

GLOBAL STABILITY ANALYSIS FOR SEIS MODELS WITH n LATENT CLASSES

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(Communicated by Yang Kuang)

ABSTRACT. We compute the basic reproduction ratio of a SEIS model with n classes of latent individuals and bilinear incidence. The system exhibits the traditional behaviour. We prove that if $\mathcal{R}_0 \leq 1$, then the disease-free equilibrium is globally asymptotically stable on the nonnegative orthant and if $\mathcal{R}_0 > 1$, an endemic equilibrium exists and is globally asymptotically stable on the positive orthant.

1. Introduction. Global stability properties of a nonlinear system generally are a difficult problem. The global stability of SIR or SIRS models is known since the eighties. Since the stability of these systems can be reduced to the study of a two-dimensional system, the Poincaré-Bendixson criterion is used to establish the global stability. Global stability for *SEIR* and *SEIS* has long been conjectured. If the global stability of the disease-free equilibrium was known when the basic reproduction number \mathcal{R}_0 satisfies $\mathcal{R}_0 \leq 1$ on the other hand, the global stability for the endemic equilibrium, when $\mathcal{R}_0 > 1$, was an open problem. This was solved in 1995 by M.Y. Li and J. Muldowney [27] using the Poincaré-Bendixson properties of competitive systems in dimension 3 combined with sophisticated use of compound matrices. Using these techniques, the study of global properties of various models of the *SEIRS* type was developed [9, 30]. Nevertheless the systems considered

2000 *Mathematics Subject Classification.* 34D23,34A34,92D30.

Key words and phrases. nonlinear dynamical systems, epidemic models, global stability.

are three-dimensional or their stability properties are reduced to the study of a three-dimensional system. The main reason is that three-dimensional competitive systems satisfy the Poincaré-Bendixson condition. As far as we know, the only exception is [13], but it turns out that the global stability is reduced to the global stability of a three-dimensional subsystem.

In 2004 Korobeinikov [21, 23] introduced a class of Lyapunov functions and used them to establish global properties of the $SEIR$ and $SEIS$ models. It should be pointed out that this kind of Lyapunov function has a long history of applications to Lotka-Volterra models [11, 3] and was originally discovered by Volterra himself, although he did not use the vocabulary and the theory of Lyapunov functions. Such type of Lyapunov functions has also been used for epidemiological systems [2, 28]. More recently these functions also have been used for other low-dimensional systems [34].

The most promising method for high-dimensional systems is the Lyapunov method, using the Lyapunov-Volterra type functions. X. Lin and J. W. H. So study n groups of SIRS systems. They prove the global stability of the endemic equilibrium when $\mathcal{R}_0 > 1$ in the case where the interaction between groups is small. Essentially this is a perturbation result. Beretta and Capasso [2] use a skew-symmetry condition to provide a necessary condition for the global stability of the endemic equilibrium of n SIR models with constant population size. These results do not consider latent classes in model. The stability for differential stability models with mass action is completely studied in [31]. In [12, 16] the stability for staged progression models, with or without latent classes, is solved, and finally in [33] the stability of a model with an arbitrary number of latent classes is also completely treated.

In this paper we use a generalized Lyapunov function analogous to the one proposed in [21, 22, 37, 34] for low-dimensional systems and in [14] for other systems. We address the global dynamics of the generalized $SEIS$ and $SEIR$ models with n latent classes, namely: the $SE_1 \cdots E_n IS$ and $SE_1 \cdots E_n IR$ models. We also consider more general structured models. In some cases the residence time in a compartment can be described by a gamma distribution. This can be a motivation for considering systems that we could call “differential and staged progression ” exposed classes or DESP models. This gives staged progression models in parallel as in figure (1).

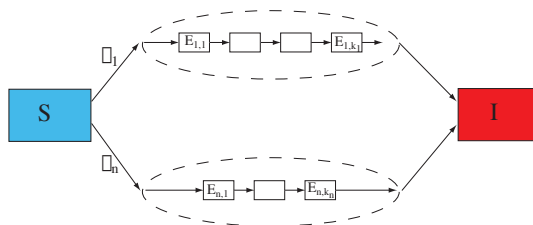


FIGURE 1. A set of linear chains in parallel

This paper is organised as follows: in section 2 we give the model formulation; in section 3 we provide the stability analysis for a linear chain of compartments; in section 4, relying on the results of section 3, we consider the case of parallel chains of compartments and explain the relationship with models incorporating continuous delays; finally in section 5 we conclude our discussion.

2. The model formulation. We assume homogeneity of the susceptible populations and we neglect variations in susceptibility associated with. The population being considered is divided into disjoint classes of susceptible, exposed, infective, and recovered individuals, with numbers at time t denoted by $S(t), E(t), I(t), R(t)$, respectively. All recruitment is into the susceptible class, and occurs at a constant rate Λ . On adequate contact with an infective, a susceptible individual becomes infected but not yet infective. This individual remains in the exposed class for a certain latent period, passing through n stages (E_1, \dots, E_n) before becoming infective. Once infective, an individual may either die or, after an infective period, pass into the recovered class. For diseases that confer temporary immunity, the individual returns to the susceptible class after an immune period. The transfer diagram for the system $SE_1 \dots E_n I S$ is given in the figure below:

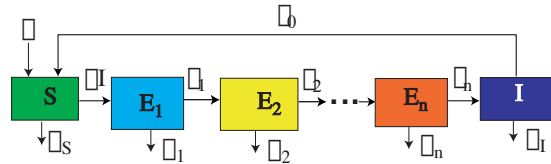


FIGURE 2. SEIS model

We write the model under a unique form.

