



the
abdus salam
international centre for theoretical physics



H4.SMR/1202-38

**"Fifth Course on Mathematical Ecology
including and introduction to Ecological Economics"**

28 February - 24 March 2000

**LOCAL STABILITY OF THE ENDEMIC STATE IN A CLASS OF
EPIDEMIC MODELS**

Jorge X. Velasco-Hernández

Departamento de Matemáticas
UNAM-Iztapalapa
México D.F.
Mexico



Submitted Jan, 2000

R_0 and local asymptotic stability of endemic states

1

Local stability of the endemic state in a class of epidemic models

Lourdes Esteva-Peralta
Departamento de Matemáticas
Facultad de Ciencias-UNAM
México, D.F. 04510

Jorge X. Velasco-Hernández
Departamento de Matemáticas
UAM-Iztapalapa
Apdo. Postal 55-534, México, D.F. 09340

Keywords: Basic reproduction number, epidemic models, monotone systems, SIS, next-generation operator

Summary

There are examples of models where the threshold parameter can give a more precise description of their solution trajectories, namely, the existence of endemic equilibrium points and/or information on its local stability. In this paper we attempt a characterization of a class of epidemic models for which $R_0 > 1$ implies the existence of a unique (endemic) interior equilibrium. For these models we show that $R_0 > 1$ implies not only the instability of the disease-free equilibrium but also the local asymptotic stability of the endemic state.

1 Introduction

The basic reproductive number, denoted by R_0 also called the basic reproduction number or contact number [6] describes the number of secondary infections produced by an infectious individual introduced into a completely susceptible population during the length of time in which it is infectious. As it is known in many mathematical models of infectious diseases $R_0 = 1$ is a threshold value. Values of R_0 above one imply the lack of stability of the disease free equilibrium which is interpreted as the triggering of an epidemic outbreak; values below it imply the local asymptotic stability of this equilibrium point. There are examples of models where the threshold parameter can give a more precise description of their solution trajectories, namely, the existence of endemic equilibrium points and/or information on its local stability [7]. We will show several examples below. For the moment, it suffices to say that there exists a well known pattern in the stability of the endemic state when $R_0 > 1$.

We define an endemic state as an equilibrium point for which at least one coordinate corresponding to some infectious stage in the disease being modeled is positive. When at least one of these coordinates is zero we speak of *boundary-equilibria*. Such points are not considered in this work; we are only concerned with endemic equilibrium points with all coordinates corresponding to infectious stages being positive, called *interior-equilibria*. Roughly speaking, whenever the model nonlinearities are quadratic, the only possible behavior around the interior equilibrium point (endemic state) is local asymptotic stability (e.g., [11], [7]). Only when either the nonlinearities are more than quadratic (e.g., [12],[13],[8], [9]), or there is non constant recruitment (e.g., [16]) or there is non-autonomous forcing (e.g., [14], [10]), the endemic equilibrium may be unstable with a limit cycle or more complex attractor around it.

In this paper we attempt a characterization of a class of epidemic models for which $R_0 > 1$ implies the existence of a unique (endemic) interior equilibrium. For these models we show that $R_0 > 1$ implies not only the instability of the disease-free equilibrium but also the local asymptotic stability of the endemic state.

2 Local asymptotic stability of the endemic state: examples

In this section we review two simple epidemiological models where $R_0 > 1$ implies the local asymptotic stability of the endemic equilibrium. Both models assume constant total population size, and no disease-induced mortality.

2.1 The classical *SIS* epidemic model

Under certain conditions the epidemic outbreak ends up with the establishment of the disease in the population in a so-called endemic state where the prevalence remains roughly constant. There exists certain class of mathematical models where the existence of an epidemic outbreak (meaning $R_0 > 1$).

implies the existence of an endemic equilibrium point and also its (local) asymptotic stability. A very simple example of this is the classical *SIS* epidemic model. Let i represent the fraction of infected individuals in a population of constant total size equal to N . Then, if β and μ are the infection and cure rates, respectively, the model is given by

$$\frac{d}{dt}i(t) = \beta i(t)(1 - i(t)) - \mu i(t). \quad (1)$$

There are two equilibrium points, $i_* = 0$ and $i^* = 1 - \mu/\beta$. The basic reproduction number in this case is $R_0 = \beta/\mu$. R_0 is the spectral radius of the next-generation operator [3], associated with the disease-free equilibrium, that can be obtained from (1), in this trivial case, taking the derivative of the fixed point equation $i = \beta/\mu(1 - i)i$. In this case we obtain

$$K(i) = R_0(1 - 2i),$$

of which the dominant eigenvalue at $i = 0$ is R_0 .

