Global asymptotic stability for a class of epidemic models with delays

Yoichi Enatsu[1]
(Joint work with Yukihiko Nakata[1] and Yoshiaki Muroya[2])

[1]International Research Training Group 1529
Department of Pure and Applied Mathematics, Waseda University

[2]Department of Mathematics, Waseda University

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Outline

Keywords

Epidemiological concern - the spread of disease in time (e.g., measles, H5N1 influenza, etc.).

- Basic reproduction number
  Threshold value - the infectious disease will die out or persists?
- Time delay effect
  Incubation (Latent) period - caused by a vector
- Incidence rate of the diseases

Basic SIR model

Consider the following model.

$$\begin{cases} S'(t) = B - \beta S(t)I(t) - \mu S(t), \\ I'(t) = \beta S(t)I(t) - (\mu+\gamma)I(t), \\ R'(t) = \gamma I(t) - \mu R(t), \ t \geq 0, \\ S(0) > 0, \ I(0) > 0, \ R(0) > 0. \end{cases} \tag{1.1}$$

B: birth rate, β: contact rate (infection force), μ: death rate, γ: recovery rate

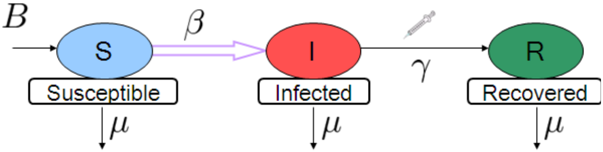


Figure: Diagram of disease transmission of system (1.1)

Basic properties

$$\begin{cases} S'(t) = B - \beta S(t)I(t) - \mu S(t), \\ I'(t) = \beta S(t)I(t) - (\mu+\gamma)I(t), \\ R'(t) = \gamma I(t) - \mu R(t). \end{cases}$$

Basic reproduction number $R_0 = \dfrac{B\beta}{\mu(\mu+\gamma)}$

R_0: the expected number of secondary cases by a unit of infected individual

	DFE: $E_0 = (S_0, 0, 0)$	**EE:** $E_* = (S_*, I_*, R_*)$
$R_0 < 1$	**GAS** (=globally asymptotically stable)*	**(no existence)**
$R_0 > 1$	**unstable**	**GAS**

Note: DFE = Disease-free equilibrium, EE = Endemic equilibrium

*globally asymptotically stable = uniformly stable + globally attractive

Time delay effect

$$\begin{cases} S'(t) = B - \beta S(t)I(t) - \mu S(t), \\ I'(t) = \beta S(t)I(t) - (\mu + \gamma)I(t), \\ R'(t) = \gamma I(t) - \mu R(t). \end{cases}$$

$\Downarrow$ Time delay effect

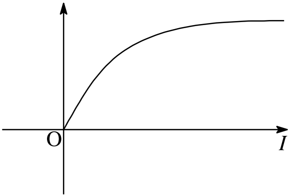
Cooke (1979), Beretta *et al.* (1997), Takeuchi *et al.* (2002), etc.

$$\begin{cases} S'(t) = B - \beta S(t)I(t-\tau) - \mu S(t), \\ I'(t) = \beta S(t)I(t-\tau) - (\mu + \gamma)I(t), \\ R'(t) = \gamma I(t) - \mu R(t), \ \tau \geq 0. \end{cases}$$

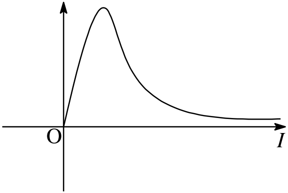
Incidence rate

Examples of nonlinear incidence rates:

- Saturation effect [Cholera, Holling functional response]
  Capasso and Serio (1976), Xu and Ma (2009), etc.
  (e.g., $G_1(I) \equiv I/(1+\alpha I^p)$, $p \leq 1$)
- Psychological effect [SARS pandemic]
  Xiao and Ruan (2007), Huo and Ma (2010), etc.
  (e.g., $G_2(I) \equiv I/(1+\alpha I^p)$, $p > 1$)



Saturated effect



psychological effect

SIRS model

Huo and Ma (2010), psychological effect [SARS]

$$\begin{cases} S'(t) = b - dS(t) - k\mathrm{e}^{-d\tau}S(t)\dfrac{I(t-\tau)}{1+\alpha I^2(t-\tau)} + \gamma R(t), \\ I'(t) = k\mathrm{e}^{-d\tau}S(t)\dfrac{I(t-\tau)}{1+\alpha I^2(t-\tau)} - (d+\mu)I(t), \\ R'(t) = \mu I(t) - (d+\gamma)R(t),\ \tau \geq 0,\ t \geq 0, \end{cases} \tag{2.1}$$

parameter setting

b: recruitment rate d: natural death rate μ: natural recovery rate

$\frac{k\mathrm{e}^{-d\tau}S(t)I(t-\tau)}{1+\alpha I^2(t-\tau)}$: infection force

