Global asymptotic stability for a class of epidemic models with delays

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Outline

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   - Main result
   - Numerical simulations
   - An application
   - Conclusion
Global asymptotic stability for a class of epidemic models with delays

Introduction

Keywords

- Epidemiological concern - the spread of disease in time (e.g., measles, H5N1 influenza, etc.).
- Basic reproduction number
  \(\text{Threshold value}\) - the infectious disease will die out or persists?
- Time delay effect
  \(\text{Incubation (Latent) period}\) - caused by a vector
- Incidence rate of the diseases
Basic SIR model

Consider the following model.

\[
\begin{align*}
S'(t) &= B - \beta S(t)I(t) - \mu S(t), \\
I'(t) &= \beta S(t)I(t) - (\mu + \gamma)I(t), \\
R'(t) &= \gamma I(t) - \mu R(t), \quad t \geq 0, \\
S(0) &> 0, \quad I(0) > 0, \quad R(0) > 0.
\end{align*}
\]

(1.1)

\(B\): birth rate, \(\beta\): contact rate (infection force), \(\mu\): death rate, \(\gamma\): recovery rate

Figure: Diagram of disease transmission of system (1.1)
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Introduction

Basic properties

\[
\begin{align*}
S'(t) &= B - \beta S(t)I(t) - \mu S(t), \\
I'(t) &= \beta S(t)I(t) - (\mu + \gamma)I(t), \\
R'(t) &= \gamma I(t) - \mu R(t).
\end{align*}
\]

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

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

<table>
<thead>
<tr>
<th>(R_0)</th>
<th>DFE: (E_0 = (S_0, 0, 0))</th>
<th>EE: (E_* = (S_<em>, I_</em>, R_*))</th>
</tr>
</thead>
<tbody>
<tr>
<td>(&lt; 1)</td>
<td>(\text{GAS (globally asymptotically stable)*})</td>
<td>(\text{(no existence)})</td>
</tr>
<tr>
<td>(&gt; 1)</td>
<td>(\text{unstable})</td>
<td>(\text{GAS})</td>
</tr>
</tbody>
</table>

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

*globally asymptotically stable = uniformly stable + globally attractive
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Introduction

Time delay effect

\[
\begin{aligned}
S'(t) &= B - \beta S(t)I(t) - \mu S(t), \\
I'(t) &= \beta S(t)I(t) - (\mu + \gamma)I(t), \\
R'(t) &= \gamma I(t) - \mu R(t).
\end{aligned}
\]

Time delay effect

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

\[
\begin{aligned}
S'(t) &= B - \beta S(t)I(t - \tau) - \mu S(t), \\
I'(t) &= \beta S(t)I(t - \tau) - (\mu + \gamma)I(t), \\
R'(t) &= \gamma I(t) - \mu R(t), \quad \tau \geq 0.
\end{aligned}
\]
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Introduction

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., $G_2(I) \equiv I/(1 + \alpha I^p)$, $p > 1$)

---

![Graphs showing saturated effect and psychological effect](image.png)

Saturated effect  
psychological effect
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Delayed SIRS epidemic model with a nonlinear incidence rate

SIRS model

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

\[
\begin{aligned}
S'(t) &= b - dS(t) - ke^{-d\tau}S(t)\frac{I(t-\tau)}{1+\alpha I^2(t-\tau)} + \gamma R(t), \\
I'(t) &= ke^{-d\tau}S(t)\frac{I(t-\tau)}{1+\alpha I^2(t-\tau)} - (d + \mu)I(t), \\
R'(t) &= \mu I(t) - (d + \gamma)R(t), \quad \tau \geq 0, \quad t \geq 0,
\end{aligned}
\] (2.1)

Parameter setting

\begin{itemize}
\item \(b\): recruitment rate
\item \(d\): natural death rate
\item \(\mu\): natural recovery rate
\item \(ke^{-d\tau}S(t)I(t-\tau)/(1+\alpha I^2(t-\tau))\): infection force
\item \(\gamma\): rate at which recovered individuals lose immunity
\item \(\alpha\): parameter which measures the psychological effect
\end{itemize}

Note: SIRS = SIR + immunity lost
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SIRS model

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

\[
\begin{align*}
S'(t) &= b - dS(t) - ke^{-dt}S(t)\frac{I(t-\tau)}{1 + \alpha I^2(t-\tau)} + \gamma R(t), \\
I'(t) &= ke^{-dt}S(t)\frac{I(t-\tau)}{1 + \alpha I^2(t-\tau)} - (d + \mu)I(t), \\
R'(t) &= \mu I(t) - (d + \gamma)R(t), \quad \tau \geq 0, \quad t \geq 0,
\end{align*}
\]

with initial conditions:

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

where \( \mathbb{R}_+^3 = \{(x_1, x_2, x_3) : x_i \geq 0, \ i = 1, 2, 3\} \).
### Known results and a new result

**Basic properties:**

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

<table>
<thead>
<tr>
<th>( R_0 &lt; 1 )</th>
<th>( R_0 &gt; 1 )</th>
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<tr>
<td>GAS</td>
<td>unstable</td>
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</table>

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<tr>
<th>( \tau = 0 )</th>
<th>( \tau \geq 0 )</th>
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</table>

**NEW RESULT**

Monotone iterative technique

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

\( *\text{LAS} = \text{locally asymptotically stable} \)
Outline of monotone iterative technique

Step 1: derivation of reduced system
Step 2: permanence
Step 3: formulation of the iterate map
Global asymptotic stability for a class of epidemic models with delays
Delayed SIRS epidemic model with a nonlinear incidence rate
Monotone iterative technique

Step 1: derivation of reduced system

Lemma 1 (invariant set)

For system (2.1), it holds that

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

\[ \rightarrow \] 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):

\[
\begin{align*}
I'(t) &= ke^{-d\tau} \left( \frac{b}{d} - I(t) - R(t) \right) \frac{I(t-\tau)}{1 + \alpha I^2(t-\tau)} - (d + \mu)I(t), \\
R'(t) &= \mu I(t) - (d + \gamma)R(t), \quad \tau \geq 0, \quad t \geq 0,
\end{align*}
\]
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Step 2: permanence

Reduced system of (2.1):

\[
\begin{align*}
I'(t) &= k e^{-d\tau} \left( \frac{b}{d} - I(t) - R(t) \right) \frac{I(t - \tau)}{1 + \alpha I^2(t - \tau)} - (d + \mu) I(t), \\
R'(t) &= \mu I(t) - (d + \gamma) R(t), \quad \tau \geq 0, \ t \geq 0,
\end{align*}
\]

Lemma 2 (permanence)

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

\[
\limsup_{t \to +\infty} I(t) \equiv \bar{I} \leq \frac{b}{d}, \quad \limsup_{t \to +\infty} R(t) \equiv \bar{R} \leq \frac{b}{d},
\]

\[
\liminf_{t \to +\infty} I(t) \equiv \underline{I} \geq \nu, \quad \liminf_{t \to +\infty} R(t) \equiv \underline{R} \geq \frac{\mu}{d + \gamma} \nu.
\]
Step 3: formulation of the iterate map

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

Key lemma 1

\[
\frac{b}{d} - \bar{I} - \bar{R} > 0, \quad \text{and} \quad \frac{b}{d} - \bar{I} - \bar{R} > 0.
\] (2.3)

Key lemma 2 (Modified iterate scheme)

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

\[
\begin{cases}
0 \leq k \exp(-d\tau) \left( \frac{b}{d} - \bar{I} - \bar{R} \right) \tilde{G}(\bar{I}) - (d + \mu)\bar{I}, \\
0 \geq k \exp(-d\tau) \left( \frac{b}{d} - \bar{I} - \bar{R} \right) G(I) - (d + \mu)I.
\end{cases}
\] (2.4)
Global asymptotic stability for a class of epidemic models with delays
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Monotone iterative technique

\[
\begin{align*}
0 &= k e^{-d \tau} \left( \frac{b}{d} - \bar{I}_n - \frac{\mu}{d + \gamma} I_{n-1} \right) \max_{\bar{I}_{n-1} \leq I \leq \bar{I}_n} G(I) - (d + \mu) \bar{I}_n, \\
0 &= k e^{-d \tau} \left( \frac{b}{d} - \bar{I}_n - \frac{\mu}{d + \gamma} \bar{I}_n \right) G(I_n) - (d + \mu) I_n, \quad n \geq 1.
\end{align*}
\]

\[
\begin{align*}
\left( 1 + \frac{d + \mu}{k e^{-d \tau}} \frac{\bar{h}(I_{n-1}, \bar{I}_n) - h(I_n)}{\bar{I}_n - I_n} \right) (\bar{I}_n - I_n) &= \frac{\mu}{d + \gamma} (\bar{I}_n - I_{n-1}), \\
\end{align*}
\]

\[
\begin{align*}
\bar{I}_n - I_n &= \frac{\mu}{d + \gamma} \left( 1 + \frac{d + \mu}{k e^{-d \tau}} \frac{\bar{h}(I_{n-1}, \bar{I}_n) - h(I_n)}{\bar{I}_n - I_n} \right) (\bar{I}_n - I_{n-1}), \\
\bar{h}(I, I) &= I / G(I), \quad \bar{h}(I_1, I_2) = I_2 / \max_{I_1 \leq I \leq I_2} G(I), \quad n \geq 1.
\end{align*}
\]
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Sketch of an iterative scheme

\[
\bar{I}_n - I_n = \frac{\mu}{d + \gamma} \left( \frac{1}{1 + \frac{d + \mu}{ke^{-d\tau}} \frac{\bar{h}(I_{n-1}, \bar{I}_n) - h(I_n)}{\bar{I}_n - I_n}} \right) (\bar{I}_n - I_{n-1}).
\]