The dynamics of the model are governed by the following system of differential equations:

$$\begin{cases} \dot{S} = \Lambda - \mu_S S - \beta S I + \gamma_0 I \\ \dot{E}_1 = \beta S I - \alpha_1 E_1 \\ \dot{E}_2 = \gamma_1 E_1 - \alpha_2 E_2 \\ \dots \\ \dot{E}_i = \gamma_{i-1} E_{i-1} - \alpha_i E_i \\ \dots \\ \dot{E}_n = \gamma_{n-1} E_{n-1} - \alpha_n E_n \\ \dot{I} = \gamma_n E_n - \alpha_{n+1} I \\ \dot{R} = \gamma_{n+1} I - \mu_R R. \end{cases} \quad (1)$$

The SE_iIR model is the model with $\gamma_0 = 0$. Since R does not appear in the $n + 2$ equations, (1) is a triangular system of the form

$$\begin{cases} \dot{X} &= f(X) \\ \dot{Y} &= g(X, Y) \end{cases} \quad (2)$$

where for any constant value of \bar{X} , the system $\dot{Y} = g(\bar{X}, Y)$ is globally asymptotically stable. It is well known that the stability analysis of the equilibria of (2) is equivalent to the stability analysis of the “reduced system” [43] and moreover, if all the trajectories of (2) are forward bounded, then the global stability analysis is also equivalent to the analysis of the reduced system [38]. Therefore we will consider the system (1) without the R compartment.

We can prove the result for positive coefficients, but for biological reasons we suppose that $\alpha_i = \gamma_i + \mu_i$ for $i = 1, \dots, n$ and $\alpha_{n+1} = \gamma_0 + \mu_I$, in others words $\alpha_i > \gamma_i$. This model allows, considering different death rates. It is biologically sensible to suppose that the mortality of the susceptible individuals is less than the mortality of the other compartments. Thus we will assume in the sequel that

$$\mu = \mu_S \leq \min_{i=1, \dots, n} (\mu_i, \mu_I).$$

3. Analysis of the system.

If we let $x = S$, $y_i = E_i$ for $i = 1, \dots, n$ and $y_{n+1} = I$, then (1) can be written under a general form.

$$\begin{cases} \dot{x} = \varphi(x) - \beta x \langle y | e_\omega \rangle + \gamma_0 y_{n+1} \\ \dot{y} = \beta x \langle y | e_\omega \rangle e_1 + A y \end{cases} \quad (3)$$

where $e_1 = (1, 0, 0, \dots, 0)^T$, $e_\omega = (0, 0, \dots, 0, 1)^T$, $\varphi(x) = \Lambda - \mu_S x$ and $\langle | \rangle$ denotes the usual inner product.

The matrix A is given by

$$A = \begin{bmatrix} -\alpha_1 & 0 & 0 & \dots & 0 & 0 \\ \gamma_1 & -\alpha_2 & 0 & \dots & 0 & 0 \\ 0 & \gamma_2 & -\alpha_3 & \dots & 0 & 0 \\ \vdots & \ddots & \ddots & \ddots & \vdots & \vdots \\ 0 & 0 & \dots & \gamma_{n-1} & -\alpha_n & 0 \\ 0 & 0 & \dots & 0 & \gamma_n & -\alpha_{n+1} \end{bmatrix}.$$

Using the fact that A is a non-singular Metzler matrix, we can deduce that the matrix $-A^{-1}$ is nonnegative[19]. We give the explicit expression of $-A^{-1}$ since we will need it later.

$$-A^{-1} = \begin{bmatrix} \frac{1}{\alpha_1} & 0 & 0 & \dots & 0 \\ \frac{\gamma_1}{\alpha_1 \alpha_2} & \frac{1}{\alpha_2} & 0 & \dots & 0 \\ \vdots & \ddots & \ddots & \ddots & \vdots \\ \frac{\gamma_1 \dots \gamma_{n-1}}{\alpha_1 \dots \alpha_n} & \dots & \frac{\gamma_{n-1}}{\alpha_{n-1} \alpha_n} & \frac{1}{\alpha_n} & 0 \\ \frac{\gamma_1 \dots \gamma_n}{\alpha_1 \dots \alpha_{n+1}} & \dots & \dots & \frac{\gamma_n}{\alpha_n \alpha_{n+1}} & \frac{1}{\alpha_{n+1}} \end{bmatrix} \quad (4)$$

The positive invariance of the nonnegative orthant by (3) is immediate with the assumptions on the model. From (1), if we denote by N the entire population

$N = S + E_1 + \dots + E_n + I$, then $\dot{N} = \Lambda - \mu_S S - (\mu_1 E_1 + \dots + \mu_n E_n) - \mu_I I$. With the hypothesis on μ we have $\dot{N} \leq \Lambda - \mu N$. It follows that $\lim_{t \rightarrow +\infty} N(t) = \frac{\Lambda}{\mu} = x^*$. It is straightforward to prove that for $\epsilon \geq 0$ the simplex

$$\Omega_\epsilon = \left\{ (S, E_1, \dots, E_n, I) \in \mathbb{R}_+^{n+2} \mid N \leq \frac{\Lambda}{\mu} + \epsilon \right\}$$

is a compact forward invariant set for the system (1) and that for $\epsilon > 0$ this set is absorbing, and so we limit our study to this simplex for $\epsilon > 0$.