γ: rate at which recovered individuals lose immunity

α: parameter which measures the psychological effect

Note: SIRS = SIR + immunity lost

SIRS model

Huo and Ma (2010), psychological effect [SARS]

$$\begin{cases} S'(t) = b - dS(t) - k\mathrm{e}^{-d\tau} S(t) \dfrac{I(t-\tau)}{1+\alpha I^2(t-\tau)} + \gamma R(t), \\ I'(t) = k\mathrm{e}^{-d\tau} S(t) \dfrac{I(t-\tau)}{1+\alpha I^2(t-\tau)} - (d+\mu)I(t), \\ R'(t) = \mu I(t) - (d+\gamma)R(t), \ \tau \geq 0, \ t \geq 0, \end{cases}$$

with initial conditions:

$$\begin{cases} S(\theta) = \phi_1(\theta), \ \ I(\theta) = \phi_2(\theta), \ \ R(\theta) = \phi_3(\theta), \\ \phi_i(\theta) \geq 0, \ \ \theta \in [-\tau, 0], \ \phi_i(0) > 0, \ \ i = 1, 2, 3, \\ (\phi_1(\theta), \phi_2(\theta), \phi_3(\theta)) \in C([-\tau, 0], \mathbb{R}^3_{+0}), \end{cases}$$

where $\mathbb{R}^3_{+0} = \{(x_1, x_2, x_3) : x_i \geq 0, \ i = 1, 2, 3\}$.

Known results and a new result

Basic properties:

Basic reproduction number $R_0 = \dfrac{bk\exp(-d\tau)}{d(d+\mu)}$

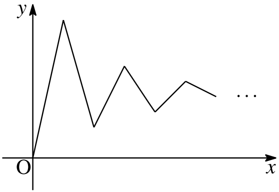
	DFE $E_0 = (S_0, 0, 0)$	EE $E_* = (S_*, I_*, R_*)$	
$R_0 < 1$	**GAS**	**(no existence)**	
$R_0 > 1$	**unstable**	$\tau = 0$	**GAS** **Xiao and Ruan (2007)** **Dulac functional technique**
		$\tau \geq 0$	**LAS*[+permanence]** **Huo and Ma (2010)**
			GAS(+under some conditions) **NEW RESULT** **Monotone iterative technique**

Our result partially solves the conjecture in Huo and Ma (2010).

*LAS = locally asymptotically stable

Outline of monotone iterative technique

Step 1	:	derivation of reduced system
Step 2	:	permanence
Step 3	:	formulation of the iterate map



Step 1: derivation of reduced system

Lemma 1 (invariant set)

For system (2.1), it holds that

$$\lim_{t\to+\infty}(S(t)+I(t)+R(t))=\frac{b}{d}. \tag{2.2}$$

$\rightarrow$ the limit set of system (2.1) in the first octant of $\mathbb{R}^3$ locates on the plane $S(t)+I(t)+R(t)=b/d$.

Reduced system of (2.1):

$$\begin{cases} I'(t)=k\mathrm{e}^{-d\tau}\left(\frac{b}{d}-I(t)-R(t)\right)\frac{I(t-\tau)}{1+\alpha I^2(t-\tau)}-(d+\mu)I(t), \\ R'(t)=\mu I(t)-(d+\gamma)R(t),\ \tau\geq 0,\ t\geq 0, \end{cases}$$

Step 2: permanence

Reduced system of (2.1):

$$\begin{cases} I'(t) = k\mathrm{e}^{-d\tau}\left(\frac{b}{d} - I(t) - R(t)\right)\frac{I(t-\tau)}{1+\alpha I^2(t-\tau)} - (d+\mu)I(t), \\ R'(t) = \mu I(t) - (d+\gamma)R(t), \ \tau \geq 0, \ t \geq 0, \end{cases}$$

Lemma 2 (permanence)

(Huo and Ma (2010)) There exists a positive constants v such that for any initial conditions of system (2.1),

$$\limsup_{t\to+\infty} I(t) \equiv \overline{I} \leq \frac{b}{d}, \ \limsup_{t\to+\infty} R(t) \equiv \overline{R} \leq \frac{b}{d},$$
$$\liminf_{t\to+\infty} I(t) \equiv \underline{I} \geq v, \ \liminf_{t\to+\infty} R(t) \equiv \underline{R} \geq \frac{\mu}{d+\gamma}v.$$

Step 3: formulation of the iterate map

Note: $G(I) = I/(1+\alpha I^2)$, $\bar{G}(I_1, I_2) = \max_{I_1 \le I \le I_2} G(I)$.

