

GLOBAL RESULTS FOR AN EPIDEMIC MODEL WITH VACCINATION THAT EXHIBITS BACKWARD BIFURCATION*

JULIEN ARINO[†], C. CONNELL MCCLUSKEY[†], AND P. VAN DEN DRIESSCHE[†]

Abstract. Vaccination of both newborns and susceptibles is included in a transmission model for a disease that confers immunity. The interplay of the vaccination strategy together with the vaccine efficacy and waning is studied. In particular, it is shown that a backward bifurcation leading to bistability can occur. Under mild parameter constraints, compound matrices are used to show that each orbit limits to an equilibrium. In the case of bistability, this global result requires a novel approach since there is no compact absorbing set.

Key words. epidemic model, vaccination, backward bifurcation, compound matrices, global dynamics

AMS subject classifications. 92D30, 34D23

DOI. 10.1137/S0036139902413829

1. Introduction. Vaccination is a commonly used method for controlling diseases, e.g., pertussis, measles, or influenza. Mathematical models including vaccination aid in deciding on a vaccination strategy and in determining changes in qualitative behavior that could result from such a control measure (see, e.g., [5, 6]). If the vaccine is not totally effective, then recent models show that a backward bifurcation is possible for some parameter values [9, 10]. In such a case, the basic reproduction number as modified by vaccination must be reduced below a certain threshold (that is less than one) in order to ensure that the disease dies out. Backward bifurcation has been observed in other disease transmission models, for example the HIV/AIDS models discussed in [2, 8] and the bovine respiratory syncytial virus model in [4].

Our model is a generalization of that of [10], allowing individuals recovering from the disease to go into a temporarily immune class rather than directly back into the susceptible class. A recent model [9] allows for a recovered class and considers vaccination for a disease that has acute and chronic infective stages as well as variable infectivity.

In section 2, we develop our model with general parameters, and illustrate its behavior in section 3 by using vaccination-related values appropriate for pertussis [1, 5]. In particular, we focus on the vaccination parameters and how changes in these may alter the qualitative behavior of the model by leading to subthreshold endemic states via backward bifurcation. Some local stability results are proved.

Previous investigations of the stability of subthreshold endemic states associated with backward bifurcations rely mainly on local results. We use compound matrices and geometric ideas to develop global results under mild parameter restrictions. These tools have been used for analyzing other models of disease transmission in which there is a unique endemic equilibrium; see, e.g., [11, 14, 16, 18]. In section 4, we present a brief summary of this geometric approach for studying the global dynamics of our model, concentrating on the novel features. This method is then used in section 5 to

*Received by the editors August 30, 2002; accepted for publication (in revised form) February 28, 2003; published electronically November 19, 2003. The research of the first and third authors was supported in part by an NSERC research grant and by MITACS.

<http://www.siam.org/journals/siap/64-1/41382.html>

[†]Department of Mathematics and Statistics, University of Victoria, Victoria, BC, Canada V8W 3P4 (arino@math.mcmaster.ca, mccluskc@math.mcmaster.ca, pvdd@math.uvic.ca).

prove global results for the model. (Some technical details are placed in Appendices A and B.) Concluding remarks are given in section 6.

2. Formulation of an *SIRS* model with vaccination. Following [10], but with newborn vaccination and a recovered class, the model has the flow diagram given in Figure 2.1 with the following assumptions. Each of the N individuals can be in one of four states: susceptible, infective, recovered, and vaccinated; the numbers in these states are denoted by S , I , R , and V , respectively. Thus, $N = S + I + R + V$. Birth occurs in the system with rate constant $d > 0$. Of these newborns, a fraction $\alpha \in [0, 1]$ are vaccinated at birth. Death occurs with the same rate constant d as birth; thus the total population N is constant. The transmission coefficient β is the number of contacts made by one infective per unit time multiplied by the probability that a contact with a susceptible leads to infection. The disease is transmitted horizontally, with the transmission modeled using a standard incidence function; thus the rate at which susceptibles become infective is $\beta SI/N$. For contacts between infectives and vaccinated individuals this coefficient is multiplied by a factor $\sigma \in [0, 1]$. Thus $1 - \sigma$ is the vaccine efficacy. Susceptible individuals are vaccinated with rate constant ϕ , and the vaccine protection wanes with rate constant $\theta > 0$. Infective individuals recover with rate constant $\gamma > 0$ and then have temporary immunity. They leave the recovered state with rate constant ν . We assume $\alpha d + \phi > 0$ to ensure that there is a nonzero flow of individuals into class V .

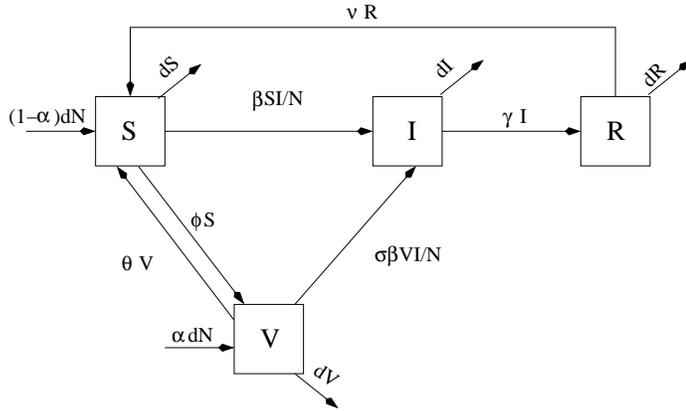


FIG. 2.1. The flow diagram of the *SIRV* model.

The model is formulated as the following system of ordinary differential equations:

$$(2.1a) \quad \frac{dS}{dt} = (1 - \alpha)dN - dS - \beta \frac{SI}{N} - \phi S + \theta V + \nu R,$$

$$(2.1b) \quad \frac{dI}{dt} = \beta \frac{SI}{N} + \sigma \beta \frac{VI}{N} - (d + \gamma)I,$$

$$(2.1c) \quad \frac{dR}{dt} = \gamma I - (d + \nu)R,$$

$$(2.1d) \quad \frac{dV}{dt} = \alpha dN + \phi S - (d + \theta)V - \sigma \beta \frac{VI}{N},$$

with nonnegative initial conditions and $N(0) > 0$.

System (2.1) is well posed: solutions remain nonnegative for nonnegative initial conditions. As the total population is constant, the system can be rewritten in terms

of proportions as

$$(2.2a) \quad \frac{dS}{dt} = (1 - \alpha)d - dS - \beta SI - \phi S + \theta(1 - S - I - R) + \nu R,$$

$$(2.2b) \quad \frac{dI}{dt} = \beta SI + \sigma\beta(1 - S - I - R)I - (d + \gamma)I,$$

$$(2.2c) \quad \frac{dR}{dt} = \gamma I - (d + \nu)R,$$

$$(2.2d) \quad V = 1 - (S + I + R),$$

where here S, I, R, V denote the proportions in the susceptible, infective, recovered, and vaccinated states, respectively. Conclusions about system (2.1) can be easily recovered from system (2.2), and we employ system (2.2) from now on. System (2.2a)–(2.2c) can be written as $dx/dt = f(x)$ with $x = (S, I, R)^T$.

In the case $\sigma = 1$, the vaccine is totally useless, and (2.2) reduces to an SIRS model without vaccination. The behavior is then determined by $\mathcal{R}_0 = \beta/(d + \gamma)$. This is the classical basic reproduction number in the SIRS model, namely, the average number of new infections caused by one infective (in a completely susceptible population) during the infective period. From now on we assume that $\sigma < 1$.

