

Global Stability for a Virus Dynamics
Model with Nonlinear Incidence of
Infection and Removal

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$$(S) \quad \begin{cases} S' = n(S) - c(S)f(V), \\ E' = c(S)f(V) - c_1 i(E), \\ I' = c_2 i(E) - c_3 p(I), \\ V' = c_4 p(I) - r(V). \end{cases}$$

Previous related works

S. Bonhoeffer, R. M. May, G. M. Shaw, and M. A. Nowak (1997)

A. S. Perelson and P. W. Nelson (1999)

M. Nowak and R. M. May (2000)

A. Korobeinikov (2004)

Hypotheses

c, f, i, p, r, n -real locally Lipschitz functions on $[0, \infty)$,

$$\begin{aligned} c(0) = f(0) = i(0) = p(0) = r(0) = 0, \\ c(t), f(t), i(t), p(t), r(t) > 0 \quad \text{for } t > 0. \end{aligned}$$

$$(U) \quad n(0) > 0 \text{ and } n(S) = 0 \Rightarrow S = S_0$$

$$(S) \quad \begin{aligned} (n(S) - n(S^0))(S - S^0) < 0 & \quad \text{for } S \neq S^0, \\ (c(S) - c(S^0))(S - S^0) > 0 & \quad \text{for } S \neq S^0 \end{aligned}$$

$$(D) \quad \int_{0+}^1 \frac{1}{\varphi(\tau)} d\tau = +\infty \quad \text{for all } \varphi \in \{c, f, i, p\}.$$

There are $k_n, k_i, k_p, k_r, \tilde{k}_n > 0$ such that

$$(G) \quad \begin{aligned} n(S) &\leq \tilde{k}_n - k_n S & \text{for } S \geq 0, \\ i(E) &\geq k_i E & \text{for } E \geq 0, \\ p(I) &\geq k_p I & \text{for } I \geq 0, \\ r(V) &\geq k_r V & \text{for } V \geq 0. \end{aligned}$$

Stability of the disease-free equilibrium

First Lyapunov functional

$$U_1(S, E, I, V) = \int_{S_0}^S \frac{c(\tau) - c(S_0)}{c(\tau)} d\tau + E + \frac{c_1}{c_2} I + \frac{c_1 c_3}{c_2 c_4} V.$$

$$\dot{U}_1(S, E, I, V) = \left(1 - \frac{c(S_0)}{c(S)}\right) (n(S) - n(S_0)) + \left[c(S_0) f(V) - \frac{c_1 c_3}{c_2 c_4} r(V) \right].$$

Local stability result

Suppose that $\exists V_R > 0$ such that

$$c(S_0) \frac{f(V) c_2 c_4}{r(V) c_1 c_3} \leq 1 \quad \text{for } V \in (0, V_R),$$

and let $m = V(S_0, 0, 0, V_R)$. Then $(S_0, 0, 0, 0)$ is LAS and its domain of attraction includes

$$M_m = \{(S, E, I, V); U_1(S, E, I, V) < m\}.$$

Second Lyapunov functional

$$U_2(S, E, I, V) = E + \frac{c_1}{c_2}I + \frac{c_1 c_3}{c_2 c_4}V.$$

Persistence result

Assume that there is a number $V_R > 0$ such that

$$c(S_0) \frac{f(V) c_2 c_4}{r(V) c_1 c_3} > 1 \quad \text{for } V \in (0, V_R).$$

Then (S) is uniformly persistent and the disease-free equilibrium $(S_0, 0, 0, 0)$ is unstable, with the positive semiaxis $[OS$ as its stable variety.

Suppose that f/r is nonincreasing on $(0, \infty)$.

Basic reproduction number

$$R_0 = c(S_0) \frac{c_2 c_4}{c_1 c_3} \lim_{V \rightarrow 0} \frac{f(V)}{r(V)}$$

If $f, g \in C^1$, then

$$R_0 = c(S_0) \frac{c_2 c_4}{c_1 c_3} \lim_{V \rightarrow 0} \frac{f'(V)}{r'(V)}$$

Global stability result

Suppose that f/r is nonincreasing on $(0, \infty)$.

- 1. If $R_0 \leq 1$, then the disease-free equilibrium $(S_0, 0, 0, 0)$ is GAS.*
- 2. If $R_0 > 1$, then (S) is uniformly persistent and the disease-free equilibrium $(S_0, 0, 0, 0)$ is unstable, with the positive semiaxis $[OS$ as its stable variety.*

The endemic equilibrium

- (f/r) f/r nonincreasing on $(0, \infty)$
- (M) c, f, i, p strictly increasing on $[0, \infty)$,
 n strictly decreasing on $[0, \infty)$
- (LIM) $\lim_{x \rightarrow \infty} i(x) = \lim_{x \rightarrow \infty} p(x) = +\infty$