Key lemma 1

$$\frac{b}{d} - \underline{I} - \overline{R} > 0, \quad \text{and} \quad \frac{b}{d} - \overline{I} - \underline{R} > 0. \tag{2.3}$$

Key lemma 2 (Modified iterate scheme)

For the reduced system of (2.1), it holds that

$$\begin{cases} 0 \le k\exp(-d\tau)\left(\frac{b}{d} - \overline{I} - \underline{R}\right)\bar{G}(\underline{I}, \overline{I}) - (d+\mu)\overline{I}, \\ 0 \ge k\exp(-d\tau)\left(\frac{b}{d} - \underline{I} - \overline{R}\right)G(\underline{I}) - (d+\mu)\underline{I}. \end{cases} \tag{2.4}$$

$$\begin{cases} 0 = ke^{-d\tau}\left(\frac{b}{d} - \overline{I}_n - \frac{\mu}{d+\gamma}\underline{I}_{n-1}\right)\max\limits_{\underline{I}_{n-1}\leq I\leq \overline{I}_n} G(I) - (d+\mu)\overline{I}_n, \\ 0 = ke^{-d\tau}\left(\frac{b}{d} - \underline{I}_n - \frac{\mu}{d+\gamma}\overline{I}_n\right)G(\underline{I}_n) - (d+\mu)\underline{I}_n, \ \ n \geq 1. \end{cases}$$

$$\Downarrow$$

$$\left(1 + \frac{d+\mu}{ke^{-d\tau}}\frac{\overline{h}(\underline{I}_{n-1}, \overline{I}_n) - h(\underline{I}_n)}{\overline{I}_n - \underline{I}_n}\right)(\overline{I}_n - \underline{I}_n) = \frac{\mu}{d+\gamma}(\overline{I}_n - \underline{I}_{n-1}),$$

$$\Downarrow$$

$$\begin{cases} \overline{I}_n - \underline{I}_n = \dfrac{\frac{\mu}{d+\gamma}}{1 + \frac{d+\mu}{ke^{-d\tau}}\frac{\overline{h}(\underline{I}_{n-1}, \overline{I}_n) - h(\underline{I}_n)}{\overline{I}_n - \underline{I}_n}}(\overline{I}_n - \underline{I}_{n-1}), \\ h(I) = I/G(I), \ \overline{h}(I_1, I_2) = I_2/\max_{I_1\leq I\leq I_2} G(I), \quad n \geq 1. \end{cases}$$

Sketch of an iterative scheme

$$\overline{I}_n - \underline{I}_n = \frac{\dfrac{\mu}{d+\gamma}}{1 + \dfrac{d+\mu}{k\mathrm{e}^{-d\tau}} \dfrac{\overline{h}(\underline{I}_{n-1}, \overline{I}_n) - h(\underline{I}_n)}{\overline{I}_n - \underline{I}_n}} (\overline{I}_n - \underline{I}_{n-1}).$$

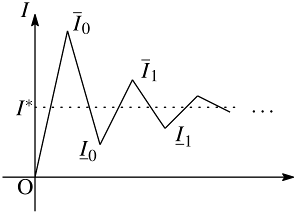
Sequences with respect to upper limits and lower limits:

$$\underline{I}_0 \le \underline{I} \le \overline{I} \le \overline{I}_0$$

$$\underline{I}_1 \le \underline{I} \le \overline{I} \le \overline{I}_1$$

$$\underline{I}_2 \le \underline{I} \le \overline{I} \le \overline{I}_2$$

$$\cdots$$



Question: When do the sequences $\{\overline{I}_n\}_{n=0}^{\infty}$ and $\{\underline{I}_n\}_{n=0}^{\infty}$ converge to I^*? $\rightarrow$ Answer for the GAS of EE E_*.