Defining a new variable $y = i - i^*$, we find that the stability of the endemic equilibrium can be studied as the stability of $y^* = 0$ of the equation

$$\frac{d}{dt}y = \beta(y + i^*)(1 - y - i^*) - \mu(y + i^*).$$

Grouping all negative linear terms in y , by applying the same procedure used to compute the next-generation operator of (1), we obtain

$$\hat{K}(y) = \frac{\beta}{\mu + \beta i^*}(1 - i^*) - \frac{2\beta}{\mu + \beta i^*}y.$$

As can be seen at $y = 0$ the dominant eigenvalue is $1/R_0$. Thus, as it is well known, in the case of the classical *SIS* model, if $R_0 > 1$ then the disease-free equilibrium is unstable, the endemic equilibrium exists and it is locally asymptotically stable. Of course, the result can be made stronger and it is well known that the endemic state is globally asymptotically stable but for the aim of this paper we wish to underline that $R_0 > 1$ implies automatically the local asymptotic stability of this point.

2.2 A model for the Dengue fever

Our next example is a model for vector transmitted diseases which was studied in detail in [4]. Let i , r and v denote the proportion of infected hosts, recovered hosts and infected vectors, respectively. Then, the model is given by:

$$\begin{aligned} \frac{d}{dt}i &= \beta(1 - i - r)v - (\gamma + \mu)i \\ \frac{d}{dt}r &= \gamma i - \mu r \\ \frac{d}{dt}v &= \delta(1 - v)i - \tilde{\mu}v, \end{aligned} \quad (2)$$

where β and δ are the infectious rates in hosts and vectors, respectively; γ the cure rate in hosts; μ and $\tilde{\mu}$ the mortality rates in hosts and vectors, respectively.

The model has two equilibrium points: the disease-free equilibrium $(0, 0, 0)$ and the endemic equilibrium (i^*, r^*, v^*) , where

$$i^* = \frac{\mu\tilde{\mu}(R_0^2 - 1)}{\tilde{\mu}(\mu + \gamma)R_0^2 + \delta\mu}, \quad r^* = \frac{\gamma\tilde{\mu}(R_0^2 - 1)}{\tilde{\mu}(\mu + \gamma)R_0^2 + \delta\mu}, \quad v^* = \frac{\delta\mu(R_0^2 - 1)}{R_0^2(\tilde{\mu}(\mu + \gamma) + \delta\mu)},$$

and

$$R_0 = \sqrt{\frac{\beta\delta}{\bar{\mu}(\mu + \gamma)}},$$

corresponds to the spectral radius of the next-generator operator

$$K(i^*, r^*, v^*) = \begin{pmatrix} 0 & 0 & \frac{\beta}{\mu + \gamma} \\ \frac{\gamma}{\mu} & 0 & 0 \\ \frac{\delta}{\mu} & 0 & 0 \end{pmatrix}.$$

If $R_0 \leq 1$, then the disease-free equilibrium is globally asymptotically stable [4], and unstable if $R_0 > 1$.

Now, as in the previous example, we make the change of coordinates: $y = i - i^*$, $z = r - r^*$, and $w = v - v^*$, and we study the stability of $(0, 0, 0)$ of the system

$$\begin{aligned} \frac{d}{dt}y &= -(\beta v^* + \mu + \gamma)y - \beta v^* z + \beta(1 - i^* - r^*)w - \beta(y + z)w \\ \frac{d}{dt}z &= \gamma y - \mu z \\ \frac{d}{dt}w &= \delta(1 - v^*)y - (\delta i^* + \bar{\mu})w - \delta y w. \end{aligned} \quad (3)$$

The fixed-point equations for system (3) are given by

$$\begin{aligned} y &= \frac{-\beta v^* z + \beta(1 - i^* - r^*)w - \beta(y + z)w}{\beta v^* + \mu + \gamma} \\ z &= \frac{\gamma y}{\mu} \\ w &= \frac{\delta(1 - v^*)y - \delta y w}{\delta i^* + \bar{\mu}}. \end{aligned} \quad (4)$$

