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Dynamical Systems/Ordinary Differential Equations

Global asymptotic stability for the disease free equilibrium for epidemiological models

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Abstract

For a general class of models, we prove the global asymptotic stability (GAS) of the disease free equilibrium (DFE) under general assumptions. These conditions are related to the basic reproductive ratio \mathcal{R}_0 . We also give a practical algorithm to compute a threshold condition equivalent to $\mathcal{R}_0 \leq 1$. We show that these two results can be applied to numerous epidemiological models from the literature. *To cite this article: J.C. Kamgang, G. Sallet, C. R. Acad. Sci. Paris, Ser. I 341 (2005).* © 2005 Académie des sciences. Published by Elsevier SAS. All rights reserved.

Résumé

Stabilité globale et asymptotique de l'équilibre sans maladie des modèles épidémiologiques. Pour une classe générale de modèles, nous prouvons la globale asymptotique stabilité de l'équilibre sans maladie sous des hypothèses générales. Ces conditions sont relatives au nombre de reproduction de base \mathcal{R}_0 . Nous donnons également un algorithme pratique permettant d'établir une condition de seuil équivalente à $\mathcal{R}_0 \leq 1$. Nous montrons que ces deux résultats peuvent être appliqués à de nombreux modèles épidémiologiques de la littérature. *Pour citer cet article : J.C. Kamgang, G. Sallet, C. R. Acad. Sci. Paris, Ser. I 341 (2005).*

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Version française abrégée

Nous considérons une classe de systèmes courants en épidémiologie. Ceux ci sont généralement des systèmes d'équations différentielles définis sur une partie Ω positivement invariante, de $\mathbb{R}^{n_1}_+ \times \mathbb{R}^{n_2}_+$. S'il n'y a pas d'immigration d'infectieux ou d'infectés ils se mettent sous la forme du système (1) :

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$$\begin{cases} \dot{\mathbf{x}}_1 = \mathbf{A}_1(\mathbf{x}) \cdot (\mathbf{x}_1 - \mathbf{x}_1^*) + A_{12}(\mathbf{x})\mathbf{x}_2, \\ \dot{\mathbf{x}}_2 = \mathbf{A}_2(\mathbf{x})\mathbf{x}_2. \end{cases}$$
(1)

Le vecteur \mathbf{x}_1 représente les « non malades » (i.e. les susceptibles, les guéris, les immuns, les mis en quarantaine, ...) et \mathbf{x}_2 représente les « porteurs de la maladie » (i.e. les infectés, infectieux, ...). La matrice $\mathbf{A}_2(\mathbf{x})$ est une matrice de Metzler (matrice dont les termes hors diagonaux sont positifs, [6]) pour tout $\mathbf{x} \in \Omega$.

Théorème 0.1. Soit $G \subset \mathcal{U} = \mathbb{R}^{n_1}_+ \times \mathbb{R}^{n_2}_+$ un sous ensemble borné, d'intérieur non vide. Soit le système (1) que l'on suppose de classe \mathcal{C}^1 (pour simplifier) défini sur \mathcal{U} . Si

- (1) *G* est positivement invariant relativement à (1);
- (2) Le système (1) réduit à la sous-variété sans maladie $G \cap (\mathbb{R}^{n_1}_+ \times \{\mathbf{0}\}) : \dot{\mathbf{x}}_1 = \mathbf{A}_1(\mathbf{x}_1, \mathbf{0}) \cdot (\mathbf{x}_1 \mathbf{x}^*_1)$ est GAS au point \mathbf{x}^*_1 ;
- (3) Pour tout $\mathbf{x} \in \overline{G}$, la matrice $\mathbf{A}_2(\mathbf{x})$ est Metzler irréductible ;
- (4) Il existe une matrice A
 ₂, qui est un majorant de M = {A₂(x) ∈ M_{n2}(ℝ) | x ∈ G} avec la propriété que si A
 ₂ ∈ M, pour tout x
 ∈ G, tel que A₂(x
) = A
 ₂, alors x
 ∈ ℝⁿ¹ × {0};
- (5) Le module de stabilité de $\bar{\mathbf{A}}_2$, $\alpha(\bar{\mathbf{A}}_2) = \max_{\lambda \in \text{Sp}(\mathbf{A})} \Re(\lambda)$ vérifie $\alpha(\bar{\mathbf{A}}_2) \leq 0$.