Main Theorem (monotone iterative technique)

Theorem 1

Assume that $R_0 > 1$, $I^* \leq \hat{I} \equiv \frac{1}{\sqrt{\alpha}}$ *and for (2.5), it holds*

$$\frac{\frac{\mu}{d+\gamma}}{1 + \frac{d+\mu}{k\exp(-d\tau)} \frac{\bar{h}(\underline{I}_0, \bar{I}_1) - h(\underline{I}_1)}{\bar{I}_1 - \underline{I}_1}} \leq 1, \text{ for } \underline{I}_1 < \bar{I}_1, \qquad (2.5)$$

and suppose that either $\sigma \leq 1$ *or*

$$\sigma > 1, \text{ and } c > a(I^* - \underline{I}_0) \text{ or } c \geq (\sigma - 1) + a(\hat{I} - I^*). \qquad (2.6)$$

Then, EE $E_* = (S^*, I^*, R^*)$ *of system (2.1) is GAS.*

Simulations for the case $R_0 < 1$ and $R_0 > 1$ ($p = 2$)

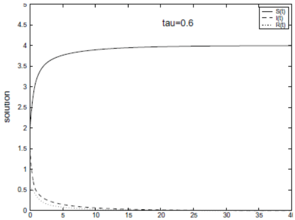


Figure: $\tau = 0.6$, $b = 4$, $k = 0.8$, $d = \alpha = \gamma = \mu = 1$ ($i.e.$ $R_0 < 1$).

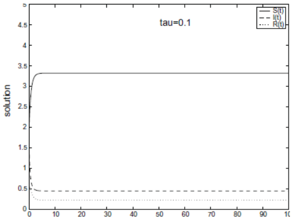


Figure: $\tau = 0.1$, $b = 4$, $k = 0.8$, $d = \alpha = \gamma = \mu = 1$ ($i.e.$ $R_0 > 1$).

Huo and Ma (2010) say:

"$\cdots$, *we give an interesting open problem: whether we can also obtain that EE E_* is GAS when $R_0 > 1$.*"

$\Downarrow$

Our results show that E_* is GAS for the above parameter case.

Application: improved result ($p = 1$)

Xu and Ma (2009), $\frac{\beta S(t)I(t-\tau)}{1+\alpha I(t-\tau)}$: saturated effect

$$\begin{cases} S'(t) = b - dS(t) - \beta S(t)\dfrac{I(t-\tau)}{1+\alpha I(t-\tau)} + \gamma R(t), \\ I'(t) = \beta S(t)\dfrac{I(t-\tau)}{1+\alpha I(t-\tau)} - (d+\mu)I(t), \\ R'(t) = \mu I(t) - (d+\gamma)R(t), \ \tau \geq 0, \ t \geq 0. \end{cases} \tag{2.7}$$

GAS condition:

	DFE: E_0	**EE:** $E_* \ (R_0 > 1)$
Xu and Ma (2009)	$R_0 < 1$	$\{\alpha(d+\mu) - \beta\}(d+\gamma) > \beta\mu$
NEW RESULT		$\{\alpha(d+\mu) + \beta\}(d+\gamma) > \beta\mu$

Difference: iterate scheme!

Difference between the iterate schemes

Key Lemma 2 (Modified iterate scheme)

For the reduced system of (2.1), it holds that

$$\begin{cases} 0 \leq k\exp(-d\tau)\left(\dfrac{b}{d} - \overline{I} - \underline{R}\right)\bar{G}(\underline{I}, \overline{I}) - (d+\mu)\overline{I}, \\ 0 \geq k\exp(-d\tau)\left(\dfrac{b}{d} - \underline{I} - \overline{R}\right)G(\underline{I}) - (d+\mu)\underline{I}. \end{cases}$$

Xu and Ma (2009) -type scheme:

$$\begin{cases} 0 \leq k\exp(-d\tau)\left(\dfrac{b}{d} - \underline{I} - \underline{R}\right)\bar{G}(\underline{I}, \underline{I}) - (d+\mu)\underline{I} \\ 0 \geq k\exp(-d\tau)\left(\dfrac{b}{d} - \overline{I} - \overline{R}\right)G(\overline{I}) - (d+\mu)\overline{I}. \end{cases}$$

Concluding remarks

We established a new iterate scheme which enables us to

- partially solve the conjecture in Huo and Ma (2010)
- improve the result in Xu and Ma (2009)

concerning GAS of an endemic equilibrium (EE) for an SIRS models with a delay and nonlinear incidence rate.

Some open problems are still left concerning GAS of EE E_* for $R_0 > 1$ on a class of epidemic models (even with a bilinear incidence rate).

Related topics:

SIRS model with temporary immunity, SIS model with disease-induced death rate, Discrete SIR model (with Mickens' approximation), etc.

