \epsilon = \frac{\lambda SI}{E}, \tag{14}$$

$$\frac{I'}{I} + d + \gamma + \alpha = \frac{\epsilon E}{I}. \tag{15}$$

Substituting (14) into (12) and (15) into (13), and using (11), we have $\mu(B) \leqslant E'/E - d$ for $t > \bar{t}$. Along each solution $x(t, x_0)$ to (1) such that $x_0 \in K$, where K is the compact absorbing set, we thus have

$$\frac{1}{t}\int_0^t \mu(B)\,\mathrm{d}s \leqslant \frac{1}{t}\log\frac{E(t)}{E(\bar{t})} + \frac{1}{t}\int_0^{\bar{t}} \mu(B)\,\mathrm{d}s - \mathrm{d}\frac{t-\bar{t}}{t},$$

which implies $\bar{q}_2 \leqslant -d/2 < 0$, proving Theorem 2.2.

5. Summary

This paper presents a mathematical study on the global dynamics of an SEIS epidemiological model that incorporates constant recruitment, exponential natural death as well as the disease-related death, so that the population size may vary in time. The incidence rate is of the simple mass-action incidences frequently used in the literature.

It is rigorously established in Theorems 2.1 and 2.2 that the basic reproduction number R_0 in (4) is a sharp threshold parameter and completely determines the global dynamics of (1) in the feasible region T. If $R_0 \leqslant 1$, the disease-free equilibrium is globally stable in T and the disease always dies out. If $R_0 > 1$, a unique endemic equilibrium is globally stable in the interior of the feasible region T, so that the disease persists at the endemic equilibrium if it is initially present. The proof of the global stability of P^* when $R_0 > 1$ utilizes a new approach of Li and Muldowney [3] to global-stability problems in $\mathbb{R}^n$.

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Appendix A. The second additive compound matrix

Let A be a linear operator on $\mathbb{R}^n$ and also denote its matrix representation with respect to the standard basis of $\mathbb{R}^n$. Let $\wedge^2\mathbb{R}^n$ denote the exterior product of $\mathbb{R}^n$. A induces canonically a linear operator $A^{[2]}$ on $\wedge^2\mathbb{R}^n$: for $u_1, u_2 \in \mathbb{R}^n$, define

$$A^{[2]}(u_1 \wedge u_2) := A(u_1) \wedge u_2 + u_1 \wedge A(u_2)$$

and extend the definition over $\wedge^2\mathbb{R}^n$ by linearity. The matrix representation of $A^{[2]}$ with respect to the canonical basis in $\wedge^2\mathbb{R}^n$ is called the *second additive compound matrix* of A. This is an $\binom{n}{2} \times \binom{n}{2}$ matrix and satisfies the property $(A+B)^{[2]} = A^{[2]} + B^{[2]}$. In the special case when $n = 2$, we have $A^{[2]}_{2\times 2} = \mathrm{tr}A$. In general, each entry of $A^{[2]}$ is a linear expression of those of A. For instance, when $n = 3$, the second additive compound matrix of $A = (a_{ij})$ is

$$A^{[2]} = \begin{bmatrix} a_{11}+a_{22} & a_{23} & -a_{13} \\ a_{32} & a_{11}+a_{33} & a_{12} \\ -a_{31} & a_{21} & a_{22}+a_{33} \end{bmatrix}.$$

For detailed discussions of compound matrices and their properties we refer the reader to [21,22]. A comprehensive survey on compound matrices and their relations to differential equations is given in [22].

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