The jacobian matrix of the previous system, evaluated at $(0,0,0)$, gives the following

$$\hat{K}(i, r, v) = \begin{pmatrix} 0 & \frac{-\beta v^*}{\beta v^* + \mu + \gamma} & \frac{\beta(1 - i^* - r^*)}{\beta v^* + \mu + \gamma} \\ \frac{\gamma}{\mu} & 0 & 0 \\ \frac{\delta(1 - v^*)}{\delta i^* + \bar{\mu}} & 0 & 0 \end{pmatrix}, \quad (5)$$

with dominant eigenvalue equal to

$$\lambda = \sqrt{\frac{\delta\beta(1 - i^* - r^*)(1 - v^*)}{(\beta v^* + \mu + \gamma)(\delta i^* + \bar{\mu})} - \frac{\gamma\beta v^*}{\mu(\beta v^* + \mu + \gamma)}}.$$

Using equations (2) at equilibrium and after some calculations we obtain the following expression for λ

$$\lambda = \sqrt{\frac{1/R_0 - r^*}{1 - r^*}}.$$

Thus, if $R_0 > 1$, $\lambda < 1$ and the endemic equilibrium is locally asymptotically stable (since $0 < r^* < 1$). In [4] was shown that for $R_0 > 1$ the endemic equilibrium is globally asymptotically stable.

3 Multigroup models and the implications of $R_0 > 1$

In this section we present the analysis of models for which $R_0 > 1$ implies the local asymptotic stability of the unique interior (endemic) equilibrium if it exists. It should come as no surprise to see that the property of the flow being monotone [15] is essential for the results that follow.

3.1 The classical multigroup SIS gonorrhoea model

Lajmanovich and Yorke in a well-known paper [11] studied the model

$$\frac{d}{dt}y = (c_i - y_i) \sum_{j=1}^n \beta_{ij}y_j - \alpha_i y_i, \quad i = 1, \dots, n, \quad (6)$$

where y_i represents the porportion of the population of subgroup i that is infected; the total constant population is subdivided into n groups each of size c_i , β_{ij} is the infection rate from infected individuals in group j toward susceptible individuals in group i . For system (6) we have the following result

Theorem 1 ([11]) *If the basic reproduction number of (6) is greater than one, then there exist a unique interior endemic equilibrium point. Moreover, the disease-free equilibrium is unstable.*

3.1.1 Stability of the endemic equilibrium

Consider the general SIS model written as

$$\frac{d}{dt}y = F(y) - My \quad (7)$$

where y represents the infected class, M is a $n \times n$ positive diagonal matrix. In models where there is no disease-induced mortality and the total population is constant or asymptotically constant, the mixing/contact terms are quadratic and thus we can assume that F has the form

$$F(y) = (C - \text{diag}(y))Gy$$

with C and G $n \times n$ non-negative constant matrices.

We will assume that system (7) has a unique endemic equilibrium y^* in the interior of the first orthant R_+^n . Making the change of coordinates $z = y - y^*$, system (7) becomes:

$$\frac{d}{dt}z = F(z + y^*) - M(z + y^*).$$

Substituting F and using the fact that y^* is an equilibrium point of (7), we get

$$\frac{d}{dt}z = (C - \text{diag}(z + y^*))Gz - (\text{diag}(Gy^*) + M)z \quad (8)$$

The jacobian matrix of system (8) around $z = 0$

$$J = (C - \text{diag}(y^*))G - (\text{diag}(Gy^*) + M). \quad (9)$$

Equating (8) to zero and solving for the linear part in terms of z we obtain the mapping $\tilde{\phi} : R^n \rightarrow R^n$ given by

$$\tilde{\phi}(z) = [\text{diag}(Gy^*) + M]^{-1}[C - \text{diag}(z + y^*)]Gz,$$

whose fixed points are the equilibria of (8). In particular $z = 0$ corresponds to the endemic equilibrium point of (7). Computing the Jacobian matrix of $\tilde{\phi}$ in $z = 0$ we obtain the new operator

$$\hat{K} = [\text{diag}(Gy^*) + M]^{-1}[C - \text{diag}(y^*)]G. \quad (10)$$

Put $H = (C - \text{diag}(y^*))G$ and $N = \text{diag}(Gy^*) + M$, then $J = H - N$ and $\hat{K} = N^{-1}H$. Next, we recall the following definitions:

Definition 1 The quantity $s(A) = \sup\{\text{Re}\lambda \mid \lambda \in \text{spec}(A)\}$ is called the spectral bound of the matrix A .

Definition 2 The spectral radius of a matrix A is defined as $\rho(A) = \max\{|\lambda| \mid \lambda \in \text{spec}(A)\}$.

The next theorem relates the spectral bound of J with the spectral radius of \hat{K} .

Theorem 2 Assume H and N are $n \times n$ matrices such that $H \geq 0$, N is diagonal with positive diagonal elements, and $H - N$ has nonnegative off diagonal elements. Then $s(H - N) < 0$ if and only if $\rho(N^{-1}H) < 1$ (see [6], Theorem 1.6; [3]).