Alors le DFE $(\mathbf{x}_1^*, \mathbf{0})$ est GAS dans \overline{G} .

1. Introduction

For epidemiological models, the basic reproduction ratio \mathcal{R}_0 is typically defined as the average number of new cases produced by a typical infectious individual during its entire infections period (Diekmann and Heesterbeck [5,4]). It is shown that \mathcal{R}_0 can be computed as the dominant eigenvalue of a positive compact operator. In general, the spectral radius of a positive operator is not easy to compute. The same remark applies for the Routh–Hurwitz criterion for systems of dimension higher than four. We provide a simple algorithm to compute a threshold condition equivalent to $\mathcal{R}_0 \leq 1$ for the stability of the DFE. Furthermore we prove for a general class of epidemiological ODE systems that $\mathcal{R}_0 \leq 1$ is a necessary and sufficient condition for the GAS of the DFE.

In the following we use the following classical notations and definitions. Let $\mathbf{A} = (a_{i\,j})$ and $\mathbf{B} = (b_{i\,j})$ be two real matrices; we say that $\mathbf{A} \leq \mathbf{B}$ if and only if $a_{i\,j} \leq b_{i\,j}$ for all (i, j), $\mathbf{A} < \mathbf{B}$ if and only if $\mathbf{A} \leq \mathbf{B}$ and $\mathbf{A} \neq \mathbf{B}$, and we note $\mathbf{A} \ll \mathbf{B}$ if and only if $a_{i\,j} < b_{i\,j}$ for all (i, j). We denote by $\alpha(\mathbf{A}) = \max_{\lambda \in S_p(\mathbf{A})} \Re(\lambda)$ the stability modulus of a square matrix $\mathbf{A} = (a_{i\,j})$, i.e. the greatest real part of eigenvalues of \mathbf{A} .

2. A theorem of stability

We consider systems arising from epidemiological problems, when modeled as compartmental deterministic systems [6]. This includes also intra-hosts models from virology [11]. It can be shown that under general hypotheses the system can be written as system (1) and is defined on a forward invariant compact subset Ω of $\mathbb{R}^{n_1}_+ \times \mathbb{R}^{n_2}_+$.

The nonnegative vector \mathbf{x}_1 can be considered as the vector representing the state of different compartments of *non transmitting individuals* (e.g. susceptible, immune, quarantine, ...), the vector \mathbf{x}_2 can be interpreted as the state of compartments of different *transmitting individuals* (e.g. infected, latent, infectious, ...). We assume that the matrix $\mathbf{A}_2(\mathbf{x})$ is Metzler¹ for all $\mathbf{x} \in \Omega$. Moreover, we suppose fulfilled the following natural biological

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¹ Matrix such that off diagonal terms are nonnegative.

assumption: The system $\dot{\mathbf{x}}_1 = \mathbf{A}_1(\mathbf{x}_1, \mathbf{0}) \cdot (\mathbf{x}_1 - \mathbf{x}_1^*)$ is GAS at \mathbf{x}_1^* . In other words there is a demographic asymptotic equilibrium when there is no disease in the population.

