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STABILITY ANALYSIS OF A MODEL FOR A VECTOR-BORNE DISEASE WITH AN ASYMPTOMATIC CLASS*

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We introduce a model for a vector-borne disease with symptomatic and asymptomatic carrier classes described by a system of ordinary differential equations. We analyse the local and the global stability of the disease-free and the endemic equilibria using appropriately chosen Lyapunov functions.

Introduction. Mosquito-transmitted diseases are among the major health challenges in tropical climates and could emerge in new regions such as Europe due to the establishment of invasive mosquito species [3]. Individuals infected with the pathogen but displaying no apparent symptoms (asymptomatic) or mild symptoms and remaining undetected by health surveillance systems (preclinical) could play a major role in the epidemic dynamics [4]. Also, individuals showing no symptoms are estimated to contribute to 88% of infections in the case of dengue fever [9], thus serving as a hidden reservoir for the pathogen. Compartmental models of vector-borne diseases sometimes include a compartment for asymptomatic carriers of the pathogen, for example, in modelling malaria [6]. We present a simple model for a vector-borne disease with asymptomatic carriers and study its equilibria and the asymptotic behaviour depending on the basic reproduction number.

Model description. The compartments of the model for the host population are formed by susceptible S, infected symptomatic I_s, infected asymptomatic I_a and removed individuals R. The total human population $N = S(t) + I_s(t) + I_a(t) + R(t)$ is assumed constant in time. The compartments of the model for the vector population are susceptible U and infected mosquitos V. The total vector population $M = U(t) + V(t)$ is assumed constant in time. The natural removal rates of hosts and vectors are denoted by μ, ν with $\mu \ll \nu$. The pathogen is transmitted from the infected hosts in both compartments I_s, I_a to the susceptible vector U, and from the infected vector V to the susceptible host S. Vectors in V cannot recover from the infection. The rate of removal/recovery of infected hosts is γ. The share of symptomatic carriers among all infected persons is denoted by $\sigma \in (0, 1)$.

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Encounters between vectors and hosts are modeled by the law of mass action with the following parameters: β denotes the infection rate of hosts per infected vector. ϑ_a denotes the infection rate of vectors per asymptomatic host, and ϑ_s denotes the infection rate of vectors per symptomatic host. There is no clear evidence whether infection rates from symptomatic and asymptomatic hosts to mosquitoes differ or not, due to physiological factors [1, 7] or simply because symptomatic carriers are more likely to be detected by health surveillance systems.

We nondimensionalise the variables $S := S/N$, $I_s := I_s/N$, $I_a := I_a/N$, $U := U/M$, $V := V/M$ and work with proportions instead. We consider the following system, which describes the temporal dynamics of the population proportion in each compartment:

$$\text{(1a)}\qquad \dot{S} = -\beta SV + \mu(1-S), \qquad \dot{R} = \gamma(I_s + I_a) - \mu R$$

$$\text{(1b)}\qquad \dot{I}_s = \sigma\beta SV - (\gamma+\mu)I_s, \qquad \dot{U} = -(\vartheta_a I_a + \vartheta_s I_s)U + \nu(1-U)$$

$$\text{(1c)}\qquad \dot{I}_a = (1-\sigma)\beta SV - (\gamma+\mu)I_a, \qquad \dot{V} = (\vartheta_a I_a + \vartheta_s I_s)U - \nu V.$$

Using the constraints $S + I_s + I_a + R = 1, U + V = 1$, it is possible to recast (1) as an equivalent system of ODEs for S, I_s, I_a, V.

$$\text{(2a)}\qquad \dot{S} = -\beta SV + \mu(1-S)$$

$$\text{(2b)}\qquad \dot{I}_s = \sigma\beta SV - (\gamma+\mu)I_s$$

$$\text{(2c)}\qquad \dot{I}_a = (1-\sigma)\beta SV - (\gamma+\mu)I_a$$

$$\text{(2d)}\qquad \dot{V} = \vartheta_a(1-V)I_a + \vartheta_s(1-V)I_s - \nu V\ .$$

One can show following [2] that the biologically relevant domain of the model (2) is the subset $\Omega = \{(S, I_s, I_a, V) \mid 0 \le S + I_s + I_a \le 1, 0 \le V \le 1\}$ of the positive orthant $\mathbb{R}^4_+$, and this domain is positively invariant by the flow of (2).