The dynamics of the model (3) are determined by the basic reproduction ratio. Using the techniques of [42, 7, 8] the next generation matrix is given by $M = \beta x^* e_1 e_\omega^T (-A^{-1})$, and the basic reproduction ratio \mathcal{R}_0 is the spectral radius of this M . Since M is a rank one matrix, the only nonzero eigenvalue is given by $\beta x^* e_\omega^T (-A^{-1}) e_1$ or, using the inner product and (4)

$$\mathcal{R}_0 = \beta x^* \langle e_\omega \mid -A^{-1} e_1 \rangle = \beta x^* \frac{\gamma_1 \dots \gamma_n}{\alpha_1 \dots \alpha_n} \frac{1}{\alpha_{n+1}}. \quad (5)$$

3.1. Stability of the DFE.

There exists an evident equilibrium for (3) which is $(x^*, \mathbf{0})$, with $x^* = \frac{\Lambda}{\mu}$, called the disease-free equilibrium (DFE). We have the following theorem, in which \mathcal{R}_0 is used as a threshold parameter.

THEOREM 3.1. *We consider the system (3). If $\mathcal{R}_0 \leq 1$, the DFE is globally asymptotically stable in Ω_ϵ implying the global stability on the nonnegative orthant. This means that the disease naturally dies out.*

Proof: Consider the following Lyapunov-LaSalle function:

$$V_{DFE} = \langle -A^{-T} e_\omega \mid y \rangle$$

time derivative along the trajectories of (3) is

$$\dot{V}_{DFE} = \langle -A^{-T} e_\omega \mid \dot{y} \rangle = \langle -A^{-T} e_\omega \mid \beta x \langle y \mid e_\omega \rangle e_1 + Ay \rangle \quad (6)$$

$$= \beta x \langle y \mid e_\omega \rangle \langle -A^{-T} e_\omega \mid e_1 \rangle + \langle -A^{-T} e_\omega \mid Ay \rangle \quad (7)$$

$$= x \langle e_\omega \mid y \rangle \frac{\mathcal{R}_0}{x^*} - \langle e_\omega \mid y \rangle = y_{n+1} \left(\mathcal{R}_0 \frac{x}{x^*} - 1 \right). \quad (8)$$

We distinguish two cases. The first is $\mathcal{R}_0 < 1$.

Let ϵ be defined such that $\frac{x^*}{\mathcal{R}_0} = x^* + 2\epsilon$ and consider the positively compact invariant absorbing set Ω_ϵ . The largest invariant set in Ω_ϵ , contained in the set

$$\{(x, y) : \dot{V}_{DFE}(x) = 0\}$$

is reduced to the DFE. By LaSalle's invariance principle, this proves the global asymptotic stability on Ω_ϵ ([5], Theorem 3.7.11, page 346). Since Ω_ϵ is absorbing, this proves the global asymptotic stability on the nonnegative orthant for $\mathcal{R}_0 < 1$. We stress the need to consider a positively invariant compact set to establish the stability of the DFE since V_{DFE} is not positive definite. Generally, when applied on a non-compact positively invariant set, the LaSalle's invariance principle proves nothing but the attractivity of the equilibrium. Considering Ω_ϵ permits us to conclude to the stability of the system [5, 26, 25]. This fact is often overlooked in the literature when using LaSalle's invariance principle.

In the second case, we suppose $\mathcal{R}_0 = 1$. We claim that with this hypothesis the half space

$$H = \{(x, y) \in \mathbb{R}_+^{n+2} \mid x \leq x^*\}$$

is positively invariant. Indeed on the boundary, defined by $x = x^*$, of H we have

$$\dot{x} = (\gamma_0 - \beta x^*) y_{n+1}.$$

Now we have

$$\mathcal{R}_0 = \beta x^* \langle e_\omega \mid -A^{-1}e_1 \rangle = \beta x^* \frac{\gamma_1 \cdots \gamma_n}{\alpha_1 \cdots \alpha_n} \frac{1}{\alpha_{n+1}} = 1,$$