3. Equilibria and bifurcations. For system (2.2), there is always the disease-free equilibrium (DFE)

$$(3.1) \quad X_0 = (S_{DFE}, 0, 0, V_{DFE}) = \left(\frac{\theta + d(1 - \alpha)}{d + \theta + \phi}, 0, 0, \frac{\phi + d\alpha}{d + \theta + \phi} \right).$$

Now consider endemic equilibria with $I = I^* > 0$. From (2.2b) at an endemic equilibrium, $\beta(S + \sigma V) = d + \gamma$. Since $S + \sigma V < 1$, this can be true only for $\beta > d + \gamma$; hence, for $\mathcal{R}_0 \leq 1$ there exists no endemic equilibrium. For $\mathcal{R}_0 > 1$, the existence of endemic equilibria is determined by the presence in $(0, 1]$ of positive real solutions of the quadratic

$$P(I) = AI^2 + BI + C = 0,$$

with

$$A = -\sigma\beta^2 \frac{d + \nu + \gamma}{d + \nu},$$

$$B = \sigma\beta^2 - \beta(d + \theta + \sigma(d + \gamma + \phi)) - \frac{\beta\gamma}{d + \nu}(d + \theta + \sigma\phi),$$

$$C = (d + \theta + \sigma\phi - d\alpha(1 - \sigma))\beta - (d + \gamma)(d + \theta + \phi).$$

Thus, depending on parameter values, the number of endemic equilibria is zero, one, or two. For $\sigma = 0$ (the vaccine is totally effective), at most one endemic equilibrium is possible. From now on we make the realistic assumption that the vaccine is not totally effective, and thus $0 < \sigma < 1$. From (2.2a)–(2.2d), it can be shown that if I^* is a positive solution of $P(I) = 0$, then S^*, R^* , and V^* are positive; thus the equilibrium is biologically relevant. For a positive real solution I^* to $P(I) = 0$, the endemic equilibrium point (EEP) in system (2.2) is given by

$$(S^*, I^*, R^*, V^*) = \left(\frac{(1 - \alpha)d + \frac{(\nu - \theta)\gamma I^*}{d + \nu} + (1 - I^*)\theta}{d + \beta I^* + \phi + \theta}, I^*, \frac{\gamma I^*}{d + \nu}, 1 - S^* - I^* - R^* \right).$$

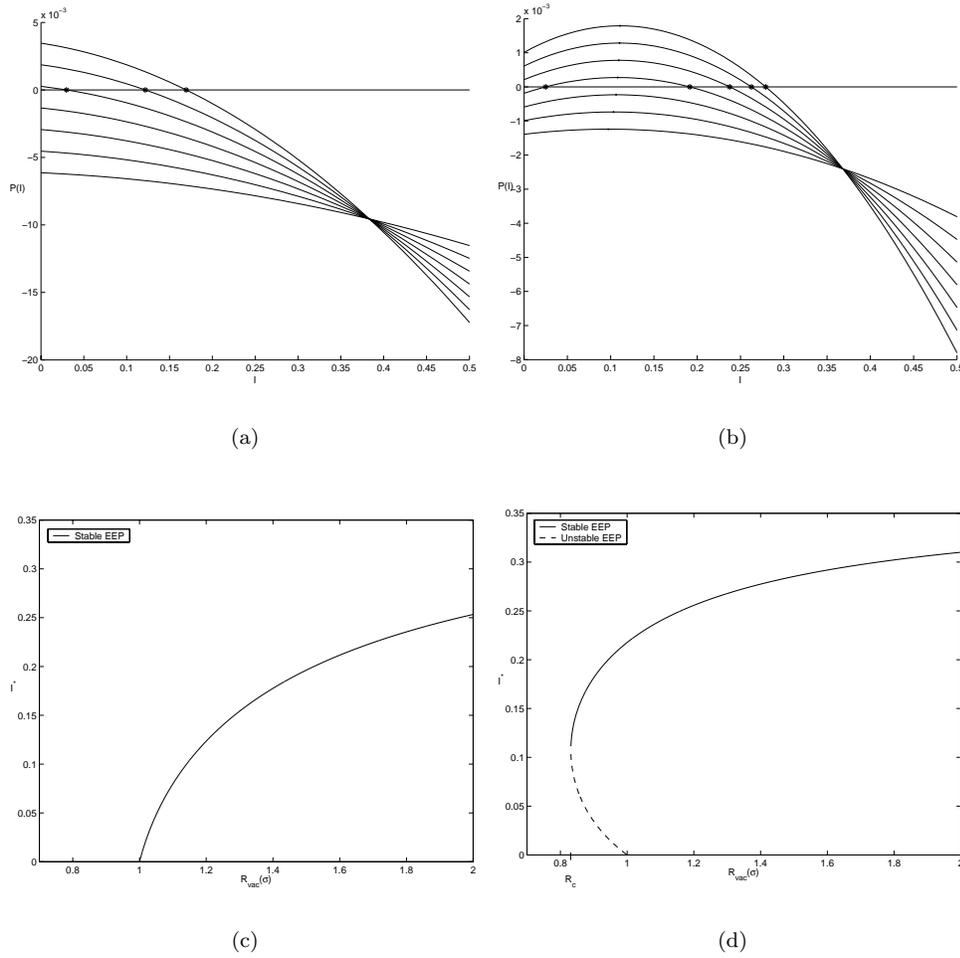


FIG. 3.1. (a) Plot of the quadratic $P(I)$, with increasing values of σ (at left, from bottom to top, $\sigma = 0.04, 0.06, \dots, 0.16$) in the forward bifurcation case, $\phi = 0.2$. (b) As (a) but in the backward bifurcation case, $\phi = 0.05$. (c) Bifurcation in the $(\mathcal{R}_{vac}(\sigma), I^*)$ -plane, $\phi = 0.2$. (d) Bifurcation in the $(\mathcal{R}_{vac}(\sigma), I^*)$ -plane, $\phi = 0.05$.

In Figure 3.1, $P(I)$ is plotted versus I for increasing values of σ and $\phi = 0.2$ or 0.05 (all other parameters being fixed at the values indicated in Table 3.1). The values of γ , d and the vaccination parameters of Table 3.1 are appropriate for pertussis [1, 5], whereas β and ν are estimated to illustrate our bifurcation results. Figure 3.1(a) shows the situation that prevails when the bifurcation is a classical forward one. In this case, an increase in σ through some critical value σ_c (which depends on the other parameter values) leads through a transcritical bifurcation to a unique endemic equilibrium. Figure 3.1(b) shows the occurrence of the backward bifurcation. In this case, an increase of σ leads to the curve $P(I)$ becoming tangent to the horizontal axis defining a critical value σ_c at a saddle-node bifurcation. As σ becomes larger than σ_c , two equilibria exist. We expect bistability with the DFE and the equilibrium with the larger I value being stable. As σ increases further, the equilibrium with the smaller

TABLE 3.1
Parameter values used in simulations.

Parameter	Typical value or range	Meaning
β	0.4 /day	Transmission coefficient
γ	1/(21 days)	Average infectious period 21 days
d	1/(75 years)	Average lifespan 75 years
ν	1/(31 days)	Average period of immunity 31 days
α	0.9	Proportion of vaccinated newborns
ϕ	0.05 to 0.2/day	Vaccination rate constant
σ	0.04 to 0.2	Vaccine is between 80% and 96% effective
θ	1/(5 years)	Average vaccine waning time 5 years

I value moves to the left. When this equilibrium leaves the positive orthant through a transcritical bifurcation with the DFE, there is only one endemic equilibrium.

Since the concavity of the quadratic $P(I)$ is fixed (as $A < 0$), observation of Figure 3.1(b) gives necessary conditions for the existence of two equilibria: $P'(0) = B > 0$ and $P(0) = C < 0$. Together with the fact that the roots of $P(I)$ are real, this gives the bistability region $B > 0, C < 0$ and $\Delta = B^2 - 4AC > 0$. Figure 3.2 shows this region as a function of σ and ϕ , with all other parameters fixed as in Table 3.1.

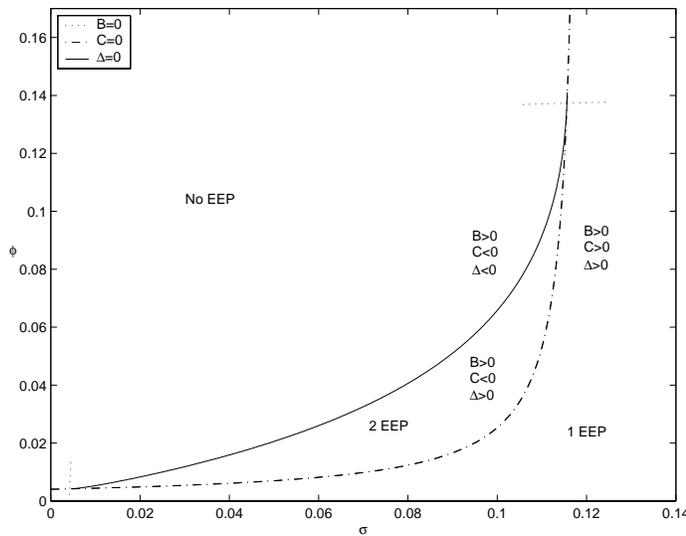


FIG. 3.2. Bifurcation diagram in the (σ, ϕ) -plane.