Assume J and \hat{K} satisfy the conditions of Theorem (2), then the stability of the endemic equilibrium y^* will follow if we show that $\rho(\hat{K}) < 1$. To this end we need the following definitions and results (see [1]).

Definition 3 A is a non-singular M -matrix if and only if $A = sI - B$ with B positive and $s > \rho(B)$.

Definition 4 A matrix A is semipositive in a cone W if and only if $A(\text{int}W) \cap \text{int}(W) \neq \emptyset$.

Theorem 3 Consider B a positive $n \times n$ matrix. Then $A = sI - B$ is a non-singular M matrix if and only if A is W -semipositive.

In the case of the Lajmanovich and Yorke's model W is the standard cone R_+^n and $A = I - \tilde{K}$. To show that A is R_+^n -semipositive we observe that since y^* is an equilibrium point of system (7), $y^* = [\text{diag}(Gy^* + M)]^{-1}CGy^*$ and therefore

$$\begin{aligned} Ay^* &= y^* - \tilde{K}y^* \\ &= y^* - [\text{diag}(Gy^*) + M]^{-1}(C - \text{diag}(y^*))Gy^* \\ &= [\text{diag}(Gy^*) + M]^{-1}\text{diag}(y^*)Gy^* \end{aligned}$$

which implies that $Ay^* \in \text{int}(R_+^n)$. Therefore, $I - \tilde{K}$ is a non-singular M -matrix and $\rho(\tilde{K}) < 1$. From Theorem (2) and (3) we have the following corollary. Note that (6) has the form (7) and that its Jacobian J given by (9) has nonnegative off-diagonal elements while the corresponding operator \hat{K} given by (10) is positive.

Corollary 1 Assume $R_0 > 1$. Then, $y^* \in R_+^n$ is a unique endemic equilibrium of system (6) which is locally asymptotically stable.

3.2 A SEIRS model with multiple infectious stages

The next example is a model developed in [5]. The model equations are the following

$$\begin{aligned} \frac{d}{dt}S &= \mu + \delta R - S \sum_{j=1}^k \beta_j I_j - \mu S, \\ \frac{d}{dt}E &= S \sum_{j=1}^k \beta_j I_j - (\mu + \sigma)E, \end{aligned}$$

$$\begin{aligned}
 \frac{d}{dt} I_1 &= \sigma E - (\mu + \gamma_1) I_1, \\
 \frac{d}{dt} I_j &= \gamma_{j-1} I_{j-1} - (\mu + \gamma_j) I_j; \quad \text{for } j = 2 \dots, k-1, \\
 \frac{d}{dt} I_k &= \gamma_{k-1} I_{k-1} - (\mu + \gamma_k) I_k, \\
 \frac{d}{dt} R &= \gamma_k I_k - (\mu + \delta) R,
 \end{aligned} \tag{11}$$

where the total population is constant, S , I_j and R represent the susceptible, infectious in the j th stage and recovered individuals respectively; β_j are the transmission rates of the j th stage, γ_j^{-1} is the average duration of the j th stage and δ^{-1} is the duration of the temporary immunity after recovery from infection.

Since in this model $1 = S + E + R + \sum_{j=1}^k I_j$, we will eliminate the equation for S from our analysis through the substitution $S = 1 - (E + R + \sum_{j=1}^k I_j)$ obtaining a system of $k + 2$ equations (all matrices below are $k + 2$ square matrices). This system can be written in the form (7) with

$$M = \begin{pmatrix} \mu + \sigma & 0 & \dots & 0 & 0 \\ 0 & \mu + \gamma_1 & \dots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \dots & \mu + \gamma_k & 0 \\ 0 & 0 & \dots & 0 & \mu + \delta \end{pmatrix}$$

and

$$F(y) = AGy; \quad y = (E, I_1, \dots, I_k, R)^T,$$

where

$$G = \begin{pmatrix} 0 & \beta_1 & \beta_2 & \dots & \beta_{k-1} & \beta_k & 0 \\ \sigma & 0 & 0 & \dots & 0 & 0 & 0 \\ 0 & \gamma_1 & 0 & \dots & 0 & 0 & 0 \\ \vdots & \vdots & \ddots & \ddots & 0 & 0 & \vdots \\ 0 & 0 & \dots & 0 & 0 & 0 & 0 \\ 0 & 0 & \dots & 0 & \gamma_{k-1} & 0 & 0 \\ 0 & 0 & \dots & 0 & 0 & \gamma_k & 0 \end{pmatrix},$$

and

$$A = \begin{pmatrix} S & 0 & 0 & \dots & 0 & 0 \\ 0 & 1 & 0 & \dots & 0 & 0 \\ 0 & 0 & 1 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & 0 \\ 0 & 0 & 0 & \dots & 1 & 0 \\ 0 & 0 & 0 & \dots & 0 & 1 \end{pmatrix}.$$