which gives $\beta x^* = \frac{\alpha_1 \cdots \alpha_n}{\gamma_1 \cdots \gamma_n} \alpha_{n+1} > \alpha_{n+1} > \gamma_0$, which in turn proves $\dot{x} \leq 0$ on the boundary of H . A similar argument, as for the case $\mathcal{R}_0 > 1$, proves that the DFE is globally asymptotically stable on $\Omega_\epsilon \cap H$. We will prove the stability of the DFE on the nonnegative orthant, in other words, we have to examine what happens on the “right-side” of H . We will use on the nonnegative orthant the $\|\cdot\|_1$ norm, i.e., $\|(x, y)\|_1 = x + \sum y_i$. Consider for any $\epsilon > 0$ the corresponding open ball $B((x^*, \mathbf{0}), \epsilon)$, centered on the DFE with radius ϵ . By stability of the DFE on $\Omega_\epsilon \cap H$, there exists $\eta > 0$ such that for any initial condition in $B((x^*, \mathbf{0}), \eta) \cap H$ the corresponding forward trajectory stays in $B((x^*, \mathbf{0}), \epsilon) \cap H$. We remark that this is the trace of $B(\mathbf{0}, x^* + \eta)$ on the nonnegative orthant. Hence $B((x^*, \mathbf{0}), \eta) \subset \Omega_\eta$. Let an initial condition (x_0, y_0) be in $B((x^*, \mathbf{0}), \eta)$ that moreover satisfies $x_0 > x^*$. By invariance of Ω_η the corresponding trajectory either stays in $\overline{B((x, \mathbf{0}), \eta)} \cap \{x \geq x^*\}$ or enters $B((x, \mathbf{0}), \epsilon) \cap H$. In any case the trajectory stays in $B((x, \mathbf{0}), \epsilon)$, which proves the stability of the DFE on the nonnegative orthant. For the attractivity of the DFE, let us consider a trajectory. This trajectory is forward bounded and enters Ω_ϵ . On the one hand, if the trajectory enters $\Omega_\epsilon \cap H$, since the DFE is globally asymptotically stable on this set, we are finished. On the other hand, if the trajectory remains in $\Omega_\epsilon \cap \{x \geq x^*\}$, we note that on the trajectory V is an increasing bounded function. LaSalle’s invariance principle proves that the ω -limit points of the trajectory are contained in the largest invariant set in $\dot{V} = 0$, reduced to the DFE. This proves the attractivity of the DFE and ends the proof of the theorem.

3.2. Stability of the SE₁...E_nS model.

A nonnegative equilibrium (\bar{x}, \bar{y}) of (3) is called endemic if $\bar{y}_i > 0$ form some i . It is called a strongly endemic equilibrium if $\bar{y}_i > 0$ for all $i = 1, \dots, n$ [41].

We have the following theorem when $\mathcal{R}_0 > 1$.

THEOREM 3.2. *We consider the system (3). If $\mathcal{R}_0 > 1$, there exists a strongly endemic equilibrium which is globally asymptotically stable on the nonnegative orthant except for the half x -axis.*

Proof: An equilibrium (\bar{x}, \bar{y}) of the system (3) satisfies

$$\varphi(\bar{x}) = (\beta \bar{x} - \gamma_0) \langle \bar{y} \mid e_\omega \rangle \tag{9}$$

$$\beta \bar{x} \langle \bar{y} \mid e_\omega \rangle e_1 = -A \bar{y}. \tag{10}$$

which gives $\bar{y} = \beta \bar{x} \langle \bar{y} \mid e_\omega \rangle (-A^{-1})e_1$, and replacing in $\langle \bar{y} \mid e_\omega \rangle$ we have

$$\langle \bar{y} \mid e_\omega \rangle = \beta \bar{x} \langle \bar{y} \mid e_\omega \rangle \langle (-A^{-1})e_1 \mid e_\omega \rangle.$$

The case $\langle \bar{y} | e_\omega \rangle = 0$ implies $\varphi(\bar{x}) = 0$ and $-A\bar{y} = 0$. Since A is nonsingular this gives the DFE.

For the other case, simplifying by $\langle \bar{y} | e_\omega \rangle$ gives, with (5),

$$\bar{x} = \frac{x^*}{\mathcal{R}_0} > 0.$$

With $\mathcal{R}_0 > 1$ we have $\bar{x} < x^*$, $\varphi(\bar{x}) > 0$ and

$$\beta \bar{x} = \frac{\alpha_1 \dots \alpha_n}{\gamma_1 \dots \gamma_n} \alpha_{n+1} > \alpha_{n+1} > \gamma_0$$

hence

$$y_{n+1} = \frac{\varphi(\bar{x})}{\beta \bar{x} - \gamma_0} > 0.$$

and finally

$$\bar{y} = \frac{\beta \bar{x}}{\beta \bar{x} - \gamma_0} \varphi(\bar{x}) (-A^{-1}) e_1.$$

Since the first column of $-A^{-1}$ is a positive vector (see (4)), we have proved that $\bar{y} \gg 0$, is a strongly endemic equilibrium.

Let us consider the following function V_{EE} , defined on the positive orthant

$$V = a_0(x - \bar{x} \ln x) + \sum_{i=1}^{n+1} a_i(y_i - \bar{y}_i \ln y_i).$$

We claim that we can choose the coefficients $(a_0, a) \in \mathbb{R}_+^{n+2}$ such that in the expression of \dot{V}_{EE} all the linear terms in x, y_1, \dots, y_n and the bilinear term in $x y_{n+1}$ cancel. We are looking for a solution of

$$\begin{bmatrix} -1 & e_1^T \\ \beta \bar{x} e_\omega & A^T \end{bmatrix} \begin{bmatrix} a_0 \\ a \end{bmatrix} = 0.$$

Using the Schur complement, we can compute the determinant of the block matrix to obtain

$$\det \begin{bmatrix} -1 & e_1^T \\ \beta \bar{x} e_\omega & A^T \end{bmatrix} = -1 + \beta \bar{x} e_1^T (-A^{-T}) e_\omega = -1 + \beta \bar{x} \langle (-A^{-1}) e_1 | e_\omega \rangle.$$

using the formula (5), for \mathcal{R}_0 we finally get

$$\det \begin{bmatrix} -1 & e_1^T \\ \beta \bar{x} e_\omega & A^T \end{bmatrix} = -1 + \bar{x} \frac{\mathcal{R}_0}{x^*} = 0.$$

The matrix is a rank $n+1$ matrix, since its kernel is one dimensional. This means that we have one degree of freedom to choose any $a_0 > 0$. When a_0 is chosen, a is defined by $a = a_0 \beta \bar{x} (-A^{-T}) e_\omega$. In other words, a is up to a multiplication by a positive scalar, the last row of A^{-1} . Then the coefficients of the Lyapunov function are positive, this proves that V_{EE} has a unique minimum.