Sequences with respect to upper limits and lower limits:

\[I_0 \leq I \leq \bar{I} \leq \bar{I}_0\]
\[I_1 \leq I \leq \bar{I} \leq \bar{I}_1\]
\[I_2 \leq I \leq \bar{I} \leq \bar{I}_2\]

Question: When do the sequences \(\{\bar{I}_n\}_{n=0}^\infty\) and \(\{I_n\}_{n=0}^\infty\) converge to \(I^*\)? → Answer for the GAS of EE \(E_*\).
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Main result

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

\[
\frac{\mu}{d + \gamma} \leq 1, \quad \text{for } I_1 < \bar{I}_1, \tag{2.5}
\]

and suppose that either \( \sigma \leq 1 \) or

\[
\sigma > 1, \quad \text{and } c > a(I^* - I_0) \quad \text{or} \quad c \geq (\sigma - 1) + a(\hat{I} - I^*). \tag{2.6}
\]

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

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:

“... we give an interesting open problem: whether we can also obtain that EE $E_\ast$ is GAS when $R_0 > 1.$”

↓

Our results show that $E_\ast$ 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

\[
\begin{align*}
S'(t) &= b - dS(t) - \beta S(t) \frac{I(t-\tau)}{1 + \alpha I(t-\tau)} + \gamma R(t), \\
I'(t) &= \beta S(t) \frac{I(t-\tau)}{1 + \alpha I(t-\tau)} - (d + \mu)I(t), \\
R'(t) &= \mu I(t) - (d + \gamma)R(t), \quad \tau \geq 0, \ t \geq 0.
\end{align*}
\] (2.7)

GAS condition:

<table>
<thead>
<tr>
<th></th>
<th>DFE: (E_0)</th>
<th>EE: (E^*_0) ((R_0 &gt; 1))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xu and Ma (2009)</td>
<td>(R_0 &lt; 1)</td>
<td>({\alpha(d + \mu) - \beta}(d + \gamma) &gt; \beta \mu)</td>
</tr>
<tr>
<td><strong>NEW RESULT</strong></td>
<td></td>
<td>({\alpha(d + \mu) + \beta}(d + \gamma) &gt; \beta \mu)</td>
</tr>
</tbody>
</table>

Difference: iterate scheme!
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An application

**Difference between the iterate schemes**

**Key Lemma 2 (Modified iterate scheme)**

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

\[
\begin{aligned}
0 & \leq k \exp(-d\tau) \left( \frac{b}{d} - \bar{I} - \bar{R} \right) \bar{G}(\bar{I}, \bar{I}) - (d + \mu)\bar{I}, \\
0 & \geq k \exp(-d\tau) \left( \frac{b}{d} - \bar{I} - \bar{R} \right) G(I) - (d + \mu)\bar{I}.
\end{aligned}
\]

**Xu and Ma (2009) -type scheme:**

\[
\begin{aligned}
0 & \leq k \exp(-d\tau) \left( \frac{b}{d} - \bar{I} - \bar{R} \right) \bar{G}(\bar{I}, \bar{I}) - (d + \mu)\bar{I} \\
0 & \geq k \exp(-d\tau) \left( \frac{b}{d} - \bar{I} - \bar{R} \right) G(\bar{I}) - (d + \mu)\bar{I}.
\end{aligned}
\]
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)
Global asymptotic stability for a class of epidemic models with delays
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Conclusion

**Contraction of iterate maps**

**Key Lemma 3 (Contraction of \( \{I_n\}_{n=1}^{\infty} \) and \( \{\bar{I}_n\}_{n=1}^{\infty} \))**

If

\[
\frac{\mu}{d + \gamma} \leq 1, \text{ for } I_1 < \bar{I}_1,
\]

\[
1 + \frac{d + \mu}{k \exp(-d\tau)} \frac{h(I_0, \bar{I}_1) - h(I_1)}{\bar{I}_1 - I_1}
\]

then

1. \( I_{n-1} \leq I_n \leq \bar{I}_n \leq \bar{I}_{n-1}, \quad n \geq 1, \)
2. \( I_n \) monotonically increasingly converges to \( I^* \), and
   \( \bar{I}_n \) monotonically decreasingly converges to \( \bar{I} \) as \( n \to +\infty \),
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Contraction of iterate maps