The existence of the endemic equilibrium

Assume that conditions (f/r), (M) and (LIM) are satisfied. Then there is a unique positive endemic equilibrium (S^, E^*, I^*, V^*) of (S) if and only if $R_0 > 1$, where R_0 is the basic reproduction number for the system (S).*

(P)

$$\begin{aligned}(c(S) - c(S^*)) (S - S^*) &> 0 && \text{for } S \neq S^*, S \geq 0, \\(f(V) - f(V^*)) (V - V^*) &> 0 && \text{for } V \neq V^*, V \geq 0, \\(i(E) - f(E^*)) (E - E^*) &> 0 && \text{for } E \neq E^*, E \geq 0, \\(p(I) - p(I^*)) (I - I^*) &> 0 && \text{for } I \neq I^*, I \geq 0\end{aligned}$$

and

(N)

$$(n(S) - n(S^*)) (S - S^*) \leq 0 \quad \text{for all } S \geq 0.$$

The third Lyapunov functional

$$\begin{aligned}U_3(S, E, I, V) &= \int_{S^*}^S \frac{c(\tau) - c(S^*)}{c(\tau)} d\tau \\&+ \int_{E^*}^E \frac{i(\tau) - i(E^*)}{i(\tau)} d\tau + \frac{c_1}{c_2} \int_{I^*}^I \frac{p(\tau) - p(I^*)}{p(\tau)} d\tau \\&+ \frac{c_1 c_3}{c_2 c_4} \int_{V^*}^V \frac{f(\tau) - f(V^*)}{f(\tau)} d\tau.\end{aligned}$$

Local stability result

Assume that the sign conditions (P) and (N) are satisfied and there are V_L and V_R such that

$$\begin{aligned} \frac{f(V)}{r(V)} &\leq \frac{f(V^*)}{r(V^*)} && \text{for } V^* \leq V < V_R, \\ \frac{f(V)}{r(V)} &\geq \frac{f(V^*)}{r(V^*)} && \text{for } V_L < V \leq V^*. \end{aligned}$$

Define

$$m = \min (U_3(S^*, E^*, I^*, V_L), U_3(S^*, E^*, I^*, V_R)).$$

Then (S^*, E^*, I^*, V^*) is LAS and its domain of attraction includes the set

$$M_m = \{(S, E, I, V); U_3(S, E, I, V) < m\}.$$

$$(B) \quad \lim_{y \rightarrow \infty} \left(y - \varphi(x) \int_x^y \frac{1}{\varphi(\tau)} d\tau \right) = +\infty$$

for all $x > 0$ and $\varphi \in \{c, f, i, p\}$.

(satisfied if $\lim_{y \rightarrow \infty} \varphi(y) = +\infty$ or
 $\varphi(x) = x^p / (1 + ax^p), 0 < p \leq 1$)

$$(D') \quad \int_{0+}^1 \frac{1}{\varphi(\tau)} d\tau = +\infty \quad \text{for some } \varphi \in \{f, i, p\}.$$

Global stability result

Suppose that f/r is nonincreasing on $(0, \infty)$ and conditions (M), (LIM), (B) and (D') are satisfied.

- 1. If $R_0 \leq 1$, then the disease-free equilibrium is GAS.*
- 2. If $R_0 > 1$, then the system (S) admits a unique positive endemic equilibrium which is GAS. The disease-free equilibrium is unstable, with the positive semiaxis $[OS$ as its stable variety.*

(The “stable” variety of the endemic equilibrium actually excludes $[OS$.)

$$(RS) \quad \begin{cases} S' = b - mS - \beta S \frac{V^p}{1 + aV^p}, \\ E' = \beta S \frac{V^p}{1 + a_1V^p} - c_1E, \\ I' = c_2E - c_3I, \\ V' = c_4I - kV^\gamma, \end{cases}$$

for $b, m, \beta, k > 0$, $a \geq 0$ and $0 < p \leq \gamma \leq 1$.

Here, $c(S) = \beta S$, $f(V) = V^p/(1 + aV^p)$, $i(E) = E$, $p(I) = I$, $r(V) = V^\gamma$, $n(S) = b - mS$.

The stability analysis

1. If $p < \gamma$, the basic reproduction number R_0 of the system (RS) is $+\infty$. The system (RS) admits a positive endemic equilibrium which is GAS. The disease-free equilibrium is unstable, with the positive semiaxis $[OS$ as its stable variety.
2. If $p = \gamma$, the basic reproduction number R_0 of the system (RS) is

$$R_0 = \frac{\beta b c_2 c_4}{m c_1 c_3 k}.$$

In this case, if $R_0 \leq 1$, then the disease-free equilibrium is GAS, while if $R_0 > 1$ the system (RS) admits a positive endemic equilibrium which is GAS. The disease-free equilibrium is unstable with the positive semiaxis $[OS$ as its stable variety.

(The “stable” variety of the endemic equilibrium actually excludes $[OS$.)