2.1. A theorem for the GAS of the DFE

Theorem 2.1. Let $G \subset U = \mathbb{R}^{n_1}_+ \times \mathbb{R}^{n_2}_+$ be a bounded set with nonempty interior. Let (1) be a given system supposed to be of class C^1 defined on U. If

- (1) *G* is positively invariant relative to (1);
- (2) The system (1) reduced to the disease free sub-manifold $G \cap (\mathbb{R}^{n_1}_+ \times \{\mathbf{0}\})$: $\dot{\mathbf{x}}_1 = \mathbf{A}_1(\mathbf{x}_1, \mathbf{0}) \cdot (\mathbf{x}_1 \mathbf{x}_1^*)$ is GAS at \mathbf{x}_1^* ;
- (3) For any $\mathbf{x} \in \overline{G}$, the matrix $\mathbf{A}_2(\mathbf{x})$ is Metzler irreducible;
- (4) There exists a matrix A
 ₂, which is an upper bound of the set M = {A₂(x) ∈ M_{n2}(ℝ) | x ∈ G
 } with the property that if A
 ₂ ∈ M, for any x
 _i ∈ G, such that A₂(x
 _i) = A
 ₂, then x
 _i ∈ ℝⁿ¹ × {0};
- (5) The stability modulus of $\bar{\mathbf{A}}_2$ satisfies $\alpha(\bar{\mathbf{A}}_2) \leq 0$.

Then the DFE $(\mathbf{x}_1^*, \mathbf{0})$ is GAS in \overline{G} .

Sketch of proof. By the Perron–Frobenius theorem, there exists $\mathbf{u} \gg \mathbf{0}$ such that $\mathbf{u}^T \bar{\mathbf{A}}_2 = \alpha(\bar{\mathbf{A}}_2)\mathbf{u}^T$. We use the Lyapunov function $L(\mathbf{x}) = \langle \mathbf{u}, \mathbf{x}_2 \rangle$ which satisfies $\dot{L}(\mathbf{x}) \leq 0$. Using the irreducibility property of $\mathbf{A}_2(\bar{\mathbf{x}})$ and $\bar{\mathbf{A}}_2$, we prove that the greatest invariant set contained in the set $\mathcal{L} = \{\mathbf{x} \in \overline{G} \mid \dot{L}(\mathbf{x}) = 0\}$ is contained in $\overline{G} \cap (\mathbb{R}^{n_1}_+ \times \{\mathbf{0}\})$. However, on this set, the reduced system is GAS on $(\mathbf{x}_1^*, \mathbf{0})$. This proves that the greatest invariant set in \mathcal{L} is $\{(\mathbf{x}_1^*, \mathbf{0})\}$. Hence by the LaSalle principle [7] this equilibrium is GAS on \overline{G} . \Box

Corollary 2.2. With the same notations and the same hypothesis than in Theorem 2.1, if furthermore we have $\bar{A}_2 = A_2(\mathbf{x}_1^*, \mathbf{0})$, then the DFE is GAS if and only if $\mathcal{R}_0 \leq 1$.

Sketch of proof. The Jacobian of the system at the DFE is

 $\mathbf{J} = \begin{pmatrix} \mathbf{A}_1(\mathbf{x}_1^*, \mathbf{0}) & A_{12}(\mathbf{x}_1^*, \mathbf{0}) \\ \mathbf{0} & \mathbf{A}_2(\mathbf{x}_1^*, \mathbf{0}) \end{pmatrix}.$

Hence $\alpha(\mathbf{A}_2) \leq 0$ is a necessary condition; this is equivalent to $\mathcal{R}_0 \leq 1$ [4]. The condition is sufficient by the preceding theorem. \Box

3. Computation of conditions for a Metzler matrix M to satisfy $\alpha(M) < 0$

Proposition 3.1. Let **M** be a square Metzler matrix written in block form $\mathbf{M} = \begin{pmatrix} \mathbf{A} & \mathbf{B} \\ \mathbf{C} & \mathbf{D} \end{pmatrix}$, with **A** and **D** square matrices. **M** is Metzler stable if and only if matrices **A** and **D** – $\mathbf{C}\mathbf{A}^{-1}\mathbf{B}$ are Metzler stable.