Stability analysis of equilibrium points. Denote in the following $\Theta = \sigma\theta_s + (1-\sigma)\theta_a$. System (2) has a trivial, disease-free equilibrium $\mathcal{E}_0 = (1, 0, 0, 0)$, and an endemic equilibrium $\mathcal{E}^* = (S^*, I_s^*, I_a^*, V^*)$,

$$\text{(3)}\qquad \begin{aligned} S^* &= \frac{\nu(\gamma+\mu)+\mu\Theta}{(\beta+\mu)\Theta}, & V^* &= \mu\frac{\beta\Theta - \nu(\gamma+\mu)}{\beta(\nu(\gamma+\mu)+\mu\Theta)}, \\ I_s^* &= \sigma\mu\frac{\beta\Theta-\nu(\gamma+\mu)}{(\gamma+\mu)(\beta+\mu)\Theta}, & I_a^* &= (1-\sigma)\mu\frac{\beta\Theta-\nu(\gamma+\mu)}{(\gamma+\mu)(\beta+\mu)\Theta}, \end{aligned}$$

which lies inside the positive orthant $\mathbb{R}^4_+$ if and only if the basic reproduction number

$$\text{(4)}\qquad \mathcal{R}_0 = \frac{\beta\Theta}{\nu(\gamma+\mu)} > 1\ .$$

In the algebraic manipulations inside this section, we use the identities

$$\text{(5)}\qquad \theta_s I_s^* + \theta_a I_a^* = \frac{\nu V^*}{1-V^*}, \qquad \frac{1}{1-V^*} = \mathcal{R}_0 S^*.$$

The local asymptotic stability of the endemic equilibrium $\mathcal{E}^*$ is characterised in

Proposition 1. *Let $\mathcal{R}_0 > 1$. The endemic equilibrium $\mathcal{E}^*$ is locally asymptotically stable. It is a spiral when $\mu \approx 0$.*

Proof. The Jacobian matrix of (2) evaluated at the endemic equilibrium $\mathcal{E}^*$ is

$$\mathbb{J} = \begin{bmatrix} -\beta V^* - \mu & 0 & 0 & -\beta S^* \\ \sigma\beta V^* & -(\gamma+\mu) & 0 & \sigma\beta S^* \\ (1-\sigma)\beta V^* & 0 & -(\gamma+\mu) & (1-\sigma)\beta S^* \\ 0 & \theta_s(1-V^*) & \theta_a(1-V^*) & -\nu\mathcal{R}_0 S^* \end{bmatrix}.$$

The characteristic polynomial of $\mathbb{J}$ factors as $P(\lambda) = \det(\lambda\mathbb{I} - \mathbb{J}) = (\lambda+\gamma+\mu)Q(\lambda)$, with $Q(\lambda) = \lambda^3 + q_1\lambda^2 + q_2\lambda + q_3$. The polynomial Q has coefficients

$$\begin{aligned} q_1 &= \gamma + 2\mu + \nu\mathcal{R}_0 S^* + \beta V^*, \\ q_2 &= (\gamma+2\mu)\nu\mathcal{R}_0 S^* + (\gamma+\mu)(\beta V^* + \mu) + \beta(\mathcal{R}_0 - 1)\nu S^* V^*, \\ q_3 &= (\beta V^* + \mu)\gamma\nu\mathcal{R}_0 S^* + \mu^2\nu\mathcal{R}_0 + \beta\mu\nu(\mathcal{R}_0 - 1)S^* V^* . \end{aligned}$$

One sees immediately that $\mathcal{R}_0 > 1$ implies $Q(\lambda) > 0$ for all $\lambda > 0$. Furthermore, $q_1 q_2 > q_3$ holds, so the Routh-Hurwitz criterion implies that all roots of Q lie in the left half of the complex plane. Hence, all roots of P have a negative real part.

The discriminant Δ of Q can be rewritten as a polynomial in μ, $\Delta(\mu)$, whereby we ignore the terms μ in the sums $\beta+\mu, \gamma+\mu$ due to being negligible ($\beta \gg \mu, \gamma \gg \mu$). Whenever $\Delta < 0$, Cardano's formula tells us the cubic $Q(\lambda)$ has a pair of imaginary roots. Gathering terms of $\mathcal{O}(\mu)$ in $\Delta(\mu)$ we have

$$\Delta(\mu) = -\frac{\mathcal{R}_0^2\gamma^6\nu^4}{108\Theta^2(\beta+\mu)^2}\left(1 - \frac{\mathcal{R}_0\nu^2}{\Theta(\beta+\mu)}\right)^2 + \mathcal{O}(\mu),$$

so $\lim_{\mu\to 0}\Delta(\mu) < 0$, which completes the proof. □

The global asymptotic stability of the equilibria depending on the magnitude of $\mathcal{R}_0$ is established in

Proposition 2. *If $\mathcal{R}_0 \le 1$, the disease-free equilibrium $\mathcal{E}_0$ is globally asymptotically stable. If $\mathcal{R}_0 > 1$, the endemic equilibrium $\mathcal{E}^*$ is globally asymptotically stable.*