Using for example the method of [20], the basic reproduction number as modified by vaccination is

$$\mathcal{R}_{vac} = \frac{\beta}{d + \gamma} (S_{DFE} + \sigma V_{DFE}),$$

which from (3.1) gives

$$(3.2) \quad \mathcal{R}_{vac} = \mathcal{R}_0 \frac{d + \theta + \sigma\phi - d\alpha(1 - \sigma)}{d + \theta + \phi}.$$

We write $\mathcal{R}_{vac}(\sigma)$ to indicate σ as the bifurcation parameter when all other parameters are fixed. Note that $\mathcal{R}_0(d(1 - \alpha) + \theta)/(d + \theta + \phi) < \mathcal{R}_{vac}(\sigma) < \mathcal{R}_0$ (equalities are achieved at $\sigma = 0$ and $\sigma = 1$, respectively). The constant term C in the polynomial $P(I)$ can be written as $(d + \gamma)(d + \theta + \phi)(\mathcal{R}_{vac} - 1)$; thus $P(0)$ has the same sign as $\mathcal{R}_{vac} - 1$. Define $\mathcal{R}_c = \mathcal{R}_{vac}(\sigma_c)$. For a forward bifurcation, this gives $\mathcal{R}_c = 1$; see Figure 3.1(c). For a backward bifurcation, $\mathcal{R}_c < 1$; see Figure 3.1(d). The existence of endemic equilibria is summarized as follows.

PROPOSITION 3.1. *For model (2.2), if $\mathcal{R}_{vac} < \mathcal{R}_c$ or $\mathcal{R}_{vac} = \mathcal{R}_c = 1$, there is no endemic equilibrium; if $\mathcal{R}_c < \mathcal{R}_{vac} < 1$, then there are two distinct endemic equilibria; if $\mathcal{R}_c = \mathcal{R}_{vac} < 1$, $\mathcal{R}_c < \mathcal{R}_{vac} = 1$, or $\mathcal{R}_{vac} > 1$, there is a unique endemic equilibrium.*

When two endemic equilibria are present, let X^* and X_* be the endemic equilibria with the larger and smaller value of I^* , respectively; when $\mathcal{R}_{vac} \neq \mathcal{R}_c$ and a unique endemic equilibrium exists, it is denoted by X^* ; when $\mathcal{R}_{vac} = \mathcal{R}_c$ and a unique endemic equilibrium exists, it is denoted by X_c . A global result (for $\mathcal{R}_0 < 1$) and local stability of the equilibria are summarized in the following theorem, which justifies the stability of equilibria as shown in Figures 3.1(c) and 3.1(d).

THEOREM 3.2. *If $\mathcal{R}_0 < 1$, then the DFE X_0 is the only equilibrium for system (2.2a)–(2.2c), and it is globally asymptotically stable; X_0 is locally asymptotically stable for $\mathcal{R}_{vac} < 1$ and unstable for $\mathcal{R}_{vac} > 1$. When present, the endemic equilibrium X_* is unstable, and if $\theta \leq \nu$, then X^* is locally asymptotically stable.*

Proof. As remarked earlier, for $\mathcal{R}_0 \leq 1$ there exists no endemic equilibrium. Further, if $\mathcal{R}_0 < 1$, then I can be used as a Lyapunov function to show that the DFE is globally asymptotically stable.

From [20, Theorem 2], \mathcal{R}_{vac} is a threshold value, with X_0 being locally asymptotically stable if $\mathcal{R}_{vac} < 1$ and unstable if $\mathcal{R}_{vac} > 1$. Linearizing (2.2a)–(2.2c) about an endemic equilibrium gives the Jacobian matrix

$$\frac{\partial f}{\partial x}(S^*, I^*, R^*) = \begin{bmatrix} -d - \beta I^* - \phi - \theta & -\beta S^* - \theta & \nu - \theta \\ (1 - \sigma)\beta I^* & -\sigma\beta I^* & -\sigma\beta I^* \\ 0 & \gamma & -(d + \nu) \end{bmatrix}.$$

In the case in which two endemic equilibria exist, $\det(\frac{\partial f}{\partial x}(X_*)) > 0$ and $\text{tr}(\frac{\partial f}{\partial x}(X_*)) < 0$. Thus $\frac{\partial f}{\partial x}(X_*)$ has a positive eigenvalue and two eigenvalues with negative real part, making X_* unstable hyperbolic.

Let λ_j , $j = 1, 2, 3$, be the eigenvalues of $\frac{\partial f}{\partial x}(X^*)$ with $\Re(\lambda_1) \leq \Re(\lambda_2) \leq \Re(\lambda_3)$. It can be shown that $\det(\frac{\partial f}{\partial x}(X^*)) < 0$ and so $\lambda_1\lambda_2\lambda_3 < 0$. This means that either $\Re(\lambda_j) < 0$ for $j = 1, 2, 3$ or $\Re(\lambda_1) < 0 \leq \Re(\lambda_2) \leq \Re(\lambda_3)$. Since $\text{tr}(\frac{\partial f}{\partial x}(X^*)) < 0$, it follows that $\lambda_1 + \lambda_2 + \lambda_3 < 0$, which implies that $\Re(\lambda_1 + \lambda_2) < 0$ and $\Re(\lambda_1 + \lambda_3) < 0$.

Assume now that $\theta \leq \nu$, and consider the second additive compound [12] of the Jacobian matrix

$$\frac{\partial f^{[2]}}{\partial x}(X^*) = \begin{bmatrix} -\left(\begin{matrix} (1 + \sigma)\beta I^* \\ + d + \phi + \theta \end{matrix} \right) & -\sigma\beta I^* & \theta - \nu \\ \gamma & -\left(\begin{matrix} \beta I^* + 2d \\ + \phi + \theta + \nu \end{matrix} \right) & -\beta S^* - \theta \\ 0 & (1 - \sigma)\beta I^* & -(\sigma\beta I^* + d + \nu) \end{bmatrix}.$$

Using the signs of the matrix elements, it is easily shown that $\det(\frac{\partial f^{[2]}}{\partial x}(X^*)) < 0$.

The eigenvalues of $\frac{\partial f^{[2]}}{\partial x}(X^*)$ are $\lambda_i + \lambda_j$, $1 \leq i < j \leq 3$, and so

$$\begin{aligned} -1 &= \operatorname{sgn} \left(\det \left(\frac{\partial f^{[2]}}{\partial x}(X^*) \right) \right) \\ &= \operatorname{sgn} (\Re(\lambda_1 + \lambda_2) \Re(\lambda_1 + \lambda_3) \Re(\lambda_2 + \lambda_3)) \\ &= \operatorname{sgn} (\Re(\lambda_2 + \lambda_3)). \end{aligned}$$

Thus, $\Re(\lambda_j) < 0$ for $j = 1, 2, 3$, and therefore X^* is locally asymptotically stable. \square

Remark 3.3. For all of the numerical simulations performed here, the parameters satisfy $\theta \leq \nu$; i.e., the average period of immunity is no longer than the average vaccine waning time. If $\theta \geq \nu$, then there is no endemic equilibrium for $\mathcal{R}_{vac} \leq 1$, since each of the coefficients in $P(I)$ is nonpositive; thus there can be no bistability.

More general techniques are needed to determine the global dynamics for the case $\mathcal{R}_0 > 1$.

4. A geometric approach to global dynamics. In this section, a brief outline of a general mathematical framework for studying global dynamics is given. This approach to global dynamics is developed in the papers of Smith [17] and Li and Muldowney [12, 13, 15]. While this method is usually applied to demonstrate the global stability of a unique equilibrium [11, 14], here it is used to demonstrate bistability for a system that exhibits a backward bifurcation. In [11, 14], compound matrix techniques together with the existence of a compact absorbing set are used to prove global asymptotic stability of the endemic equilibrium point. For cases in which our model exhibits bistability, no such compact absorbing set exists; thus, a sequence of surfaces that exists for time $\epsilon > 0$ and minimizes the functional measuring surface area must be considered.

Let B be the Euclidean ball in \mathbb{R}^2 , and let \bar{B} and ∂B be its closure and boundary, respectively. Letting $\operatorname{Lip}(X \rightarrow Y)$ denote the set of Lipschitzian functions from X to Y , a function $\varphi \in \operatorname{Lip}(\bar{B} \rightarrow \mathcal{D})$ is a (simply connected rectifiable) surface in \mathcal{D} . A function $\psi \in \operatorname{Lip}(\partial B \rightarrow \mathcal{D})$ is a closed rectifiable curve in \mathcal{D} and is called simple if it is one-to-one. Let $\Sigma(\psi, \mathcal{D}) = \{\varphi \in \operatorname{Lip}(\bar{B} \rightarrow \mathcal{D}) : \varphi|_{\partial B} = \psi\}$. In [15], it is shown that if ψ is contained in a simply connected open subset of \mathcal{D} , then $\Sigma(\psi, \mathcal{D})$ is nonempty.