We prove the necessity of the condition. Any principal sub-matrix of a Metzler stable matrix is also Metzler stable, **A** and **D** are Metzler stable. Since **M** is Metzler stable there exists a positive block column vector $\mathbf{c} = (\mathbf{c}_1; \mathbf{c}_2) \gg \mathbf{0}$ such that $\mathbf{M} \cdot \mathbf{c} \ll \mathbf{0}$. This means $\mathbf{A}\mathbf{c}_1 + \mathbf{B}\mathbf{c}_2 \ll \mathbf{0}$ and $\mathbf{C}\mathbf{c}_1 + \mathbf{D}\mathbf{c}_2 \ll \mathbf{0}$. Since **A** is Metzler stable $-\mathbf{A}^{-1} \ge 0$ and **C** is nonnegative, we pre-multiply by $-\mathbf{C}\mathbf{A}^{-1} \ge \mathbf{0}$ to obtain $-\mathbf{C}\mathbf{c}_1 - \mathbf{C}\mathbf{A}^{-1}\mathbf{B}\mathbf{c}_2 \leqslant \mathbf{0}$. Hence $(\mathbf{D} - \mathbf{C}\mathbf{A}^{-1}\mathbf{B})\mathbf{c}_2 \ll \mathbf{0}$ which proves that $\mathbf{D} - \mathbf{C}\mathbf{A}^{-1}\mathbf{B}$ is Metzler stable. The necessity has been proven.

The condition is sufficient. If **A** and **D** – **CA**⁻¹**B** are stable Metzler matrices, there exists $\mathbf{c}_2 \gg 0$ such that $(\mathbf{D} - \mathbf{C}\mathbf{A}^{-1}\mathbf{B})\mathbf{c}_2 \ll \mathbf{0}$. Let $\mathbf{c}_3 = -\mathbf{A}^{-1}\mathbf{B}\mathbf{c}_2$. Since **A** is Metzler stable, **B** nonnegative and $\mathbf{c}_2 \gg 0$ it follows $\mathbf{c}_3 \ge 0$

and the inequalities $\mathbf{Cc}_3 + \mathbf{Dc}_2 \ll 0$ and $\mathbf{Ac}_3 + \mathbf{Bc}_2 = \mathbf{0}$ hold. Since \mathbf{A} is Metzler stable, let $\mathbf{v} \gg 0$ such that $\mathbf{Av} \ll 0$. We define $\mathbf{c}_1 = \mathbf{c}_3 + \varepsilon \mathbf{v} \gg 0$ for $\varepsilon > 0$. Hence $\mathbf{Cc}_1 + \mathbf{Dc}_2 = \mathbf{Cc}_3 + \mathbf{Dc}_2 + \varepsilon \mathbf{Cv}$. Since $\mathbf{Cc}_3 + \mathbf{Dc}_2 \ll 0$ and $\mathbf{v} \gg 0$ we can choose ε sufficiently small such that $\mathbf{Cc}_1 + \mathbf{Dc}_2 \ll 0$. This gives $\mathbf{Ac}_1 + \mathbf{Bc}_2 = \mathbf{Ac}_3 + \mathbf{Bc}_2 + \varepsilon \mathbf{Av} = \varepsilon \mathbf{Av} \ll 0$ which proves that \mathbf{M} is Metzler stable, hence the condition is sufficient.

4. Examples

Our results can be applied to numerous examples of the literature, improving some results on the GAS of the DFE [1,8–10]. As illustrations, we choose two examples from the biological literature and give also an original example in dimension 13.

4.1. The bovine viral diarrhea virus (BVDV) model [3]

The example is based on a model by Cherry et al. [3]. The reader is referred to this paper for the description of the model. We change the original notation to adhere to the classical compartment's name (S susceptible, ...).

$$\begin{cases} \dot{M} = \mu R_1 - (\mu + \sigma)M, & \dot{S} = \sigma M + \mu (S + E) + \Delta - \mu S - (\beta_1 I + \beta_2 P)S, \\ \dot{E} = (\beta_1 I + \beta_2 P)S - (\mu + \alpha)E, & \dot{I} = \alpha E - (\mu + \gamma)I, \\ \dot{R}_1 = \gamma \pi_1 I + \phi_3 Z + 2\phi_2 R_2 - \mu R_1, & \dot{R}_2 = \gamma \pi_2 I - (\mu + \phi_2) R_2, \\ \dot{Z} = \gamma \pi_3 I - (\mu + \phi_3)Z, & \dot{P} = \theta \phi_3 Z + (\mu - a)P - (\mu + b)P. \end{cases}$$
(2)