Proof. First we consider the case $\mathcal{R}_0 \le 1$. Similar to [8], we set as a candidate for a Lyapunov function

$$\mathcal{L}(t) = S(t) - \ln S(t) + \frac{\theta_s}{\Theta}I_s(t) + \frac{\theta_a}{\Theta}I_a(t) + \frac{\beta}{\nu}V(t).$$

Differentiating $\mathcal{L}$ with respect to t gives

$$\begin{aligned} \dot{\mathcal{L}} &= \left(1 - \frac{1}{S}\right)\dot{S} + \frac{\theta_s}{\Theta}\dot{I}_s + \frac{\theta_a}{\Theta}\dot{I}_a + \frac{\beta}{\nu}\dot{V} \\ &= -\mu\frac{(1-S)^2}{S} + (\theta_s I_s + \theta_a I_a)\left(\frac{\beta}{\nu} - \frac{\gamma+\mu}{\Theta}\right) - \frac{\beta}{\nu}(\theta_s I_s + \theta_a I_a)V. \end{aligned} \tag{6}$$

Since $\mathcal{R}_0 \le 1$, $\frac{\beta}{\nu} - \frac{\gamma+\mu}{\Theta} \le 0$, we have $\dot{\mathcal{L}} < 0$ unless $V = 0, S = 1, I_s = I_a = 0$. Thus, the disease-free equilibrium is globally asymptotically stable in the case $\mathcal{R}_0 \le 1$.

Next we consider the case $\mathcal{R}_0 > 1$ and show that $\mathcal{E}^*$ is globally asymptotically stable.

We set as a candidate for a Lyapunov function

$$\mathcal{L}(t) = S(t) - S^* - S^* \ln \frac{S(t)}{S^*} + \frac{\beta S^*}{\nu}\left(V(t) - V^* - V^* \ln \frac{V(t)}{V^*}\right)$$
$$+ \frac{1}{\Theta}\left(\theta_s I_s(t) + \theta_a I_a(t) - (\theta_s I_s^* + \theta_a I_a^*)\right) - \frac{\theta_s I_s^* + \theta_a I_a^*}{\Theta} \ln \frac{\theta_s I_s(t) + \theta_a I_a(t)}{\theta_s I_s^* + \theta_a I_a^*},$$

where S^*, I_s^*, I_a^*, V^* are given by (3). Differentiating with respect to t gives

$$\begin{aligned}\dot{\mathcal{L}} = & \left(1 - \frac{S^*}{S}\right)\dot{S} + \frac{1}{\Theta}\left(\theta_s - \frac{\theta_s(\theta_s I_s^* + \theta_a I_a^*)}{\theta_s I_s + \theta_a I_a}\right)\dot{I}_s \\ & + \frac{1}{\Theta}\left(\theta_a - \frac{\theta_a(\theta_s I_s^* + \theta_a I_a^*)}{\theta_s I_s + \theta_a I_a}\right)\dot{I}_a + \frac{\beta S^*}{\nu}\left(1 - \frac{V^*}{V}\right)\dot{V}\,.\end{aligned} \tag{7}$$

After some algebraic transformations, we arrive to

$$\begin{aligned}\dot{\mathcal{L}} = & \mu(1-S) - \mu(1-S)\frac{S^*}{S} + \beta S^* V - \beta S V \\ & + \beta S V - \frac{\gamma+\mu}{\Theta}(\theta_s I_s + \theta_a I_a) - \frac{\beta S V(\theta_s I_s^* + \theta_a I_a^*)}{\theta_s I_s + \theta_a I_a} + \frac{\gamma+\mu}{\Theta}(\theta_s I_s^* + \theta_a I_a^*) \\ & + \frac{\beta S^*}{\nu}(\theta_s I_s + \theta_a I_a)\left(1 - V + V^* - \frac{V^*}{V}\right) - \beta S^* V + \beta S^* V^*.\end{aligned} \tag{8}$$

Adding and subtracting $\frac{\beta S^*}{\nu}(\theta_s I_s + \theta_a I_a)V^*$ in (8) and using the identities

$$\Theta \beta S^* V^* = (\gamma+\mu)(\theta_s I_s^* + \theta_a I_a^*), \quad \beta S^* V^* = \mu(1 - S^*)$$

gives

$$\begin{aligned}\dot{\mathcal{L}} = & \mu\left(3 - S - S^* - \frac{S^*}{S}\right) + \frac{\beta S^*}{\nu}(\theta_s I_s + \theta_a I_a)\left(2V^* - V - \frac{V^*}{V}\right) \\ & - \frac{\beta S V(\theta_s I_s^* + \theta_a I_a^*)}{\theta_s I_s + \theta_a I_a} + \left(\frac{\beta S^*}{\nu}(1 - V^*) - \frac{\gamma+\mu}{\Theta}\right)(\theta_s I_s + \theta_a I_a)\,.\end{aligned} \tag{9}$$

The last summand in (9) vanishes due to (5).