Let $\|\cdot\|$ be a norm on $\mathbb{R}^{\binom{n}{2}}$. Consider a functional \mathcal{S} on surfaces in \mathcal{D} defined by

$$(4.1) \quad \mathcal{S}\varphi = \int_{\bar{B}} \left\| P \cdot \left(\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2} \right) \right\| du,$$

where $u = (u_1, u_2)$, $u \mapsto \varphi(u)$ is Lipschitzian on \bar{B} , the wedge product $\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2}$ is a vector in $\mathbb{R}^{\binom{n}{2}}$ (see [19]), and P is an $\binom{n}{2} \times \binom{n}{2}$ matrix such that $\|P^{-1}\|$ is bounded on $\varphi(\bar{B})$. The following result follows from the development in [12] and [15].

PROPOSITION 4.1. *Suppose that ψ is a simple closed rectifiable curve in \mathbb{R}^n . Then there exists $\delta > 0$ such that*

$$\mathcal{S}\varphi \geq \delta$$

for all $\varphi \in \Sigma(\psi, \mathbb{R}^n)$.

Functionals of the form (4.1) give a measure of the surface area of the surface φ . In this context, Proposition 4.1 can be interpreted as stating that, given a curve $\psi \subset \mathbb{R}^n$ and a measure of surface area, all surfaces with boundary ψ have surface area uniformly bounded away from zero.

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

$$(4.2) \quad \frac{dx}{dt} = f(x).$$

(This is used in section 5 with $x = (S, I, R)^T$ for the system (2.2a)–(2.2c).) For any surface φ , the new surface φ_t is defined by $\varphi_t(u) = x(t, \varphi(u))$. Note that when viewed as a function of t , $\varphi_t(u)$ gives the solution to (4.2) that passes through the point $\varphi(u)$ at $t = 0$.

It is shown in [15] that $D_+\mathcal{S}\varphi_t$, the right-hand derivative of $\mathcal{S}\varphi_t$, is given by

$$(4.3) \quad D_+\mathcal{S}\varphi_t = \int_{\bar{B}} \lim_{h \rightarrow 0^+} \frac{1}{h} \left[\|z + hQ(\varphi_t(u))z\| - \|z\| \right] du,$$

where the matrix $Q = P_f P^{-1} + P \frac{\partial f}{\partial x} P^{-1}$. Here P_f is the directional derivative of P in the direction of the vector field f , $\frac{\partial f}{\partial x}$ is the second additive compound [12] of $\frac{\partial f}{\partial x}$, and $z = P \cdot \left(\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2} \right)$ is a solution to the differential equation

$$(4.4) \quad \frac{dz}{dt} = Q(\varphi_t(u))z.$$

Thus, (4.3) can be rewritten as

$$D_+\mathcal{S}\varphi_t = \int_{\bar{B}} D_+\|z\| du.$$

If there exists $\eta > 0$ such that $D_+\|z\| \leq -\eta\|z\|$ for all $z \in \mathbb{R}^{\binom{n}{2}}$ and all $x \in \mathcal{D}$, then $D_+\mathcal{S}\varphi_t \leq \int_{\bar{B}} -\eta\|z\| du = -\eta\mathcal{S}\varphi_t$, and so $\mathcal{S}\varphi_t \leq \mathcal{S}\varphi e^{-\eta t}$ as long as φ_t remains in \mathcal{D} . If $\varphi_t \subset \mathcal{D}$ for all t , then $\lim_{t \rightarrow \infty} \mathcal{S}\varphi_t = 0$.

Suppose that ψ is the trace of a periodic solution of (4.2). Then ψ is invariant under the flow described by (4.2). Let $\varphi \in \Sigma(\psi, \mathcal{D})$. Then $\varphi_t(\partial B) = x(t, \varphi(\partial B)) = x(t, \psi(\partial B)) = \psi(\partial B)$. Thus, $\varphi_t \in \Sigma(\psi, \mathcal{D})$ as long as $\varphi_t \subset \mathcal{D}$. If \mathcal{D} is positively invariant, then $\varphi_t \in \Sigma(\psi, \mathcal{D})$ for all $t \geq 0$, and therefore, by Proposition 4.1, $\mathcal{S}\varphi_t \geq \delta$ for all $t \geq 0$. Thus, by the remarks of the previous paragraph, the condition that $D_+\|z\| \leq -\eta\|z\|$ for all z and x precludes the existence of periodic solutions to (4.2).

In the absence of a compact absorbing set, a surface may not remain in \mathcal{D} for all time. Thus, we consider a sequence of surfaces $\{\varphi^k\}$ in $\Sigma(\psi, \mathcal{D})$ such that $\lim_{k \rightarrow \infty} \mathcal{S}\varphi^k = \delta$, where $\delta = \inf\{\mathcal{S}\varphi : \varphi \in \Sigma(\psi, \mathcal{D})\}$ and for which there exists $\epsilon > 0$ such that $\varphi_t^k(\bar{B}) \subset \mathcal{D}$ for $t \in [0, \epsilon]$ and $k = 1, 2, \dots$. If $D_+\|z\| \leq -\eta\|z\|$ for all $z \in \mathbb{R}^{\binom{n}{2}}$ and all $x \in \mathcal{D}$, then $\mathcal{S}\varphi_\epsilon^k \leq \mathcal{S}\varphi^k e^{-\eta\epsilon}$, and therefore there exists l such that $\mathcal{S}\varphi_\epsilon^l < \delta$. This implies that the boundary of φ_ϵ^l is not ψ , and therefore ψ is not invariant under (4.2). Thus, if for every simple closed curve ψ in \mathcal{D} there is a sequence of surfaces $\{\varphi^k\}$ in $\Sigma(\psi, \mathcal{D})$ that all remain in \mathcal{D} for some time $\epsilon > 0$, and there is a surface functional \mathcal{S} of the form given in (4.1), then the condition $D_+\|z\| \leq -\eta\|z\|$ precludes the existence of invariant closed curves, including periodic orbits, homoclinic orbits, and heteroclinic cycles.

The above conditions are robust under local C^1 perturbations to the original differential equation (4.2). Thus, if (4.2) satisfies the above hypotheses, then so do all systems that are sufficiently C^1 -close to (4.2). Therefore, Pugh’s closing lemma [7] leads to the following result in the spirit of Criterion 3.1 in [15], giving conditions that preclude the existence of nonconstant nonwandering points.

THEOREM 4.2. *Suppose there exists a norm $\|\cdot\|$ on $\mathbb{R}^{\binom{2}{2}}$ and $\eta > 0$ such that $D_+\|z\| \leq -\eta\|z\|$ for all $z \in \mathbb{R}^{\binom{2}{2}}$ satisfying (4.4) and all $x \in \mathcal{D}$ for \mathcal{D} simply connected. Further, suppose that for any simple closed curve ψ in \mathcal{D} there exists a sequence of surfaces $\{\varphi^k\}$ that minimizes \mathcal{S} relative to $\Sigma(\psi, \mathcal{D})$ and there exists $\epsilon > 0$ such that $\varphi_t^k \subset \mathcal{D}$ for $t \in [0, \epsilon]$ and $k = 1, 2, \dots$. Then any omega limit point of (4.2) in the interior of \mathcal{D} is an equilibrium.*

In order to apply the theorem to a particular system, it is necessary to find a norm $\|\cdot\|$ and a matrix P (which then determines the matrix Q) such that $D_+\|z\| \leq -\eta\|z\|$ and to show that an appropriate sequence of surfaces exists.