Note that A can be written as

$$A = \text{diag}(1, 1, \dots, 1) - \text{diag}(E + \sum_{j=1}^k I_j + R, 0 \dots, 0).$$

The disease-free equilibrium of (11) is given by $(1, 0, \dots, 0)$. The unique endemic equilibrium of (11) can be found explicitly from the equations. It is unique and is biologically feasible provided the basic

reproduction number $R_0 = \frac{\sigma}{\mu + \sigma} \sum_{j=1}^k \beta_j \frac{\prod_{i=1}^{j-1} \gamma_i}{\prod_{i=1}^j (\mu + \gamma_i)}$ is greater than unity [5]. The next-generation

operator of the disease-free equilibrium is given by

$$K_{gen} = \begin{pmatrix} 0 & \frac{\beta_1}{\mu+\sigma} & \frac{\beta_2}{\mu+\sigma} & \dots & \frac{\beta_{k-1}}{\mu+\sigma} & \frac{\beta_k}{\mu+\sigma} & 0 \\ \frac{\sigma}{\mu+\gamma_1} & 0 & 0 & \dots & 0 & 0 & 0 \\ 0 & \frac{\gamma_1}{\mu+\gamma_2} & 0 & \dots & 0 & 0 & 0 \\ \vdots & \vdots & \ddots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \dots & 0 & 0 & 0 \\ 0 & 0 & 0 & \dots & \frac{\gamma_{k-1}}{\mu+\gamma_k} & 0 & 0 \\ 0 & 0 & 0 & \dots & 0 & \frac{\gamma_k}{\mu+\delta} & 0 \end{pmatrix}.$$

R_0 is the spectral radius of the above matrix. Proceeding as in the previous section, we perform the change of variables

$$z_0 = E - E^*, \quad z_i = I - I_i^*, \quad i = 1, \dots, k, \quad z_{k+1} = R - R^*,$$

we obtain the system

$$z' = AG(z + y^*) - M(z + y^*)$$

with

$$z = (z_0, \dots, z_{k+1})^{tr}, \quad y^* = (y_0^*, \dots, y_{k+1}^*)^{tr}.$$

The jacobian matrix of the this system evaluated at $z = 0$ is given by

$$J_0 = \text{diag}(1 - \sum_{j=0}^{k+1} y_j^*, 1, \dots, 1)G - \bar{G} - N, \quad (12)$$

where

$$N = \begin{pmatrix} \mu + \sigma + \sum_{j=1}^k \beta_j y_j^* & 0 & \dots & 0 & 0 \\ 0 & \mu + \gamma_1 & \dots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \dots & \mu + \gamma_k & 0 \\ 0 & 0 & \dots & 0 & \mu + \delta \end{pmatrix},$$

$$\bar{G} = \begin{pmatrix} 0 & -\sum_{j=1}^k \beta_j y_j^* & \dots & -\sum_{j=1}^k \beta_j y_j^* & -\sum_{j=1}^k \beta_j y_j^* \\ 0 & 0 & \dots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \dots & 0 & 0 \\ 0 & 0 & \dots & 0 & 0 \end{pmatrix}.$$

Defining

$$H = \text{diag}(1 - \sum_{j=0}^{k+1} y_j^*, 1, \dots, 1)G - \bar{G},$$

we can obtain the $(k+2) \times (k+2)$ -matrix

$$K_{gen}(y^*) = N^{-1}H \quad (13)$$

given by

$$\begin{pmatrix} 0 & \frac{\theta\beta_1}{\mu+\sigma+\Psi} - \frac{\Psi}{(\mu+\sigma+\Psi)} & \frac{\theta\beta_2}{\mu+\sigma+\Psi} - \frac{\Psi}{(\mu+\sigma+\Psi)} & \dots & \frac{\theta\beta_k}{\mu+\sigma+\Psi} - \frac{\Psi}{(\mu+\sigma+\Psi)} & -\frac{\Psi\beta_k}{\mu+\sigma+\Psi} \\ \frac{\sigma}{\mu+\gamma_1} & 0 & 0 & \dots & 0 & 0 \\ 0 & \frac{\gamma_1}{\mu+\gamma_2} & 0 & \dots & 0 & 0 \\ \vdots & \vdots & \ddots & \ddots & \vdots & \\ 0 & 0 & 0 & \dots & 0 & 0 \\ 0 & 0 & 0 & \dots & \frac{\gamma_k}{\mu+\delta} & 0 \end{pmatrix},$$

where

$$\theta = 1 - \sum_{j=0}^{k+1} y_j^*, \quad \Psi = \sum_{j=1}^k \beta_j y_j^*.$$

Note that by definition of endemic equilibrium in a population of constant size we must have $\theta = 1/R_0$.