Thank you for your kind attention.

Vielen Dank.

ご清聴ありがとうございました。

江夏 (Enatsu)　洋一 (Yoichi)

Contraction of iterate maps

Key Lemma 3 (Contraction of $\{\underline{I}_n\}_{n=1}^{\infty}$ and $\{\overline{I}_n\}_{n=1}^{\infty}$)

If

$$\frac{\frac{\mu}{d+\gamma}}{1+\frac{d+\mu}{k\exp(-d\tau)}\frac{\bar{h}(\underline{I}_0,\overline{I}_1)-h(\underline{I}_1)}{\overline{I}_1-\underline{I}_1}} \leq 1, \text{ for } \underline{I}_1 < \overline{I}_1,$$

then

1. $\underline{I}_{n-1} \leq \underline{I}_n \leq \overline{I}_n \leq \overline{I}_{n-1}, \quad n \geq 1,$
2. $\underline{I}_n$ *monotonically increasingly converges to* $\underline{I}^*$, *and* $\overline{I}_n$ *monotonically decreasingly converges to* $\overline{I}$ *as* $n \to +\infty$,

Contraction of iterate maps

Key Lemma 3 (Contraction of $\{\underline{I}_n\}_{n=1}^{\infty}$ and $\{\overline{I}_n\}_{n=1}^{\infty}$)

3. $0 < \exists \lim_{n\to+\infty} \underline{I}_n \equiv \underline{I}^* \leq \underline{I} \leq \overline{I} \leq \exists \lim_{n\to+\infty} \overline{I}_n \equiv \overline{I}^* < +\infty,$

4. $$\begin{cases} \overline{I}^* + \dfrac{\mu}{d+\gamma}\underline{I}^* + \dfrac{d+\mu}{k\exp(-d\tau)}\bar{h}(\underline{I}^*, \overline{I}^*) = \dfrac{b}{d}, \\ \underline{I}^* + \dfrac{\mu}{d+\gamma}\overline{I}^* + \dfrac{d+\mu}{k\exp(-d\tau)}h(\underline{I}^*) = \dfrac{b}{d}, \\ 1 + \dfrac{d+\mu}{k\exp(-d\tau)}\dfrac{\bar{h}(\underline{I}^*, \overline{I}^*) - h(\underline{I}^*)}{\overline{I}^* - \underline{I}^*} = \dfrac{\mu}{d+\gamma}, \quad \text{if } \underline{I}^* < \overline{I}^*. \end{cases}$$

Globally asymptotic stability

Key Lemma 4 (GAS)

Assume that Key lemma 2 holds and there exist two constants $\underline{i} < \bar{i}$ *such that*

$$\begin{aligned}
&1.\quad \underline{i} \le \underline{I} \le I^* \le \bar{I} \le \bar{i},\\
&2.\quad \frac{\frac{\mu}{d+\gamma}}{1 + \frac{d+\mu}{\mathrm{k}e^{-d\tau}} \frac{\bar{h}(\underline{i}, \bar{i}) - h(\underline{i})}{\bar{i} - \underline{i}}} < 1,\\
&3.\quad \begin{cases} \underline{i} \le \underline{I}^* \le I^* \le \bar{I}^* \le \bar{i}, \\ \bar{I}^* + \frac{d+\mu}{\mathrm{k}e^{-d\tau}} \bar{h}(\underline{I}^*, \bar{I}^*) = \frac{d}{b} - \frac{\mu}{d+\gamma} \underline{I}^*, \\ \underline{I}^* + \frac{d+\mu}{\mathrm{k}e^{-d\tau}} h(\underline{I}^*) = \frac{d}{b} - \frac{\mu}{d+\gamma} \bar{I}^*, \end{cases} \Rightarrow \underline{I}^* = \bar{I}^* = I^*.
\end{aligned} \tag{2.8}$$

Then, EE $E_* = (S^*, I^*, R^*)$ *of system (2.1) is GAS.*

Distance between $\underline{I}^*$ and $\overline{I}^*$ ($\bar{I}^* < \hat{I} \equiv \frac{1}{\sqrt{\alpha}}$)

Put $\underline{I}^* = I^* - \varepsilon$ and $\bar{I}^* = I^* + \kappa$ in Key lemma 3.