Now if we choose $a_0 = 1$, the linear part in y of V_{EE} is exactly $\beta \bar{x} V_{DFE}$. Recalling $\bar{x} = \frac{x^*}{\mathcal{R}_0}$ and using the result of the computation (8), we see when computing \dot{V}_{EE} that the only term in y_{n+1} comes from the expression of \dot{x} . Then

$$\begin{aligned}
\dot{V}_{EE} &= \varphi(x) \frac{(x - \bar{x})}{x} + \gamma_0 y_{n+1} \frac{(x - \bar{x})}{x} \\
&\quad - a_1 \beta \bar{x} \bar{y}_{n+1} \frac{x y_{n+1} \bar{y}_1}{\bar{x} \bar{y}_{n+1} y_1} - a_2 \gamma_1 \bar{y}_1 \frac{y_1 \bar{y}_2}{\bar{y}_1 y_2} - \dots - a_n \gamma_{n-1} \bar{y}_{n-1} \frac{y_{n-1} \bar{y}_n}{\bar{y}_{n-1} y_n} \\
&\quad - a_{n+1} \gamma_n \bar{y}_n \frac{y_n \bar{y}_{n+1}}{\bar{y}_n y_{n+1}} + a_1 \alpha_1 \bar{y}_1 + \dots + a_n \alpha_n \bar{y}_n + a_{n+1} \alpha_{n+1} \bar{y}_{n+1}
\end{aligned}$$

Using the definition for the coefficients a , and the relations for the endemic equilibrium, a finite recursion argument shows immediately

$$\begin{aligned}
a_1 \beta \bar{x} \bar{y}_{n+1} &= \\
a_1 \alpha_1 \bar{y}_1 &= a_2 \gamma_1 \bar{y}_1 \dots = a_i \alpha_i \bar{y}_i = a_{i+1} \gamma_i \bar{y}_i \\
&= a_{n+1} \alpha_{n+1} \bar{y}_{n+1}.
\end{aligned}$$

In others words, the coefficients in line 2 and 3 are equal. Moreover $a_0 = a_1 = 1$. we get

$$\begin{aligned}
\dot{V}_{EE} &= \varphi(x) \frac{(x - \bar{x})}{x} + \gamma_0 y_{n+1} \frac{(x - \bar{x})}{x} \\
&\quad + \beta \bar{x} \bar{y}_{n+1} \left[(n+1) - \frac{x y_{n+1} \bar{y}_1}{\bar{x} \bar{y}_{n+1} y_1} - \frac{y_1 \bar{y}_2}{\bar{y}_1 y_2} - \dots - \frac{y_{n-1} \bar{y}_n}{\bar{y}_{n-1} y_n} - \frac{y_n \bar{y}_{n+1}}{\bar{y}_n y_{n+1}} \right].
\end{aligned}$$

Using the relation $\beta \bar{x} \bar{y}_{n+1} = \varphi(\bar{x}) + \gamma_0 \bar{y}_{n+1}$ we add and subtract $\beta \bar{x} \bar{y}_{n+1} \frac{(x - \bar{x})}{x}$ to obtain

$$\begin{aligned}
\dot{V}_{EE} &= (\varphi(x) - \varphi(\bar{x})) \frac{(x - \bar{x})}{x} + \gamma_0 (y_{n+1} - \bar{y}_{n+1}) \frac{(x - \bar{x})}{x} \\
&\quad + \beta \bar{x} \bar{y}_{n+1} \left[(n+2) - \frac{\bar{x}}{x} - \frac{x y_{n+1} \bar{y}_1}{\bar{x} \bar{y}_{n+1} y_1} - \frac{y_1 \bar{y}_2}{\bar{y}_1 y_2} - \dots - \frac{y_{n-1} \bar{y}_n}{\bar{y}_{n-1} y_n} - \frac{y_n \bar{y}_{n+1}}{\bar{y}_n y_{n+1}} \right].
\end{aligned}$$

which gives us, with the definition of φ ,

$$\begin{aligned}
\dot{V}_{EE} &= -\mu \frac{(x - \bar{x})^2}{x} + \gamma_0 (y_{n+1} - \bar{y}_{n+1}) \frac{(x - \bar{x})}{x} \\
&\quad + \beta \bar{x} \bar{y}_{n+1} \left[(n+2) - \frac{\bar{x}}{x} - \frac{x y_{n+1} \bar{y}_1}{\bar{x} \bar{y}_{n+1} y_1} - \frac{y_1 \bar{y}_2}{\bar{y}_1 y_2} - \dots - \frac{y_{n-1} \bar{y}_n}{\bar{y}_{n-1} y_n} - \frac{y_n \bar{y}_{n+1}}{\bar{y}_n y_{n+1}} \right].
\end{aligned}$$