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

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

\[
\begin{align*}
\overline{I}^* + \frac{\mu}{d + \gamma} I^* + \frac{d + \mu}{k \exp(-d\tau)} \overline{h}(I^*, \overline{I}^*) &= \frac{b}{d}, \\
I^* + \frac{\mu}{d + \gamma} \overline{I}^* + \frac{d + \mu}{k \exp(-d\tau)} h(I^*) &= \frac{b}{d}, \\
1 + \frac{d + \mu}{k \exp(-d\tau)} \frac{\overline{h}(I^*, \overline{I}^*) - h(I^*)}{\overline{I}^* - I^*} &= \frac{\mu}{d + \gamma}, \quad \text{if } I^* < \overline{I}^*.
\end{align*}
\]
Globally asymptotic stability

Key Lemma 4 (GAS)

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

1. $i \leq I \leq I^* \leq \bar{I} \leq \bar{i},$
   \[ \frac{\mu}{d + \gamma} \]

2. \[ \frac{1}{1 + \frac{d + \mu}{k e^{-d\tau}} \frac{h(i, \bar{i}) - h(i)}{\bar{i} - i}} < 1, \quad (2.8) \]

3. \[ \left\{ \begin{array}{l}
   i \leq I^* \leq \bar{I}^* \leq \bar{i}, \\
   \bar{I}^* + \frac{d + \mu}{k e^{-d\tau}} h(I^*, \bar{I}^*) = \frac{d}{b} - \frac{\mu}{d + \gamma} I^*, \Rightarrow \bar{I}^* = \bar{I}^* = I^*.
   \\
   I^* + \frac{d + \mu}{k e^{-d\tau}} h(I^*) = \frac{d}{b} - \frac{\mu}{d + \gamma} I^*, \\
   \end{array} \right. \]

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

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

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

Goal: $\varepsilon = 0$

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

$$0 \leq \varepsilon \leq I^* - I_0 \quad \text{and} \quad 0 \leq \kappa < \hat{I} - I^*. \quad (2.9)$$

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

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

\[
\begin{align*}
\frac{\mu}{d + \gamma}(-\varepsilon + \sigma \kappa + a\kappa^2) &= 0, \\
\frac{\mu}{d + \gamma}(\kappa - \sigma \varepsilon + a\varepsilon^2) &= 0, \\
\sigma + a(\kappa - \varepsilon) &= 1, \quad \text{if } \varepsilon > 0,
\end{align*}
\]

where

\[
a = \frac{d+\gamma}{\mu} \frac{d+\mu}{ke-d\tau} \alpha, \quad \sigma = \frac{2(d+\gamma)}{\mu} \left(1 + \frac{d+\mu}{ke-d\tau} \alpha I^*\right), \quad c = \frac{\sigma-1+\sqrt{(\sigma-1)(\sigma+3)}}{2}.
\]

We now have that \( \varepsilon = \sigma \kappa + a\kappa^2, \quad \kappa = \sigma \varepsilon - a\varepsilon^2, \) 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 \( \sigma > 1, \quad \varepsilon = \frac{c}{a} \) and \( \kappa = \frac{c}{a} - \frac{\sigma-1}{a}. \) This contradicts to (2.9). Thus, we have \( \varepsilon = 0. \)
Distance between $I^*$ and $\bar{I}^*$ ($\bar{I}^* \geq \hat{I}$)

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

\[
\begin{align*}
(\bar{I}^* + \kappa) + \frac{\mu}{d + \gamma} (\bar{I}^* - \varepsilon) + \frac{\mu + \gamma}{ke - d\tau} \left\{ \left[ 1 + \alpha (\bar{I}^* + \kappa) \right]^2 \right. & \left. + \alpha \left( \frac{1}{G(\hat{I})} - \frac{1}{G(\bar{I}^*)} \right) \bar{I}^* \right\} = \frac{d}{b}, \\
(\bar{I}^* - \varepsilon) + \frac{\mu}{d + \gamma} (\bar{I}^* + \kappa) + \frac{\mu + \gamma}{ke - d\tau} \left\{ 1 + \alpha (\bar{I}^* - \varepsilon) \right\} = \frac{d}{b}, \\
1 + \frac{\mu + \gamma}{ke - d\tau} \alpha \{2\bar{I}^* + (\kappa - \varepsilon)\} + \frac{\mu + \gamma}{ke - d\tau} \alpha \left( \frac{1}{G(\hat{I})} - \frac{1}{G(\bar{I}^*)} \right) \bar{I}^* = \frac{\mu}{d + \gamma}, \\
& \text{if } \varepsilon > 0.
\end{align*}
\]

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

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