Since, in the model, the population of the herd (denoted by *N*) is kept constant by re-equilibration recruitment in the herd corresponding to $\Delta = \mu(M + I + R_2 + Z) + (a + b)P - (\phi_2 R_2 + \theta \phi_3 Z)$ in the class S. We can reduce to 7 states. We define $\mathbf{x}_1 = (S; R_1; R_2)$ consisting in non transmitting cattle, and $\mathbf{x}_2 = (Z; E; I; P)$. The DFE is (N, 0, 0, 0, 0, 0, 0). On the compact forward invariant set $G = \{\mathbf{x} = (\mathbf{x}_1, \mathbf{x}_2) \in \mathbb{R}^7_+ | \sum_{i=1}^7 x_i \leq N\}$ (isomorphic to the simplex of \mathbb{R}^8_+), the system can be easily written in the form of Eq. (1), with:

$$\mathbf{A}_{2}(\mathbf{x}) = \begin{pmatrix} -(\mu + \phi_{3}) & 0 & \gamma \pi_{2} & 0 \\ 0 & -(\mu + \alpha) & \beta_{1}S & \beta_{2}S \\ 0 & \alpha & -(\mu + \gamma) & 0 \\ \theta \phi_{3} & 0 & 0 & -(a + b) \end{pmatrix}.$$

The conditions (1)–(3) of Theorem 2.1 are obviously satisfied.

Let J_2 the bloc of the Jacobian matrix, computed at the DFE, corresponding to A_2 ; the expression of J_2 is $A_2(\mathbf{x})$ in which *S* is replaced by *N*. Then J_2 is irreducible and we have $A_2(\mathbf{x}) \leq J_2$.

To apply the Corollary 2.2 we have to compute the condition $\alpha(\mathbf{J}_2) \leq 0$, applying the Proposition 3.1 iteratively gives a NSC for GAS of the DFE:

$$\frac{\alpha N(\beta_1(\mu+\phi_3)(a+b)+\beta_2\theta\phi_3\gamma\pi_2)}{(\mu+\alpha)(\mu+\gamma)(\mu+\phi_3)(a+b)} \leqslant 1.$$

Then we have been able to compute a threshold condition equivalent to the condition obtained in [3], but in addition we get the GAS of the DFE on the simplex \overline{G} , the biological domain of the system, problem not treated in the quoted reference. Moreover, we consider the general problem with the two transmission parameters β_1 and β_2 .

4.2. A two strain tuberculosis model [1]

The following example shows that our result can be used iteratively. We consider the two strain tuberculosis model of Castillo Chavez et al. [1,2]. The system is given by:

$$\begin{cases} \dot{T} = rE_1 + (1 - p - q)\tilde{r}I_1 - \left(\sigma\beta_1\frac{I_1}{N} + \beta_2\frac{I_2}{N} + \mu\right)T, & \dot{S} = \Lambda - \left(\sigma\beta_1\frac{I_1}{N} + \beta_2\frac{I_2}{N} + \mu\right)S, \\ \dot{E}_1 = \sigma\beta_1\frac{I_1}{N}S + \sigma\beta_1\frac{I_1}{N}T + p\tilde{r}I_1 - \left(k_1 + r + \mu + \beta_2\frac{I_2}{N}\right)E_1, & \dot{I}_1 = k_1E_1 - (\tilde{r} + \mu + d_1)I_1, \end{cases}$$
(3)

$$\dot{E}_2 = \beta_2 \frac{I_2}{N} (S + E_1 + T) + q\tilde{r}I_1 - (k_2 + \mu)E_2, \qquad \dot{I}_2 = k_2 E_2 - (\mu + d_2)I_2.$$

The DFE is $\mathbf{x}_0 = (\frac{\Lambda}{\mu}; 0; 0; 0; 0; 0)$. We obtain easily a forward invariant absorbing compact set \overline{G} (for example $0 \le N \le \Lambda/\mu$).