With the inequality between the arithmetical and geometrical means we deduce that, except for the term $\gamma_0 (y_{n+1} - \bar{y}_{n+1}) \frac{(x - \bar{x})}{x}$, the two other terms are nonnegative. Using the relation

$$\dot{x} = -(\mu + \beta y_{n+1})(x - \bar{x}) - (y_{n+1} - \bar{y}_{n+1})(\beta \bar{x} - \gamma_0),$$

we know that $\beta \bar{x} - \gamma_0 > 0$. So, we consider the new candidate Lyapunov function

$$V(x, y) = \frac{\gamma_0}{\beta \bar{x} - \gamma_0} (x - \bar{x} \ln x) + V_{EE}.$$

The preceding computation gives

$$\begin{aligned} \dot{V} = & -\mu \frac{(x - \bar{x})^2}{x} - \frac{\gamma_0}{\beta \bar{x} - \gamma_0} (\mu + \beta y_{n+1}) \frac{(x - \bar{x})^2}{x} \\ & + \beta \bar{x} \bar{y}_{n+1} \left[(n+2) - \frac{\bar{x}}{x} - \frac{x}{\bar{x}} \frac{y_{n+1}}{\bar{y}_{n+1}} \frac{\bar{y}_1}{y_1} - \frac{y_1}{\bar{y}_1} \frac{\bar{y}_2}{y_2} - \dots - \frac{y_{n-1}}{\bar{y}_{n-1}} \frac{\bar{y}_n}{y_n} - \frac{y_n}{\bar{y}_n} \frac{\bar{y}_{n+1}}{y_{n+1}} \right]. \end{aligned}$$

This proves that \dot{V} is negative definite on the positive orthant. By considering the system on the boundary of the positive orthant, we obtain the desired conclusion.

4. The k parallel chains model.

Before addressing the stability problems of the system given by (1), we will explain why we consider such a system. Often stage transition is addressed in the spirit of compartment modeling [19]. Individuals are assumed to leave the stage at a fixed per-capita rate. This leads to a peculiar length distribution of the stage, the exponential distribution. This distribution is biologically unrealistic, since it corresponds to the assumption that the remaining time in the stage is independent of the time of entry in the stage. To have a better description would be to measure the real probability density function (pdf) and to include it explicitly in the model, a difficult task. Another method to approximate the pdf by a linear combination of Erlang distributions [20]. The Erlang distribution is a high flexible distribution that can mimic a variety of biologically plausible continuous delays.

The density function of the Erlang distribution is given by

$$g_{n,b} = \frac{t^{n-1} e^{-\frac{t}{b}}}{b^n (n-1)!}. \quad (11)$$

This distribution has for mean, $\tau = nb$, variance, nb^2 , and peak, $(n-1)b$. It can be generated by a one-way catenary chain of n compartments.

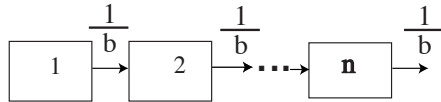


FIGURE 3. One-way catenary chain of compartments

If one injects a unit impulse into compartment 1 at $t = 0$, the outflow from compartment n , as a function of time, is exactly $g_{n,b}$ of (11). The use of a catenary chain of compartments with one-way flow to generate a distribution of lags is well known. MacDonald used it extensively in his monograph [32], calling it the ‘linear chain trick’. The preceding catenary subsystem can be inserted between two compartments of a system to generate a lag with pdf given by (11). It should be pointed out that these stages are a mathematical device used to consider pdf. In

general they need not correspond to biological features. We can now insert between two compartments parallel catenary chains of different length, as in figure (1), to generate a linear combination of Erlang distributions.

Thus, if one can find such a compartmental system and insert it between compartments, one obtains a larger compartmental system without explicit lags that behaves exactly the same as the original system. To summarize, in a compartmental system with delays, if the pdf of the delays are linear combinations of Erlang distributions, then the system is equivalent to a compartmental system without delays. More precisely, any solution of the system without delays is a solution of the system with delays. The proof of this claim can be found in numerous references [20, 35, 15, 6].

To model residence time in the latency period, whose pdf can be approximated by a pdf which is a convex sum of Erlang distributions, we consider a model with k chains as in figure (1).

Since we think that the main difficulty lies in the notations, we will develop some conventions and notations. We will write the system in a form analogous to (3) with some modifications. We will denote by y the state vector corresponding to the latent classes and decompose the vector y into k blocks $y = (y_1, y_2, \dots, y_k)$ corresponding to the k parallel chains. Each vector-block y_i is of length n_i , the length of the i th-chain. We denote $y_i = (y_{i,1}, \dots, y_{i,\omega})$ with the convention that $y_{i,\omega}$ is the last component of y_i . The notation ω plays a role similar to the syntax **end** in MATLAB. We denote by x and z the state of the susceptible and infectious respectively. The state vector y is in \mathbb{R}^n , with $n = \sum n_i$, and the system is in \mathbb{R}^{n+2} . As usual, we will take the liberty of indentifying \mathbb{R}^{n_i} with its canonical injection in \mathbb{R}^{n+2} . We need some notations for the canonical basis of \mathbb{R}^{n_i} . According to this identification, $e_{i,j}$ will denote the j -th canonical vector of \mathbb{R}^{n_i} , in other words it is the vector numbered $1 + n_1 + \dots + n_{i-1} + j$. The last vector of \mathbb{R}^{n_i} will be denoted by $e_{i,\omega}$, and the last vector of \mathbb{R}^{n+2} , corresponding to z , will be denoted by e_ω . Thus we can write the system