It can be proved by induction over k [5] that the characteristic polynomial of $K_{gen}(y^*)$ is given by

$$p(\lambda) = \lambda^{k+2} - \sum_{j=1}^k \frac{\sigma[\theta\beta_j - \Psi]}{(\mu + \sigma + \Psi)} \frac{\prod_{i=0}^{j-1} \gamma_i}{\prod_{i=1}^j (\mu + \gamma_i)} \lambda^{k+1-j} - \frac{\Psi\sigma\beta_k \prod_{j=1}^k \gamma_j}{(\mu + \sigma + \Psi) \prod_{j=1}^k (\mu + \gamma_j) (\mu + \delta)}.$$

where $\gamma_0 = 1$.

Now, we prove the following lemma

Lemma 1 Consider the non-negative $(k+2) \times (k+2)$ -matrix

$$\begin{pmatrix} 0 & a_1 - \epsilon & a_2 - \epsilon & \dots & a_k - \epsilon & -\epsilon \\ b_0 & 0 & 0 & \dots & 0 & 0 \\ 0 & b_1 & 0 & \dots & 0 & 0 \\ \vdots & \vdots & \ddots & \ddots & \vdots & \vdots \\ 0 & 0 & \dots & \ddots & 0 & 0 \\ 0 & 0 & \dots & 0 & b_k & 0 \end{pmatrix}, \quad (14)$$

where ϵ is a small positive number. Denote by $f(\lambda, \epsilon)$ the corresponding characteristic polynomial. Also assume that for $\epsilon = 0$ (14) is irreducible and primitive. Then if $\lambda = 1$ is a simple dominant root of $f(\lambda, 0) = 0$, then for ϵ small, there exist a real root r_ϵ of $f(\lambda, \epsilon) = 0$ such that r_ϵ is real and strictly less than 1. Moreover all other roots of $f(\lambda, \epsilon) = 0$ have modulus less than or equal to r_ϵ .

Proof: The characteristic polynomial of the above matrix is

$$f(\lambda, \epsilon) = \lambda^{k+2} - \sum_{j=1}^k (a_j - \epsilon) \prod_{i=0}^j b_i \lambda^{k+1-j} + \epsilon \prod_{i=0}^k b_i. \quad (15)$$

Assuming $\lambda = 1$ is a simple root of $f(\lambda, 0) = 0$ we obtain the condition

$$1 = \sum_{j=0}^k a_j \prod_{i=1}^j b_i. \quad (16)$$

Now, in a neighborhood of $\lambda = 1$, we wish to find roots of $f(\lambda, \epsilon) = 0$ of the form $r_\epsilon = 1 + \alpha\epsilon + \dots$ for ϵ small. Substituting this expression into (15), collecting in terms of powers of ϵ and neglecting terms of order ϵ^2 and higher we obtain that

$$\alpha = -\frac{1 + \sum_{j=1}^k \prod_{i=0}^{j-1} b_i}{k + 2 - \sum_{j=1}^k a_j (k + 1 - j) \prod_{i=0}^{j-1} b_i}.$$

The sign of α is obviously determined by the denominator. Using (16) we have

$$k + 2 > \sum_{j=1}^k a_j (k + 1 - j) \prod_{i=0}^{j-1} b_i.$$

We therefore conclude that $\alpha < 0$. Thus $0 < r_\epsilon < 1$ and the first claim of the lemma is proved. For the second part we observe that since the coefficients of the characteristic polynomial are continuous functions of the entries of the matrix, we have that $\frac{\partial f(r_\epsilon, \epsilon)}{\partial \lambda} \neq 0$ for sufficiently small ϵ . Therefore we can guarantee that r_ϵ is simple. There cannot be any other simple real root greater than r_ϵ since by hypothesis all other roots of (15) are to the left of the line $\lambda = r_\epsilon$ in the complex plane. The conclusion of the lemma follows.