5. Global analysis of the SIRS model with vaccination. Recalling that for $\mathcal{R}_0 < 1$ the DFE is globally asymptotically stable (Theorem 3.2), we now apply the theory outlined in the previous section to system (2.2a)–(2.2c) for $\mathcal{R}_0 > 1$. Let $\mathcal{D} = \{(S, I, R) : S, R \geq 0, I > 0, S + I + R \leq 1\}$. The Jacobian matrix at a general point $x = (S, I, R)^T$ is given by

$$(5.1) \quad \frac{\partial f}{\partial x} = \begin{bmatrix} -d - \beta I - \phi - \theta & -\beta S - \theta & \nu - \theta \\ (1 - \sigma)\beta I & \beta(S + \sigma V - \sigma I) - (d + \gamma) & -\sigma\beta I \\ 0 & \gamma & -(d + \nu) \end{bmatrix},$$

where $V = 1 - S - I - R$ from (2.2d). The second additive compound [12] of the Jacobian matrix is the 3×3 matrix given by

$$\frac{\partial f^{[2]}}{\partial x} = \begin{bmatrix} \left(\begin{matrix} \beta(S + \sigma V - (1 + \sigma)I) \\ -[2d + \phi + \theta + \gamma] \end{matrix} \right) & -\sigma\beta I & \theta - \nu \\ \gamma & -(\beta I + 2d + \phi + \theta + \nu) & -(\beta S + \theta) \\ 0 & (1 - \sigma)\beta I & \left(\begin{matrix} \beta(S + \sigma V - \sigma I) \\ -[2d + \gamma + \nu] \end{matrix} \right) \end{bmatrix}.$$

Let $P = \frac{1}{I}I_3$, where I_3 is the 3×3 identity matrix. Then $P_f P^{-1} = -\frac{1}{I} \frac{dI}{dt} I_3$ with $\frac{dI}{dt}$ given by (2.2b), and

$$(5.2) \quad Q = P_f P^{-1} + P \frac{\partial f^{[2]}}{\partial x} P^{-1} = \begin{bmatrix} -[(1 + \sigma)\beta I + d + \phi + \theta] & -\sigma\beta I & \theta - \nu \\ \gamma & \left(\begin{matrix} \gamma - [\beta(S + \sigma V + I)] \\ +d + \phi + \theta + \nu \end{matrix} \right) & -(\beta S + \theta) \\ 0 & (1 - \sigma)\beta I & -(\sigma\beta I + d + \nu) \end{bmatrix}.$$

For $z = (z_1, z_2, z_3)^T$, let $\|z\|$ be given by

$$(5.3) \quad \|z\| = \begin{cases} \max\{|z_1| + |z_3|, |z_2| + |z_3|\} & \text{if } 0 \leq z_2 z_3, \\ \max\{|z_1| + |z_3|, |z_2|\} & \text{if } z_2 z_3 \leq 0. \end{cases}$$

This norm is used as a Lyapunov function for system (4.4). The following two propositions, with proofs given in the appendices, lead to our main result.

PROPOSITION 5.1. *Assume that in system (2.2a)–(2.2c) the parameters satisfy the following inequalities:*

$$(5.4) \quad \begin{aligned} \theta &< d + 2\nu, \\ 2\gamma &< d + \phi + \theta + \nu, \\ \gamma &< d + \phi + \nu. \end{aligned}$$

Then there exists $\eta > 0$ such that $D_+ \|z\| \leq -\eta \|z\|$ for all $z \in \mathbb{R}^3$ and all $S, I, R, V \geq 0$, $I \neq 0$, where z is a solution of (4.4) with Q and $\|\cdot\|$ given by (5.2) and (5.3), respectively.

Note that inequalities (5.4) are independent of the transmission coefficient β , the proportion of newborns vaccinated α , and the vaccine efficacy σ but depend on the other model parameters.

PROPOSITION 5.2. *Let ψ be a simple closed curve in \mathcal{D} . There exist $\epsilon > 0$ and a sequence of surfaces $\{\varphi^k\}$ that minimizes \mathcal{S} given by (4.1) relative to $\Sigma(\psi, \mathcal{D})$ such that $\varphi_t^k \subset \mathcal{D}$ for all $k = 1, 2, \dots$ and all $t \in [0, \epsilon]$.*

THEOREM 5.3. *If inequalities (5.4) hold, then each positive semitrajectory of (2.2a)–(2.2c) in $\bar{\mathcal{D}}$ limits to a single equilibrium.*

Proof. Let Γ be a positive semitrajectory in $\bar{\mathcal{D}}$ with omega limit set Ω . Suppose that Ω intersects the interior of \mathcal{D} . Propositions 5.1 and 5.2 ensure that Theorem 4.2 can be applied to system (2.2a)–(2.2c). Theorem 4.2 implies that every omega limit point of (2.2a)–(2.2c) in the interior of \mathcal{D} is an equilibrium. Since the system has a finite number of equilibria, there are only a finite number of points in the interior of \mathcal{D} which can be in Ω . As Γ is bounded, Ω must be connected. Thus, Ω must consist of a single equilibrium.

Suppose, on the other hand, that Ω is contained in the boundary $\partial\mathcal{D}$ of \mathcal{D} . Since omega limit sets are invariant, Ω must be contained in the largest invariant subset of $\partial\mathcal{D}$. By considering (2.2a)–(2.2c) with the assumption that θ, γ , and $\alpha d + \phi$ are positive, it is easily shown that $\{X_0\}$ is the only invariant subset of $\partial\mathcal{D}$ and therefore $\Omega = \{X_0\}$. \square

For the parameters given in Table 3.1 and used in Figure 3.2, inequalities (5.4) are satisfied for $\phi > 0.063$, which contains part of the bistability region. With $\theta = 1/(1 \text{ year})$ and $\nu = 1/(14 \text{ days})$, and all other parameters fixed as in Table 3.1, Figure 5.1 shows a two-dimensional bifurcation diagram in the (σ, ϕ) -plane. Inequalities (5.4) are satisfied for $\phi > 0.021$, including the entire region for which bistability occurs.

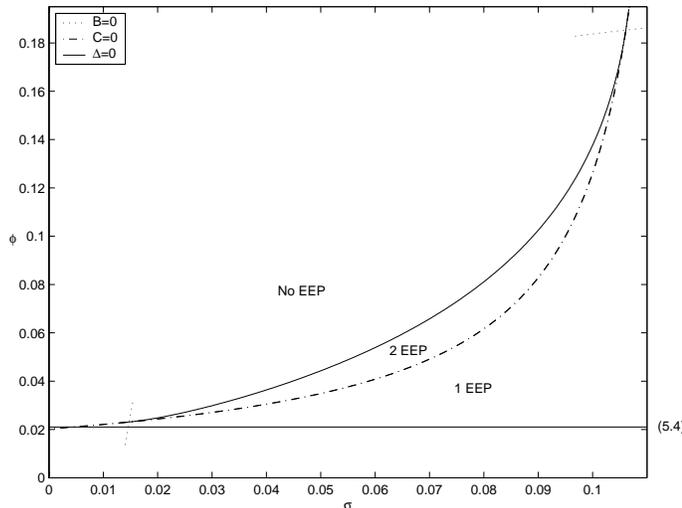


FIG. 5.1. *Bifurcation diagram in the (σ, ϕ) -plane, for $1/\theta$ equal to one year and $1/\nu$ equal to two weeks. The second inequality of (5.4) holds for ϕ above the horizontal line labeled (5.4). The other two inequalities of (5.4) hold in the whole region.*

COROLLARY 5.4. Assume that inequalities (5.4) hold for system (2.2a)–(2.2c).

(i) If there is no endemic equilibrium, then all solutions limit to the DFE X_0 .

(ii) If $\mathcal{R}_{vac} > 1$, then (S, I, R) tends to the unique endemic equilibrium X^* , provided that $I(0) > 0$.

(iii) If there are two endemic equilibria, or if X_c is the only endemic equilibrium, then depending on the initial values, the disease dies out or limits to a constant endemic value.

Proof. Statements (i) and (iii) follow directly from Theorem 5.3. For (ii), $\mathcal{R}_{vac} > 1$, and so the DFE is unstable with a two-dimensional stable manifold (see (5.1)), which is $\{I = 0\}$. Since from Theorem 5.3 every solution limits to an equilibrium, and since solutions with $I(0) > 0$ do not go to the DFE, they must limit to X^* . \square

COROLLARY 5.5. Suppose that $\theta \leq \nu$ and $2\gamma < d + \phi + \theta + \nu$. Then the conclusions of Corollary 5.4 hold. Furthermore, if system (2.2a)–(2.2c) has two endemic equilibria, then the basins of attraction of X^* and X_0 have positive measure and the basin of attraction of X_* has zero measure.

Proof. If $\theta \leq \nu$ and $2\gamma < d + \phi + \theta + \nu$, then the inequalities (5.4) are satisfied and so the conclusions of Corollary 5.4 follow. From Theorem 3.2, X^* is locally asymptotically stable. Thus it has a basin of attraction with positive measure. It is shown in section 3 that X_* is unstable hyperbolic. Thus, the set of points which limit to X_* has Lebesgue measure zero. When there are two endemic equilibria, $\mathcal{R}_{vac} < 1$, and thus X_0 is locally asymptotically stable and has a basin of attraction with positive measure. \square

Remark 5.6. For ν sufficiently large (i.e., a sufficiently short period of immunity), inequalities (5.4) hold and the conclusion of Corollary 5.5 holds. In the limiting case as ν tends to infinity, upon recovery infective individuals progress directly to the susceptible class; thus the model reduces to an *SIS* model with vaccination, similar to that considered in [10].