$$\begin{cases} \dot{x} &= \varphi(x) - \beta x z + \gamma_0 z \\ \dot{y} &= \beta x z \mathbf{b} + A y \\ \dot{z} &= \mathbf{c}^T y - \alpha z \end{cases} \quad (12)$$

where A is a $n \times n$ diagonal block matrix $A = \text{diag}(A_1, \dots, A_k)$. The i block A_i is a $n_i \times n_i$ matrix as in (3), where the coefficients α and β appearing in (3) are indexed, i.e., $\alpha_{i,j}$ for $j = 1, \dots, n_i$ and $\gamma_{i,j}$ for $j = 1, \dots, j - 1$.

The matrix \mathbf{c}^T is a $1 \times n$ matrix

$$\mathbf{c}^T = [\gamma_{1,\omega} e_{1,\omega}^T, \dots, \gamma_{k,\omega} e_{k,\omega}^T]$$

corresponding to each output of the last compartment of each latent chain entering the infectious compartment.

The vector \mathbf{b} is

$$\mathbf{b} = \pi_1 e_{1,1} + \dots + \pi_{k,1} e_{k,1}$$

corresponding to the input in each first compartment of each latent chain, with $\pi_1 + \dots + \pi_k = 1$.

We denote by \tilde{A} the block matrix

$$\tilde{A} = \begin{bmatrix} A & 0 \\ \mathbf{c}^T & -\alpha_z \end{bmatrix}.$$

We can now give the theorem of this section.

THEOREM 4.1. *We consider the system (12). The basic reproduction ratio of the system is given by*

$$\mathcal{R}_0 = \beta x^* \langle e_\omega \mid (-\tilde{A}^{-1}) \mathbf{b} \rangle$$

1. *The system (12) is globally asymptotically stable on \mathbb{R}_+^{n+2} at the DFE $(x^*, 0, \dots, 0)$ if and only if $\mathcal{R}_0 \leq 1$.*
2. *If $\mathcal{R}_0 > 1$ then the DFE is unstable, there exists a unique strongly endemic equilibrium $(\bar{x}, \bar{y}, \bar{z}) \gg 0$ in the positive orthant. The endemic equilibrium is globally asymptotically stable on the nonnegative orthant, except for initial conditions on the nonnegative x -axis.*

Proof: The argument for \mathcal{R}_0 is similar to the one-chain case. We assume $\mathcal{R}_0 \leq 1$, and we consider the Lyapunov-LaSalle function

$$V_{DFE} = \beta \langle (-\tilde{A}^{-T}) e_\omega \mid \begin{bmatrix} y \\ z \end{bmatrix} \rangle.$$

We obtain in a straightforward way

$$\dot{V} = \beta z (\mathcal{R}_0 \frac{x}{x^*} - 1).$$

and the proof of the global stability of the DFE is exactly the one-chain case.

We now prove the global existence of the EE on the positive orthant. When all the π_j but one $\pi_i = 1$. we are in the one-chain case and then we can define

$$\mathcal{R}_{0,i} = \beta x^* \frac{\gamma_{i,1} \cdots \gamma_{i,\omega}}{\alpha_{i,1} \cdots \alpha_{i,\omega}} \frac{1}{\alpha_z}.$$

With this definition and using the structure of $(-\tilde{A})^{-1}$ we obtain

$$\mathcal{R}_0 = \beta x^* \sum_{i=1}^k \frac{\pi_i \gamma_{i,\omega}}{\alpha_z} \langle (-A_i^{-1}) e_{i,1} \mid e_{i,\omega} \rangle = \sum_{i=1}^k \pi_i \mathcal{R}_{0,i}$$

and if $\mathcal{R}_0 > 1$, we obtain

$$\begin{cases} \bar{x} &= \frac{x^*}{\mathcal{R}_0} \\ \bar{y} &= \varphi(\bar{x}) (-A^{-1}) \mathbf{b} \\ \bar{z} &= \frac{\varphi(\bar{x})}{\beta \bar{x} - \gamma_0}. \end{cases} \quad (13)$$

We have, if $\mathcal{R}_0 < 1$, $0 < \bar{x} < x^*$, hence, $\varphi(\bar{x}) > 0$, which in turn implies $\bar{y} > 0$. We have to prove that $\beta \bar{x} > \gamma_0$. But

$$\beta \bar{x} = \frac{\alpha_z}{\sum_{i=1}^k \pi_i \gamma_{i,\omega} \langle (-A_i^{-1}) e_{i,1} \mid e_{i,\omega} \rangle} = \frac{\alpha_z}{\sum_{i=1}^k \pi_i \frac{\gamma_{1,i} \cdots \gamma_{i,\omega}}{\alpha_{i,1} \cdots \alpha_{i,\omega}}} > \frac{\alpha_z}{\sum \pi_i} = \alpha_z > \gamma_0.$$

This proves $\bar{z} > 0$.