In this case we cannot apply directly the theorem since the matrix $\mathbf{A}_2(\mathbf{x})$ is not irreducible. But this matrix can be decomposed in a diagonal of two block Metzler matrices. Then we apply Theorem 2.1 and Corollary 2.2 iteratively. We obtain $\mathcal{R}_1 = \frac{k_1(\sigma\beta_1 + p\tilde{r})}{(\tilde{r} + \mu + d_1)(k_1 + r + \mu)} \leq 1$ and $\mathcal{R}_2 = \frac{\beta_2 k_2}{(\mu + k_2)(\mu + d_2)} \leq 1$. As in [1], we have $\mathcal{R}_0 = \max(\mathcal{R}_1, \mathcal{R}_2)$, and we have proved that for $\mathcal{R}_0 \leq 1$, the DFE \mathbf{x}_0 is GAS in *G*. Since *G* is absorbing, the DFE is GAS on \mathbb{R}_+^4 .

In [1] (Theorems 2 and 3) the authors obtained a similar result if $\mathcal{R}_0 < 1$ with the hypothesis $d_1 = d_2 = 0$, i.e. they assume that there is no disease-induced mortality. The authors 'extend' the cases $d_1 > 0$ and $d_2 > 0$ numerically. Our result confirms this simulation. The authors obtained their results by using limiting system, which proves the attractivity of the DFE. The stability is obtained for $\mathcal{R}_0 < 1$ which ensures the local asymptotic stability. Our technique allows us to solve the problem of stability at the bifurcation value of the parameters. We stress that this stability is relative to the set \mathbb{R}^6_+ . It can be proven that the DFE for $\mathcal{R}_0 = 1$ on \mathbb{R}^6 is a saddle-node equilibrium.

4.3. Analysis of the effect of insecticide treated nets on the dynamic of malaria transmission

We give a model of the dynamic of the transmission of malaria in a population where a part of humans own and use lifelong the I.T.N. (insecticide treated bed nets) all time to protect themselves against mosquitoes bites. The human population is structured in *SI* classes giving 4 compartments according their I.T.N. status. The mosquitoes are divided in $SE_1E_2E_3I$ classes and are in a state of questing (*Q*) or resting (*R*) giving 8 classes. A special class of resting exposed E_4 mosquitoes is created giving a model of 13 compartments. Such a model implies two populations, the population of female anopheles in compartments indexed by *Q* for questing and *R* for resting and the humans population divided in two classes, a class of I.T.N. users (indexed by *B*), and a class of non users of I.T.N. (indexed by *N*).

$$\begin{split} \dot{S}_{Q} &= \mu M - (\mu + \beta) S_{Q} + \delta S_{R}, & \dot{S}_{R} = \beta (1 - d - \varphi) S_{Q} - (\mu + \delta) S_{R}, \\ \dot{E}_{R}^{(1)} &= \beta \varphi S_{Q} - (\mu + \delta) E_{R}^{(1)}, & \dot{E}_{Q}^{(1)} = \delta E_{R}^{(1)} - (\mu + \beta) E_{Q}^{(1)}, \\ \dot{E}_{R}^{(2)} &= \beta (1 - d) E_{Q}^{(1)} - (\mu + \delta) E_{R}^{(2)}, & \dot{E}_{Q}^{(2)} = \delta E_{R}^{(2)} - (\mu + \beta) E_{Q}^{(2)}, \\ \dot{E}_{R}^{(3)} &= \beta (1 - d) E_{Q}^{(2)} - (\mu + \delta) E_{R}^{(3)}, & \dot{E}_{Q}^{(3)} = \delta E_{R}^{(3)} - (\mu + \beta) E_{Q}^{(3)}, \\ \dot{E}_{R}^{(4)} &= \beta (1 - d) E_{Q}^{(3)} - (\mu + \delta) E_{R}^{(4)}, & \dot{I}_{N} = \beta h_{N} b_{2} \frac{I_{Q}}{H(1 - B)} (H(1 - B) - I_{N}) - \gamma I_{N}, \\ \dot{I}_{B} &= \beta h_{B} b_{2} \frac{I_{Q}}{HB} (HB - I_{B}) - \gamma I_{B}, & \dot{I}_{Q} = \delta E_{R}^{(4)} - (\mu + \beta) I_{Q} + \delta I_{R}, \\ \dot{I}_{R} &= \beta (1 - d) I_{Q} - (\delta + \mu) I_{R}. \end{split}$$