Goal: $\varepsilon = 0$

First, assume that $\bar{I}^* < \hat{I} \equiv \frac{1}{\sqrt{\alpha}}$. Then,

$$0 \le \varepsilon \le I^* - \underline{I}_0 \quad \text{and} \quad 0 \le \kappa < \hat{I} - I^*. \tag{2.9}$$

By $I^* + \kappa \le \hat{I}$, we have that

$$\begin{cases} (I^* + \kappa) + \dfrac{\mu}{d+\gamma}(I^* - \varepsilon) + \dfrac{d+\mu}{k\mathrm{e}^{-d\tau}}\{1 + \alpha(I^* + \kappa)^2\} = \dfrac{d}{b}, \\ (I^* - \varepsilon) + \dfrac{\mu}{d+\gamma}(I^* + \kappa) + \dfrac{\mu+\gamma}{k\mathrm{e}^{-d\tau}}\{1 + \alpha(I^* - \varepsilon)^2\} = \dfrac{d}{b}, \\ 1 + \dfrac{\mu+\gamma}{k\mathrm{e}^{-d\tau}}\alpha\{2I^* + (\kappa - \varepsilon)\} = \dfrac{\mu}{d+\gamma}, \ \text{if } \varepsilon > 0. \end{cases} \tag{2.10}$$

From (2.10), we have that

$$\begin{cases} \frac{\mu}{d+\gamma}(-\varepsilon+\sigma\kappa+a\kappa^2)=0, \\ \frac{\mu}{d+\gamma}(\kappa-\sigma\varepsilon+a\varepsilon^2)=0, \\ \sigma+a(\kappa-\varepsilon)=1, \quad \text{if } \varepsilon>0, \end{cases}$$

where

$a=\frac{d+\gamma}{\mu}\frac{d+\mu}{k\mathrm{e}^{-d\tau}}\alpha$, $\sigma=\frac{2(d+\gamma)}{\mu}(1+\frac{d+\mu}{k\mathrm{e}^{-d\tau}}\alpha I^*)$, $c=\frac{\sigma-1+\sqrt{(\sigma-1)(\sigma+3)}}{2}$.
We now have that $\varepsilon=\sigma\kappa+a\kappa^2$, $\kappa=\sigma\varepsilon-a\varepsilon^2$, and $\kappa=\varepsilon+\frac{1-\sigma}{a}$ if $\varepsilon>0$. Suppose that $\varepsilon>0$. Then,

$$a^2\varepsilon^2+a(1-\sigma)\varepsilon+(1-\sigma)=0,$$

and hence, we obtain that $\sigma>1$, $\varepsilon=\frac{c}{a}$ and $\kappa=\frac{c}{a}-\frac{\sigma-1}{a}$. This contradicts to (2.9). Thus, we have $\varepsilon=0$.

Distance between $\underline{I}^*$ and $\overline{I}^*$ $(\bar{I}^* \geq \hat{I})$

Second, we suppose that $\bar{I}^* \geq \hat{I}$. Then, since $\tilde{h}(I) = 1 + 2\alpha\frac{I}{\hat{I}}$ for $I \geq \hat{I}$, by (2.8), we have that $\frac{1}{G(\hat{I})} - \frac{1}{G(\bar{I}^*)} \leq 0$ and

$$\begin{cases} (I^* + \kappa) + \frac{\mu}{d+\gamma}(I^* - \varepsilon) + \frac{\mu+\gamma}{k e^{-d\tau}}[\{1 + \alpha(I^* + \kappa)^2\} \\ \qquad + \alpha(\frac{1}{G(\hat{I})} - \frac{1}{G(\bar{I}^*)})\bar{I}^*] = \frac{d}{b}, \\ (I^* - \varepsilon) + \frac{\mu}{d+\gamma}(I^* + \kappa) + \frac{\mu+\gamma}{k e^{-d\tau}}\{1 + \alpha(I^* - \varepsilon)^2\} = \frac{d}{b}, \\ 1 + \frac{\mu+\gamma}{k e^{-d\tau}}\alpha\{2I^* + (\kappa - \varepsilon)\} + \frac{\mu+\gamma}{k e^{-d\tau}}\alpha(\frac{1}{G(\hat{I})} - \frac{1}{G(\bar{I}^*)})\bar{I}^* = \frac{\mu}{d+\gamma}, \\ \qquad \text{if } \varepsilon > 0. \end{cases}$$

Then, similar to the above discussion, by $\frac{1}{G(\hat{I})} - \frac{1}{G(\bar{I}^*)} \leq 0$, we can derive that $\underline{I}^* \geq I^* - \frac{c}{a}$, $\bar{I}^* \leq I^* + \frac{c-(\sigma-1)}{a}$ and hence, we have $\varepsilon = 0$.