Remark 5.7. By using norms other than the norm given by (5.3), inequalities (5.4) can be replaced with other conditions which lead to the same conclusions. For example, if $\|z\|$ is given by

$$\|z\| = \max_{j=1,2,3} |z_j|,$$

then (5.4) can be replaced with

$$(5.5) \quad 2\gamma \leq d + \nu + \theta.$$

Similarly, if $\|z\|$ is given by

$$\|z\| = \begin{cases} |z_1| + |z_2| + |z_3| & \text{if } \text{sgn}(z_1) = \text{sgn}(z_2) = \text{sgn}(z_3), \\ \max\{|z_1| + |z_2|, |z_1| + |z_3|\} & \text{if } \text{sgn}(z_1) = \text{sgn}(z_2) = -\text{sgn}(z_3), \\ \max\{|z_1| + |z_3|, |z_2|\} & \text{if } \text{sgn}(z_1) = -\text{sgn}(z_2) = \text{sgn}(z_3), \\ \max\{|z_1| + |z_3|, |z_2| + |z_3|\} & \text{if } -\text{sgn}(z_1) = \text{sgn}(z_2) = \text{sgn}(z_3), \end{cases}$$

then (5.4) can be replaced with

$$(5.6) \quad \begin{aligned} \theta &< d + 2\nu, \\ \gamma &< d + \phi + \min\{\theta, \nu\}. \end{aligned}$$

For parameter values given in Table 3.1, the inequalities found in (5.4) are less restrictive than those given in (5.5) or (5.6).

6. Concluding remarks. The model formulated in section 2 incorporates vaccination for a disease in a simple manner, with vaccinated individuals in a class distinct from that of the individuals who have recovered from the disease. By contrast, in some models (e.g., [3]) these two classes are combined. The basic reproduction number as modified by vaccination, namely \mathcal{R}_{vac} as given by (3.2), is a key parameter in our model. To eradicate the disease, it may not be sufficient to reduce \mathcal{R}_{vac} below one. In the case of bistability, \mathcal{R}_{vac} must be further reduced; see Figure 3.1(d). Increasing vaccination of either newborns or the population at risk has the effect of reducing \mathcal{R}_{vac} . An important parameter in \mathcal{R}_{vac} is the efficacy of the vaccine, namely, $1 - \sigma$. Bistability may occur for a range of σ values. This range depends on the values of the other parameters in the model. The occurrence of a backward bifurcation is illustrated for some parameter values in Figures 3.1(b), 3.1(d), 3.2, 5.1. In the case of bistability, the asymptotic behavior of the proportion of infectives depends on the initial conditions. In such a situation, global analysis is more complicated than in a situation with a unique endemic equilibrium and a compact absorbing set. An appropriate sequence of surfaces that minimizes the functional measuring surface area must be considered. This novel approach is outlined in section 4 and then applied to our model in section 5. Global results are proved under mild parameter restrictions, and it is indicated that alternative restrictions arise from alternative choices of norms. The rate of vaccination of susceptibles and the vaccine waning rate play a role in these restrictions, whereas the vaccine efficacy and the proportion of newborns vaccinated do not. Theorem 5.3 rules out any complicated behavior (e.g., limit cycles) under mild parameter restrictions, and numerical simulations have found no such behavior for any parameter values. A more realistic model including vaccination should incorporate age structure and demographics (see, e.g., [5]). However, global results are then not available, and simulations must be performed to gain some insight into the model behavior and to determine vaccination strategy.

The analysis of our model can be regarded as the first application of using a minimizing sequence of surfaces in this context. This method may also be useful in other models for which there exist solutions that limit to boundary equilibria.

Appendix A. Proof of Proposition 5.1.

Proof. We demonstrate the existence of some $\eta > 0$ such that $D_+ \|z\| \leq -\eta \|z\|$, where z is a solution of (4.4). By linearity, if this inequality is true for some z , then it is also true for $-z$. The proof is subdivided into eight cases based on the octant and the definition of the norm in (5.3).

Case 1. If $0 < z_1, z_2, z_3$ and $|z_1| + |z_3| > |z_2| + |z_3|$, then $\|z\| = |z_1| + |z_3|$ and

$$\begin{aligned} D_+ \|z\| &= D_+(|z_1| + |z_3|) \\ &= D_+(z_1 + z_3) \\ &= \frac{dz_1}{dt} + \frac{dz_3}{dt} \\ &= -((1 + \sigma)\beta I + d + \phi + \theta)z_1 + (1 - 2\sigma)\beta I z_2 + (\theta - (\sigma\beta I + d + 2\nu))z_3. \end{aligned}$$

Noting that $(1 - 2\sigma)\beta I z_2 \leq (1 - \sigma)\beta I z_2 \leq (1 - \sigma)\beta I z_1$,

$$\begin{aligned} D_+ \|z\| &< -(2\sigma\beta I + d + \phi + \theta)z_1 + (\theta - (\sigma\beta I + d + 2\nu))z_3 \\ &\leq \max\{-(2\sigma\beta I + d + \phi + \theta), \theta - (\sigma\beta I + d + 2\nu)\} \|z\|. \end{aligned}$$

Thus, in order that $D_+ \|z\|$ be bounded away from zero on the negative side for all z

and all $I > 0$, we require that

$$(A.1) \quad \theta < d + 2\nu.$$

Case 2. If $0 < z_1, z_2, z_3$ and $|z_1| + |z_3| < |z_2| + |z_3|$, then $\|z\| = |z_2| + |z_3|$ and

$$\begin{aligned} D_+\|z\| &= D_+(|z_2| + |z_3|) \\ &= \frac{dz_2}{dt} + \frac{dz_3}{dt} \\ &= \gamma z_1 + (\gamma - (\beta(S + \sigma V + \sigma I) + d + \phi + \theta + \nu))z_2 - (\beta(S + \sigma I) + d + \theta + \nu)z_3. \end{aligned}$$

Since $z_1 < z_2$, this becomes

$$D_+\|z\| < (2\gamma - (\beta(S + \sigma V + \sigma I) + d + \phi + \theta + \nu))z_2 - (\beta(S + \sigma I) + d + \theta + \nu)z_3.$$

In order that $D_+\|z\|$ be bounded away from zero on the negative side for all $S, I, V > 0$, we require that

$$(A.2) \quad 2\gamma < d + \phi + \theta + \nu.$$

Case 3. If $z_1 < 0 < z_2, z_3$ and $|z_1| + |z_3| > |z_2| + |z_3|$, then $\|z\| = |z_1| + |z_3|$ and

$$\begin{aligned} D_+\|z\| &= D_+(|z_1| + |z_3|) \\ &= D_+(-z_1 + z_3) \\ &= -\frac{dz_1}{dt} + \frac{dz_3}{dt} \\ &= ((1 + \sigma)\beta I + d + \phi + \theta)z_1 + \beta I z_2 - (\sigma\beta I + d + \theta)z_3 \\ &= -((1 + \sigma)\beta I + d + \phi + \theta)|z_1| + \beta I |z_2| - (\sigma\beta I + d + \theta)|z_3|. \end{aligned}$$

Since $|z_2| < |z_1|$,

$$\begin{aligned} D_+\|z\| &< -(\sigma\beta I + d + \phi + \theta)|z_1| - (\sigma\beta I + d + \theta)|z_3| \\ &\leq -(d + \theta)\|z\|. \end{aligned}$$

Thus, in this case, $D_+\|z\|$ is automatically bounded away from zero on the negative side.