We will prove now the global stability for the EE. To continue in a similar vein we define the function

$$V_{EE} = a_0(x - \bar{x} \ln x) + \sum_{i=1}^n a_i (y_i - \bar{y}_i \ln y_i) + a_{n+2} (z - \bar{z} \ln z).$$

Using the same convention, we define the vector a of \mathbb{R}^n by defining the k blocks $a = (a_1, \dots, a_k)$ and use $a_\omega = a_{n+2}$. We choose (a_0, a, a_ω) as a positive solution of

$$\begin{bmatrix} -1 & \mathbf{b}^T \\ \beta \bar{x} e_\omega & \tilde{A}^T \end{bmatrix} \begin{bmatrix} a_0 \\ a \\ a_\omega \end{bmatrix} = 0.$$

The same argument as in section 3.2 applies. Then we can choose, for example $a_0 = 1$. When we compute \dot{V}_{DFE} the same simplifications occur

$$\begin{aligned} \dot{V}_{EE} &= \varphi(x) \left(1 - \frac{\bar{x}}{x}\right) + \gamma_0 z \frac{(x-\bar{x})}{x} \\ &+ \sum_{i=1}^k \left[-\pi_i a_{i,1} \beta \bar{x} \bar{z} \frac{y_{i,1}}{\bar{y}_{i,1}} \frac{x}{\bar{x}} \frac{z}{\bar{z}} - \sum_{j=2}^{n_i} a_{i,j} \gamma_{i,j-1} \bar{y}_{i,j-1} \frac{y_{i,j-1}}{\bar{y}_{i,j-1}} \frac{\bar{y}_{i,j}}{y_{i,j}} \right. \\ &\left. + \sum_{j=1}^{n_i} a_{i,j} \alpha_{i,j} \bar{y}_{i,j} - a_\omega \gamma_{i,\omega} \bar{y}_{i,\omega} \frac{y_{i,\omega}}{\bar{y}_{i,\omega}} \frac{\bar{z}}{z} \right] + a_\omega \alpha_z \bar{z}. \end{aligned}$$

Each diagonal block of A_i of the matrix A has the structure of the matrix considered in the one-chain case, then, we deduce the following relations between the coefficients

$$a_{i,j} \gamma_{i,j-1} \bar{y}_{i,j-1} = \pi_i a_{i,1} \varphi(\bar{x}) = a_{i,j} \alpha_{i,j} \bar{y}_{i,j} = \gamma_{i,\omega} \bar{y}_{i,\omega}$$

and $a_\omega \alpha_z \bar{z} = \beta \bar{x} \bar{z} = \varphi(\bar{x}) + \gamma_0 \bar{z}$. We recall that $a_0 = 1 = \sum_{i=1}^k \pi_i a_{i,1}$. hence

$$\begin{aligned} \dot{V}_{EE} &= a \varphi(x) \frac{(x-\bar{x})}{x} + \gamma_0 z \frac{(x-\bar{x})}{x} \\ &+ \beta \bar{x} \bar{z} \sum_{i=1}^k \pi_i a_{i,1} \left[(n_i + 1) - \frac{y_{i,1}}{\bar{y}_{i,1}} \frac{x}{\bar{x}} \frac{z}{\bar{z}} - \sum_{j=2}^{n_i} \frac{y_{i,j-1}}{\bar{y}_{i,j-1}} \frac{\bar{y}_{i,j}}{y_{i,j}} - \frac{y_{i,\omega}}{\bar{y}_{i,\omega}} \frac{\bar{z}}{z} \right]. \end{aligned}$$

Adding and subtracting $\beta \bar{x} \bar{z} \frac{(x-\bar{x})}{x}$ gives

$$\begin{aligned} \dot{V}_{EE} &= a \varphi(x) \frac{(x-\bar{x})}{x} + \gamma_0 (z - \bar{z}) \frac{(x-\bar{x})}{x} \\ &+ \beta \bar{x} \bar{z} \sum_{i=1}^k \pi_i a_{i,1} \left[(n_i + 2) - \frac{\bar{x}}{x} - \frac{y_{i,1}}{\bar{y}_{i,1}} \frac{x}{\bar{x}} \frac{z}{\bar{z}} - \sum_{j=2}^{n_i} \frac{y_{i,j-1}}{\bar{y}_{i,j-1}} \frac{\bar{y}_{i,j}}{y_{i,j}} - \frac{y_{i,\omega}}{\bar{y}_{i,\omega}} \frac{\bar{z}}{z} \right]. \end{aligned}$$

With this relation we obtain, as in section 3.2, that

$$V(x, y, z) = \frac{\gamma_0}{\beta \bar{x} - \gamma_0} (x - \bar{x} \ln x) + V_{EE}(x, y, z)$$

is a strict Lyapunov function, which ends the proof of the theorem.

5. Discussion.

We have given a complete analysis of SE_iIR systems with latent classes. The latent classes are made up of parallel chains of different lengths and are inserted between the susceptible and the infectious compartments. We compute the basic reproduction ratio \mathcal{R}_0 , and we prove that if $\mathcal{R}_0 \leq 1$, the disease-free equilibrium is globally asymptotically stable on the nonnegative orthant. If $\mathcal{R}_0 > 1$, then a unique endemic equilibrium exists in the positive orthant and is globally asymptotically stable, on the positive orthant.

Acknowledgments. Paper written during a workshop in Yaoundé organized in July 2006, by the EPIMATH group of Cameroon. Work was supported by the SARIMA project of the French ministry of Foreign Affairs. This paper is dedicated to the memory of Napoléon Bame, who died on April, 6, 2007.

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Received on October 19, 2006. Accepted on June 22, 2007.

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