We define $\mathbf{x}_1 = (S_Q; S_R)$ and $\mathbf{x}_2 = (E_R^{(1)}; E_Q^{(1)}; E_R^{(2)}; E_Q^{(2)}; E_R^{(3)}; E_Q^{(3)}; E_R^{(4)}; I_N; I_B; I_Q; I_R)$; the DFE is given by $\mathbf{x}^* = (\mathbf{x}_1^*; \mathbf{0})$ (i.e. $\mathbf{x}_2^* = \mathbf{0}$) with $\mathbf{x}_1^* = \frac{M}{\Delta}(\mu(\mu + \delta); \mu\beta(1 - d))$ with $\Delta = \mu(\mu + \delta) + \delta(\mu + \beta d)$. On $G = \mathbb{R}^{13}_+$ the system can be written in the form of system (1), with: $\mathbf{A}_2(\mathbf{x})$ a square matrix of order 11.

The conditions (1), (2) and (3) of Theorem 2.1 are satisfied. The irreducibility of the matrices $A_2(x)$ is established by following the paths interconnecting compartments corresponding to the components of x_2 .

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The upper bound of the set of matrices $A_2(\mathbf{x})$ which is matrix A_2 is attained for $\bar{\mathbf{x}} = (H(1 - B); HB; \mathbf{0})$; this matrix is also irreducible for the same reason as the matrices $A_2(\mathbf{x})$.

The condition $\alpha(\mathbf{A}_2) \leq 0$ obtained by applying iteratively the algorithm in Proposition 3.1 is equivalent to

$$\mathcal{R}_{C} = \frac{M}{H} b_{1} b_{2} \frac{(1-d)^{3} \beta^{5} \delta^{3}}{\Delta(\mu+\beta)^{3} (\mu+\delta)^{3}} \left(\frac{h_{B}^{2}}{B} + \frac{h_{N}^{2}}{1-B}\right) \leqslant 1.$$
(5)

This gives the condition for the DFE to be GAS.

We remark that since the value of the matrix A_2 is not attained to the DFE the left value in the condition (5) is not \mathcal{R}_0 . Computing the condition $\alpha(A_2(\mathbf{x}^*)) \leq 0$ by applying the Proposition 3.1, we have:

$$\mathcal{R}_{0} = \frac{M}{H} \mu b_{1} b_{2} \frac{1}{\gamma} \left(\frac{\delta}{\mu+\delta}\right)^{2} \left(\frac{\beta(1-d)}{\mu+\beta}\right)^{3} \frac{\beta^{2} \delta^{2}}{\Delta^{2}} \left(\frac{h_{N}^{2}}{1-B} + \frac{h_{B}^{2}}{B}\right) \leqslant 1$$

as it can be checked by verifying the biological signification.

We have chosen the example of the effect of I.T.N. on the dynamics of the transmission of the malaria, which is a work in progress to stress that our result can give necessary condition for GAS of the DFE. The tuberculosis and BVDV examples illustrate that our method can be applied to numerous models of the literature to improve already known results. In the following examples of the literature, we can conclude, in the same manner, to the GAS of the DFE when $\mathcal{R}_0 \leq 1$ [1,8–10]. We can for example answer affirmatively to a conjecture of Perelson in [11]; i.e. the DFE is GAS iff $\mathcal{R}_0 \leq 1$. The result has been obtained as in the preceding examples.

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