Case 4. If $z_1 < 0 < z_2, z_3$ and $|z_1| + |z_3| < |z_2| + |z_3|$, then $\|z\| = |z_2| + |z_3|$ and

$$\begin{aligned} D_+\|z\| &= D_+(|z_2| + |z_3|) \\ &= \frac{dz_2}{dt} + \frac{dz_3}{dt} \\ &= \gamma z_1 + (\gamma - (\beta(S + \sigma V + \sigma I) + d + \phi + \theta + \nu))z_2 - (\beta(S + \sigma I) + d + \theta + \nu)z_3 \\ &= -\gamma|z_1| + (\gamma - (\beta(S + \sigma V + \sigma I) + d + \phi + \theta + \nu))|z_2| \\ &\quad - (\beta(S + \sigma I) + d + \theta + \nu)|z_3| \\ &< (\gamma - (\beta(S + \sigma V + \sigma I) + d + \phi + \theta + \nu))|z_2| - (\beta(S + \sigma I) + d + \theta + \nu)|z_3| \\ &\leq \max\{\gamma - (\beta(S + \sigma V + \sigma I) + d + \phi + \theta + \nu), -(\beta(S + \sigma I) + d + \theta + \nu)\} \|z\|. \end{aligned}$$

Thus we require that

$$(A.3) \quad \gamma < d + \phi + \theta + \nu.$$

Case 5. If $z_2 < 0 < z_1, z_3$ and $|z_1| + |z_3| > |z_2|$, then $\|z\| = |z_1| + |z_3|$ and

$$\begin{aligned} D_+\|z\| &= D_+(|z_1| + |z_3|) \\ &= \frac{dz_1}{dt} + \frac{dz_3}{dt} \\ &= -((1 + \sigma)\beta I + d + \phi + \theta)z_1 + (1 - 2\sigma)\beta I z_2 + (\theta - (\sigma\beta I + d + 2\nu))z_3 \\ &= -((1 + \sigma)\beta I + d + \phi + \theta)|z_1| + (2\sigma - 1)\beta I |z_2| + (\theta - (\sigma\beta I + d + 2\nu))|z_3|. \end{aligned}$$

Since $(2\sigma - 1)\beta I |z_2| \leq \sigma\beta I |z_2| < \sigma\beta I (|z_1| + |z_3|)$,

$$\begin{aligned} D_+\|z\| &< -(\beta I + d + \phi + \theta)|z_1| + (\theta - (d + 2\nu))|z_3| \\ &\leq \max\{-(\beta I + d + \phi + \theta), \theta - (d + 2\nu)\}\|z\|. \end{aligned}$$

Thus, we require that (A.1) hold.

Case 6. If $z_2 < 0 < z_1, z_3$ and $|z_1| + |z_3| < |z_2|$, then $\|z\| = |z_2|$ and

$$\begin{aligned} D_+\|z\| &= D_+(|z_2|) \\ &= -\frac{dz_2}{dt} \\ &= -\gamma z_1 - (\gamma - (\beta(S + \sigma V + I) + d + \phi + \theta + \nu))z_2 + (\beta S + \theta)z_3 \\ &= -\gamma|z_1| + (\gamma - (\beta(S + \sigma V + I) + d + \phi + \theta + \nu))|z_2| + (\beta S + \theta)|z_3|. \end{aligned}$$

Since $-\gamma|z_1| < 0$ and $|z_3| < |z_2|$,

$$D_+\|z\| < (\gamma - (\beta(\sigma V + I) + d + \phi + \nu))|z_2|.$$

Thus, we require that

$$(A.4) \quad \gamma < d + \phi + \nu.$$

Case 7. If $z_3 < 0 < z_1, z_2$ and $|z_1| + |z_3| > |z_2|$, then $\|z\| = |z_1| + |z_3|$ and

$$\begin{aligned} D_+\|z\| &= D_+(|z_1| + |z_3|) \\ &= \frac{dz_1}{dt} - \frac{dz_3}{dt} \\ &= -((1 + \sigma)\beta I + d + \phi + \theta)z_1 - \beta I z_2 + (\theta + \sigma\beta I + d)z_3 \\ &= -((1 + \sigma)\beta I + d + \phi + \theta)|z_1| - \beta I |z_2| - (\theta + \sigma\beta I + d)|z_3| \\ &\leq -(d + \theta)\|z\|. \end{aligned}$$

Thus, in this case, $D_+\|z\|$ is automatically bounded away from zero on the negative side.

Case 8. If $z_3 < 0 < z_1, z_2$ and $|z_1| + |z_3| < |z_2|$, then $\|z\| = |z_2|$ and

$$\begin{aligned} D_+\|z\| &= D_+(|z_2|) \\ &= \frac{dz_2}{dt} \\ &= \gamma z_1 + (\gamma - (\beta(S + \sigma V + I) + d + \phi + \theta + \nu))z_2 - (\beta S + \theta)z_3 \\ &= \gamma|z_1| + (\gamma - (\beta(S + \sigma V + I) + d + \phi + \theta + \nu))|z_2| + (\beta S + \theta)|z_3|. \end{aligned}$$

Noting that $|z_1| + |z_3| < |z_2|$,

$$D_+\|z\| < (\gamma - (\beta(S + \sigma V + I) + d + \phi + \theta + \nu) + \max\{\gamma, \beta S + \theta\})\|z\|.$$

Thus, we require that (A.2) and (A.4) hold.

Note that (A.2) and (A.4) each imply (A.3). Thus, if inequalities (A.1), (A.2), and (A.4) hold, then there exists $\eta > 0$ such that $D_+\|z\| \leq -\eta\|z\|$ for almost every $z \in \mathbb{R}^3$ and all nonnegative S, I, R , and V . The boundary between the different cases, including, for example, $z_j = 0$ for some j , is resolved by continuity. Thus, (A.1), (A.2), and (A.4) (equivalently (5.4)) imply that $D_+\|z\| \leq -\eta\|z\|$ for all $z \in \mathbb{R}^3$. \square

Appendix B. Proof of Proposition 5.2.

Proof. Let $\xi = \frac{1}{2} \min\{I : (S, I, R) \in \psi\}$ and let $\epsilon > 0$. Note that the model is well posed so solutions remain in the nonnegative orthant. In \mathcal{D} , $\frac{dI}{dt} \geq -(d + \nu)I$. Thus, if a solution satisfies $I(0) \geq \xi$, then the solution remains in \mathcal{D} for time ϵ .

Therefore, it suffices to show that there exists a sequence of surfaces $\{\varphi^k\}$ that minimizes \mathcal{S} relative to $\Sigma(\psi, \tilde{\mathcal{D}})$, where $\tilde{\mathcal{D}} = \{(S, I, R) \in \mathcal{D} : I \geq \xi\}$. Let $\varphi = (S(u), I(u), R(u)) \in \Sigma(\psi, \mathcal{D})$. Define a new surface $\tilde{\varphi} = (\tilde{S}, \tilde{I}, \tilde{R})$ by

(B.1)

$$\tilde{\varphi}(u) = \begin{cases} \varphi(u) & \text{if } I(u) \geq \xi, \\ (S, \xi, R) & \text{if } I(u) < \xi \text{ and } S(u) + \xi + R(u) \leq 1, \\ \left(\frac{S}{S+R}(1-\xi), \xi, \frac{R}{S+R}(1-\xi)\right) & \text{if } I(u) < \xi \text{ and } S(u) + \xi + R(u) > 1. \end{cases}$$

Note that $\tilde{\varphi} \in \Sigma(\psi, \tilde{\mathcal{D}})$. We now demonstrate that $\mathcal{S}\tilde{\varphi} \leq \mathcal{S}\varphi$.

Since φ is Lipschitzian, the partial derivatives $\frac{\partial \varphi}{\partial u_j}$, $j = 1, 2$, exist almost everywhere. Thus,

$$\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2} = \begin{bmatrix} \frac{\partial S}{\partial u_1} \\ \frac{\partial I}{\partial u_1} \\ \frac{\partial R}{\partial u_1} \end{bmatrix} \wedge \begin{bmatrix} \frac{\partial S}{\partial u_2} \\ \frac{\partial I}{\partial u_2} \\ \frac{\partial R}{\partial u_2} \end{bmatrix} = \begin{bmatrix} \det \begin{pmatrix} \frac{\partial S}{\partial u_1} & \frac{\partial S}{\partial u_2} \\ \frac{\partial I}{\partial u_1} & \frac{\partial I}{\partial u_2} \end{pmatrix} \\ \det \begin{pmatrix} \frac{\partial S}{\partial u_1} & \frac{\partial S}{\partial u_2} \\ \frac{\partial R}{\partial u_1} & \frac{\partial R}{\partial u_2} \end{pmatrix} \\ \det \begin{pmatrix} \frac{\partial I}{\partial u_1} & \frac{\partial I}{\partial u_2} \\ \frac{\partial R}{\partial u_1} & \frac{\partial R}{\partial u_2} \end{pmatrix} \end{bmatrix}$$

is a vector in \mathbb{R}^3 for almost every $u \in B$. To examine $\|\frac{\partial \tilde{\varphi}}{\partial u_1} \wedge \frac{\partial \tilde{\varphi}}{\partial u_2}\|$, we do a case analysis based on the definition of $\tilde{\varphi}$ given in (B.1).