Thus we can now prove the following result

Proposition 1 *For model (11), if $R_0 = 1 + C\epsilon$, where C is an arbitrary positive constant and ϵ is a sufficiently small positive number, the spectral radius of $K_{gen}(y^*) < 1$.*

Proof: Note that K_{gen} and $K_{gen}(y^*)$ differ among each other only in the first row. Comparing corresponding entries we find that $(K_{gen}(y^*))_{1j} < (K_{gen})_{1j}$ for all $j = 1, \dots, k + 1$. Note also that $\theta = 1/R_0$ and that Ψ is a continuous function of R_0 . With no loss of generality take $C = 1$. Assuming $R_0 \sim 1 + \epsilon$, then we have that $\theta \sim 1 - \epsilon$ and $\Psi \sim \epsilon \sum_{i=1}^k \beta_i$. Substituting these approximations into $K_{gen}(y^*)$ and after rearranging the resulting expressions in terms of ϵ we see that

$$(K_{gen}(y^*))_{1j} \sim (K_{gen})_{1j} - O(\epsilon), \quad \text{for all } j = 1, \dots, k + 1.$$

In this case the characteristic polynomial of $K_{gen}(y^*)$ is

$$f(\lambda, \epsilon) = \lambda^{k+2} - \frac{\sigma}{\mu + \sigma} \sum_{j=1}^k \frac{\prod_{i=0}^{j-1} \gamma_i}{\prod_{i=1}^j (\mu + \gamma_i)} (\beta_j - \epsilon) \lambda^{k+1-j} + \epsilon \frac{\prod_{i=0}^j \gamma_i}{\prod_{i=1}^j (\mu + \gamma_i) (\mu + \delta)}, \quad (17)$$

where we have defined $\prod_{l=1}^m a_l = 1$ if $m < 1$.

Taking $\lambda = 1$ and $\epsilon = 0$ we obtain the corresponding condition to (16)

$$1 = \frac{\sigma}{\mu + \sigma} \sum_{j=1}^k \beta_j \frac{\prod_{i=0}^{j-1} \gamma_i}{\prod_{i=1}^j (\mu + \gamma_i)}. \quad (18)$$

Applying the lemma it follows that in a neighborhood of radius ϵ of $\lambda = 1$, there exists a simple, real, dominant root of the characteristic polynomial of the form $r_\epsilon = 1 + \alpha\epsilon + \dots$ with

$$0 > \alpha = - \frac{1 + \sigma \sum_{j=1}^k \frac{\prod_{i=1}^{j-1} \gamma_i}{\prod_{i=1}^j (\mu + \gamma_i)}}{k + 2 - \frac{\sigma}{\mu + \sigma} \sum_{j=1}^k \beta_j (k + 1 - j) \frac{\prod_{i=1}^{j-1} \gamma_i}{\prod_{i=1}^j (\mu + \gamma_i)}}.$$

Therefore, we have that, for ϵ small enough, the spectral radius of K_{gen} is less than one and the proposition is proved.

Now, from (12) we have that

$$J_0 = N(K_{gen}(y^*) - I) = NB.$$

Now, since λ is an eigenvalue of B if and only if $\lambda + 1$ is an eigenvalue of $K_{gen}(y^*)$ and $\rho(K_{gen}(y^*)) < 1$, then B is stable. Now we proceed to show that all eigenvalues of NB have negative real part.

Consider again a perturbation procedure. Let $R_0 = 1 + \epsilon$. We have proved in Proposition 1 that in this case the spectral radius of $K_{gen}(y^*)$ is strictly less than one. We want to look this matrix as

a function of the small quantity ϵ . Define $J_0(\epsilon) = N(K_{gen}(y^*, \epsilon) - I)$ and observe that $K_{gen}(y^*, 0)$ is a positive matrix such that $\rho(K_{gen}(y^*, 0)) = 1$. Therefore the matrix $J_0(0)$ has spectral bound exactly equal to zero.

We have the following theorem.

Theorem 4 *Let $p(\lambda, \epsilon)$ be the characteristic polynomial of $J_0(\epsilon)$. Assume that $p(\lambda, 0)$ has only simple roots and that $\lambda = 0$ is one of them. Also assume that all other roots have strictly negative real parts. Then $p(\lambda, \epsilon)$ has, for ϵ sufficiently small, only simple roots. Moreover, the perturbation $\lambda(\epsilon)$ of the eigenvalue $\lambda = 0$ is real and strictly negative.*