The resulting derivative of $\mathcal{L}$ is then identical in form to the derivative of the Lyapunov function suggested in [8]. Note we can bound the first and thr second summands in (9) using the inequality $x^2 + y^2 \geq 2xy$ applied to $x = \sqrt{S}, y = \frac{S^*}{\sqrt{S}}$ and $x = \sqrt{V}, y = \frac{V^*}{\sqrt{V}}$, respectively. Thus,

$$\dot{\mathcal{L}} \leq 3\mu(1-S^*) - \mu(1-S^*)\frac{S^*}{S} - \frac{\beta S^*}{\nu}(\theta_s I_s + \theta_a I_a)\frac{V^*}{V}(1-V^*) - \frac{\beta S V(\theta_s I_s^* + \theta_a I_a^*)}{\theta_s I_s + \theta_a I_a} \tag{10}$$

and the inequality in (10) is strict unless $V = V^*$, $S = S^*$. Applying the arithmetic-geometric mean inequality to the three summands on the right-hand side of (10) and using (4), (5) we obtain

$$\dot{\mathcal{L}} \leq 3\mu(1-S^*) - 3\sqrt[3]{\mu\frac{\beta^2}{\nu}(1-S^*)S^{*2}V^*(1-V^*)(\theta_s I_s^* + \theta_a I_a^*)} = 0.$$

The equality $\dot{\mathcal{L}} < 0$ is strict unless $x = y$, or $V = V^*$, $S = S^*$.

We now examine the case $V = V^*$, $S = S^*$. Applying again the inequality

$x^2 + y^2 \geq 2xy$ to $x = \sqrt{\theta_s I_s + \theta_a I_a}, y = \dfrac{\theta_s I_s^* + \theta_a I_a^*}{\sqrt{\theta_s I_s + \theta_a I_a}}$ we have

$$\dot{\mathcal{L}} = 2\mu(1 - S^*) - \frac{\gamma + \mu}{\Theta}\left(\theta_s I_s + \theta_a I_a + \frac{(\theta_s I_s^* + \theta_a I_a^*)^2}{\theta_s I_s + \theta_a I_a}\right)$$
$$\leq 2\mu(1 - S^*) - 2\frac{\gamma + \mu}{\Theta}(\theta_s I_s^* + \theta_a I_a^*) \leq 0,$$

with equality holding only in the set

$$\mathcal{X} = \{z \in \mathbb{R}_+^4 \mid \dot{\mathcal{L}}(z) = 0\} = \{(S^*, I_s, I_a, V^*) \mid \theta_s I_s + \theta_a I_a = \theta_s I_s^* + \theta_a I_a^*\}.$$

Observe that the only invariant set under the flow defined by (2) for all $t \in (-\infty, +\infty)$, which is contained in $\mathcal{X}$, is the endemic equilibrium $\mathcal{E}^* = (S^*, I_s^*, I_a^*, V^*)$. Indeed, the flow (2) restricted to $\mathcal{X}$ is given by

$$\begin{cases} \dot{I}_s &= \sigma\beta S^* V^* - (\gamma + \mu) I_s \\ \dot{I}_a &= (1 - \sigma)\beta S^* V^* - (\gamma + \mu) I_a \ . \end{cases} \tag{11}$$

The equations (11) are uncoupled and linear, and have a solution for all $t \in (-\infty, +\infty)$. The set $\mathcal{E}^*$ is the only invariant subset of $\mathcal{X}$ for all $t \in (-\infty, +\infty)$. Krasovskii–LaSalle's invariance principle [5] implies that every solution of (2) with initial data in Ω's interior converges to $\mathcal{E}^*$. $\square$

Conclusion. We investigate the asymptotic behaviour of the model (2) depending on the magnitude of the basic reproduction number $\mathcal{R}_0$. The endemic equilibrium is globally asymptotically stable if $\mathcal{R}_0 > 1$, and is a spiral if the natural removal rate of the human population is small. Thus, the asymptotic dynamics is similar to the case of models without distinction between symptomatic and asymptomatic carriers.

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АНАЛИЗ НА УСТОЙЧИВОСТТА НА МОДЕЛ НА ВЕКТОРНО-ПРЕДАВАНА БОЛЕСТ С БЕЗСИМПТОМЕН КЛАС

Петър Рашков

Представен е модел на векторно-предавана болест[1] със симптомни и безсимптомни класове, описан със система обикновени диференциални уравнения. Анализират се локалната и глобалната устойчивост на равновесията на елиминирана и на ендемична болест с помощта на подходящо избрани функции на Ляпунов.

[1]За читателите, които свързват *вектор* само с математическото понятие: болест, при която причинителите се предават с кръвосмучещи членестоноги, наречени *вектори.* (бел. ред.)