Case 1. If $I(u) \geq \xi$, then $\tilde{\varphi} = \varphi$ and therefore $\|\frac{\partial \tilde{\varphi}}{\partial u_1} \wedge \frac{\partial \tilde{\varphi}}{\partial u_2}\| = \|\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2}\|$ when all of the relevant partial derivatives exist.

Case 2. If $I(u) < \xi$ and $S(u) + \xi + R(u) \leq 1$, then $\tilde{\varphi}(v) = (S(v), \xi, R(v))$. Therefore

$$\frac{\partial \tilde{\varphi}}{\partial u_1} \wedge \frac{\partial \tilde{\varphi}}{\partial u_2} = \begin{bmatrix} \det \begin{pmatrix} \frac{\partial S}{\partial u_1} & \frac{\partial S}{\partial u_2} \\ 0 & 0 \end{pmatrix} \\ \det \begin{pmatrix} \frac{\partial S}{\partial u_1} & \frac{\partial S}{\partial u_2} \\ \frac{\partial R}{\partial u_1} & \frac{\partial R}{\partial u_2} \end{pmatrix} \\ \det \begin{pmatrix} 0 & 0 \\ \frac{\partial R}{\partial u_1} & \frac{\partial R}{\partial u_2} \end{pmatrix} \end{bmatrix} = \begin{bmatrix} 0 \\ \det \begin{pmatrix} \frac{\partial S}{\partial u_1} & \frac{\partial S}{\partial u_2} \\ \frac{\partial R}{\partial u_1} & \frac{\partial R}{\partial u_2} \end{pmatrix} \\ 0 \end{bmatrix}$$

almost everywhere. If y_j is equal to either z_j or zero for $j = 1, 2, 3$, then $\|(y_1, y_2, y_3)^T\| \leq \|(z_1, z_2, z_3)^T\|$ for the given norm. It follows that $\|\frac{\partial \tilde{\varphi}}{\partial u_1} \wedge \frac{\partial \tilde{\varphi}}{\partial u_2}\| \leq \|\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2}\|$.

Case 3. If $I(u) < \xi$ and $S(u) + \xi + R(u) > 1$, then $\tilde{\varphi}(v) = (\frac{S}{S+R}(1-\xi), \xi, \frac{R}{S+R}(1-\xi))$. Therefore

$$\frac{\partial \tilde{\varphi}}{\partial u_j} = (1 - \xi) \frac{R \frac{\partial S}{\partial u_j} - S \frac{\partial R}{\partial u_j}}{(S + R)^2} \begin{bmatrix} 1 \\ 0 \\ -1 \end{bmatrix}$$

for $j = 1, 2$. Thus, $\frac{\partial \tilde{\varphi}}{\partial u_1}$ and $\frac{\partial \tilde{\varphi}}{\partial u_2}$ are linearly dependent, and so their wedge product is zero [19]. Therefore $\|\frac{\partial \tilde{\varphi}}{\partial u_1} \wedge \frac{\partial \tilde{\varphi}}{\partial u_2}\| = 0 \leq \|\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2}\|$.

The above three cases show that $\|\frac{\partial \tilde{\varphi}}{\partial u_1} \wedge \frac{\partial \tilde{\varphi}}{\partial u_2}\| \leq \|\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2}\|$ for almost all $u \in \bar{B}$. We also note that $\tilde{I}(u) = \max\{I(u), \xi\}$ and thus $1/\tilde{I} \leq 1/I$. Therefore from (4.1),

$$\begin{aligned} \mathcal{S}\tilde{\varphi} &= \int_{\bar{B}} \frac{1}{\tilde{I}} \left\| \frac{\partial \tilde{\varphi}}{\partial u_1} \wedge \frac{\partial \tilde{\varphi}}{\partial u_2} \right\| du \\ &\leq \int_{\bar{B}} \frac{1}{I} \left\| \frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2} \right\| du \\ &= \mathcal{S}\varphi. \end{aligned}$$

Let $\{\varphi^k\}$ be a sequence of surfaces that minimizes \mathcal{S} relative to $\Sigma(\psi, \mathcal{D})$. Let $\{\tilde{\varphi}^k\}$ be a sequence of surfaces in $\Sigma(\psi, \tilde{\mathcal{D}})$ defined by the above construction. Since $\mathcal{S}\tilde{\varphi}^k \leq \mathcal{S}\varphi^k$ for each k , and $\Sigma(\psi, \tilde{\mathcal{D}})$ is a subset of $\Sigma(\psi, \mathcal{D})$, it follows that $\{\tilde{\varphi}^k\}$ minimizes \mathcal{S} relative to $\Sigma(\psi, \tilde{\mathcal{D}})$. \square

REFERENCES

- [1] J. CHIN, ED., *Control of Communicable Diseases Manual*, 17th ed., American Public Health Association, Washington, DC, 2000.
- [2] J. DUSHOFF, W. HUANG, AND C. CASTILLO-CHAVEZ, *Backwards bifurcations and catastrophe in simple models of fatal diseases*, J. Math. Biol., 36 (1998), pp. 227–248.
- [3] D. J. D. EARN, P. ROHANI, B. M. BOLKER, AND B. T. GRENFELL, *A simple model for complex dynamical transitions in epidemics*, Science, 287 (2000), pp. 667–670.
- [4] D. GREENHALGH, O. DIEKMANN, AND M. C. M. DE JONG, *Subcritical endemic steady states in mathematical models for animal infections with incomplete immunity*, Math. Biosci., 165 (2000), pp. 1–25.
- [5] H. W. HETHCOTE, *Oscillations in an endemic model for pertussis*, Canadian Appl. Math. Quart., 6 (1998), pp. 61–88.
- [6] H. W. HETHCOTE, *The mathematics of infectious diseases*, SIAM Rev., 42 (2000), pp. 599–653.
- [7] M. W. HIRSCH, *Systems of differential equations that are competitive or cooperative. VI: A local C^r closing lemma for 3-dimensional systems*, Ergodic Theory Dynam. Systems, 11 (1991), pp. 443–454.
- [8] W. HUANG, K. L. COOKE, AND C. CASTILLO-CHAVEZ, *Stability and bifurcation for a multiple-group model for the dynamics of HIV/AIDS transmission*, SIAM J. Appl. Math., 52 (1992), pp. 835–854.
- [9] C. KRIBS-ZALETA AND M. MARTCHEVA, *Vaccination strategies and backward bifurcation in an age-since-infection structured model*, Math. Biosci., 177/178 (2002), pp. 317–332.
- [10] C. KRIBS-ZALETA AND J. VELASCO-HERNÁNDEZ, *A simple vaccination model with multiple endemic states*, Math. Biosci., 164 (2000), pp. 183–201.
- [11] M. Y. LI AND J. S. MULDOWNNEY, *Global stability for the SEIR model in epidemiology*, Math. Biosci., 125 (1995), pp. 155–164.
- [12] M. Y. LI AND J. S. MULDOWNNEY, *On R. A. Smith’s autonomous convergence theorem*, Rocky Mountain J. Math., 25 (1995), pp. 365–379.
- [13] M. Y. LI AND J. S. MULDOWNNEY, *A geometric approach to global-stability problems*, SIAM J. Math. Anal., 27 (1996), pp. 1070–1083.

- [14] M. Y. LI, H. L. SMITH, AND L. WANG, *Global dynamics of an SEIR epidemic model with vertical transmission*, SIAM J. Appl. Math., 62 (2001), pp. 58–69.
- [15] Y. LI AND J. S. MULDOWNY, *On Bendixson's criterion*, J. Differential Equations, 106 (1993), pp. 27–39.
- [16] C. C. MCCLUSKEY, *A model of HIV/AIDS with staged progression and amelioration*, Math. Biosci., 181 (2003), pp. 1–16.
- [17] R. A. SMITH, *Some applications of Hausdorff dimension inequalities for ordinary differential equations*, Proc. Roy. Soc. Edinburgh Sect. A, 104 (1986), pp. 235–259.
- [18] B. SONG, C. CASTILLO-CHAVEZ, AND J. P. APARICIO, *Global dynamics of tuberculosis models with density dependent demography*, in Mathematical Approaches for Emerging and Reemerging Infectious Diseases: Models, Methods, and Theory, C. Castillo-Chavez, with S. Blower, P. van den Driessche, D. Kirschner, and A.-A. Yakubu, eds., IMA Vol. Math. Appl. 126, Springer-Verlag, New York, 2002, pp. 275–294.
- [19] M. SPIVAK, *Calculus on Manifolds*, W. A. Benjamin, New York, 1965.
- [20] P. VAN DEN DRIESSCHE AND J. WATMOUGH, *Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission*, Math. Biosci., 180 (2002), pp. 29–48.