Proof: Since $p(\lambda, 0)$ has simple roots by hypothesis, then it follows that for sufficiently small ϵ , $p(\lambda, \epsilon)$ has also simple roots. It remains to prove that the perturbation of $\lambda = 0$ cannot be non-negative (the perturbation cannot produce complex roots arising from the roots when $\epsilon = 0$ because of the assumption of being simple. In particular roots with negative real part remain in the left-half of the complex plane). To prove that the perturbation of $\lambda = 0$ cannot be non-negative, observe that, for ϵ small, the matrix B is stable. Let $p_B(\lambda)$ be the characteristic polynomial of B . Then $p_B(\lambda) > 0$ for $\lambda \geq 0$. Now recall that $p(\lambda, \epsilon)$ is the characteristic polynomial of $J_0(\epsilon) = NB$. Then

$$p(0, \epsilon) = \text{Det}N\text{Det}B = \text{Det}Np_B(0) > 0.$$

Moreover $p(\lambda, \epsilon) \rightarrow \infty$ when $\lambda \rightarrow \infty$. Therefore the perturbation of the root $\lambda = 0$ cannot be non-negative.

Corollary 2 *The endemic equilibrium point is locally asymptotically stable for $R_0 = 1 + O(\epsilon)$.*

Remark 2: Note that in theorem 1 the polynomial (17) gives, evaluated at $\lambda = 1$ and $\epsilon = 0$, that $1 - R_0 = 0$, thus obtaining R_0 directly without computing the eigenvalues of K_{gen} . R_0 is given by the right-hand side of (18).

Acknowledgements. The authors are grateful to Odo Diekmann and Hal Smith for sharing their useful commentaries and ideas. LEP acknowledges support from a CONACYT grant 1999; JXVH acknowledges support from CONACYT grant 1998-2001, México.

References

- [1] Berman A, Plemmons R. J.: Nonnegative Matrices in the Mathematical Sciences, Academic Press, New York, 1979
- [2] Busenberg S., van den Driessche P.: Analysis of a disease transmission model in a population with varying size. *Math. Biol.* **28**, 257-270 (1990)
- [3] Diekmann, O., Heesterbeek, H., Metz, J.A.J.: On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations. *J. Math. Biol.* **28**, 365-382 (1990)
- [4] Esteva, L., Vargas, C.: Analysis of a Dengue disease transmission model: *Math. Biosci.* **150**, 131-151 (1998)
- [5] Ferreira M.B., Bassanezi R.C., Yang H. M.: Modeling Directed Transmitted Infections Considering the Amount of Virus: The Basic Reproduction Ratio (preprint), Universidad de Campinas, Brasil, 1999.

- [6] Heesterbeek H. : R_0 : PhD Thesis, Centrum voor Wiskunde en Informatica, Amsterdam ,1992
- [7] Hethcote H. W. , Thieme H. R.: Stability of the Endemic Equilibrium in Epidemic Models with Subpopulations, *Math. Biosc.* **75** :205–227 (1985)
- [8] Hethcote H. W., Levin S. A.: Periodicity in epidemiological models, in *Mathematical Ecology, Volumen II* , S.A. Levin, T.G. Hallan, L. Gross, eds., Springer–Verlag, Nueva York, 1988.
- [9] Hethcote, H.W., van den Driessche P.: Some epidemiological models with nonlinear incidence. *J. Math. Biol.* **29**, 271-287 (1991)
- [10] Kuznetsov, Y.A, Piccard, C.: Bifurcation analysis of periodic SEIRS and SIR epidemic models. *J. Math. Biol.* **32**, 109-121 (1994)
- [11] Lajmanovich A., Yorke J. A.: A deterministic model for gonorrhea in a nonhomogeneous population. *Maht Biosc.* **28**, 221-236
- [12] Liu, W.M., Levin, S.A., Iwasa, Y.: Influence of nonlinear incidence rates upon the behavior of *SIRS* epidemiological models. *J. Math. Biol.* **23**, 187-204 (1986)
- [13] Liu, W.M., Hethcote, H.W., Levin, S.A.: Dynamical behavior of epidemiological models with nonlinear incidence rates, *J. Math. Biol.* **25**, 359-380 (1987)
- [14] Schwartz, I.B., Smith, H.L.: Infinite subharmonic bifurcation in a SEIR epidemic model, *J. Math. Biol.* **18**, 233-253 (1983)
- [15] Smith, H.L.: *Monotone Dynamical Systems : An Introduction to the Theory of Competitive and Cooperative Systems* (Mathematical Surveys and Monographs, No 41). Providence, RI (1995)
- [16] Velasco-Hernández, J.X., Brauer, F., Castillo-Chavez, C.: Effects of treatment and prevalence-dependent recruitment on the dynamics of a fatal disease. *IMA Journal of Mathematics Applied to Medicine and Biology*, **13**, 175-192 (1996)