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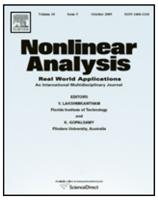

Nonlinear Analysis
Real World Applications

Global dynamics of a staged-progression model for HIV/AIDS with amelioration

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ABSTRACT

We consider a mathematical model for HIV/AIDS that incorporates staged progression and amelioration. Amelioration as a result of HAART treatment is allowed to occur across any number of stages. The global dynamics are completely determined by the basic reproduction number R_0. If $R_0 \leq 1$, then the disease-free equilibrium (DFE) is globally asymptotically stable and the disease always dies out. If $R_0 > 1$, DFE is unstable and a unique endemic equilibrium (EE) is globally asymptotically stable, and the disease persists at the endemic equilibrium. The proof of global stability utilizes a global Lyapunov function.

1. Introduction

For infectious diseases progressing through a long infectious period, infectivity or infectiousness can vary greatly over time. The progression of a typical HIV infection can take eight to ten years before the clinical syndrome (AIDS) occurs, and the progression goes through several distinct stages, marked by drastically different CD4$^+$ T-cell counts and viral RNA levels. HIV-infected individuals are highly infectious in the first few weeks after infection, then remain in an asymptotic stage of low infectiousness for many years, and become gradually more infectious as their immune system becomes compromised, until they develop AIDS.

Since the advent of highly active antiretroviral therapy (HARRT) in 1996, there has been remarkable improvement on the survival rate of HIV-infected patients. On an individual level, the viral load of averted treatment can help patients ameliorate to higher CD4+ counts and prolong patients' lives. On the population level, treatment can prolong the infectious period of HIV-infected individuals during which they may continue transmission and may even resume risky sexual or drug activities. This can have negative effects to the control and interventions of the epidemics. To fully evaluate the overall effectiveness of the antiretroviral therapies on the disease spread of HIV/AIDS, it is important to investigate the long term impact of amelioration on the population dynamics of the HIV transmission.

Mathematical modeling is a useful tool in better understanding disease dynamics, making prediction of disease outbreak and evaluations of prevention or intervention strategies. In [1,2], models of HIV infection in vivo were studied. Global properties of disease models in cellular levels were analyzed in [3,4] and recently, small world networks was derived for HIV modeling by discrete event simulation models [5].

Variability of infectiousness over time has been modeled in the literature by Markov chain models, or staged-progression (SP) models (see e.g. [6–17]). Longini et al. [14] used six stages of HIV infection for individuals who have not developed full-blown AIDS to model the progression of HIV infection. Current HAART treatments are able to significantly lengthen patients'

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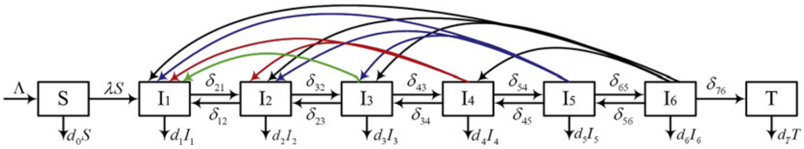

Fig. 1. The transfer diagram for model (1).

life spans. It is possible for ameliorated HIV patients to move from advanced stages back to any earlier infectious stages [8,15]. In this paper, we present a 6-stage SP model with arbitrary amelioration so that ameliorated patients can move to any of the less advanced stages. Our model is a natural generalization of those in [18,15,19], in which amelioration can only occur one stage at a time. Our goal is to establish the global dynamics of the 6-stage model with arbitrary amelioration and to investigate the effects of amelioration on the disease dynamics.

We prove that the global dynamics is completely determined by the basic reproduction number R_0. If $R_0 \leq 1$, then the DFE is globally asymptotically stable and the disease always dies out. If $R_0 > 1$, then DFE becomes unstable, and a unique EE exists in the interior of feasible region. For the case of bilinear incidence, we prove that EE is globally asymptotically stable. Our results contain earlier global-stability results in [18,15,19] when the number of stages is less than or equal to 6.

The paper is organized as follows. The 6-stage SP model is presented in Section 2 and its basic properties are given in Section 3. In Section 4, the basic reproduction number is derived using the method of next generation matrix. The global stability of EE for the bilinear incidence is proved in Section 5.

2. A 6-stage SP model with arbitrary amelioration

To formulate an SP model with disease progression and arbitrary amelioration, the total host population is partitioned into the following compartments: the susceptible (S), the infectious (I_i) whose members are in the i-th stage of the disease progression, $i = 1, \dots, 6$, and the terminal compartment (T), where individuals are non-infectious due to inactivity. In the case of HIV infection, the terminal compartment consists of people with active AIDS and they typically either become sexually inactive or isolated from the infection process, thus their infectivity is negligible. One also assumes that there is no recovery from the disease, and thus the only exit from the compartment T is death. Let δ_{ij} $(i > j,\ i = j + 1)$ be the mean progression rate from the j-th stage to the i-th stage and δ_{ij} $(i < j)$ the rate of amelioration from the j-th stage to the i-th stage, respectively, for $i, j = 1, 2, \dots, 6$. Here, we allow individuals in the j-th stage to be able to move to any other i-th stage as the result of HARRT treatment. Let λ_i be the transmission coefficient for the infection of a susceptible from an infectious in the class I_i, which takes into account of average number of contact and probability of infection for each contact, then the total incidence is given by $\lambda = \sum_{i=1}^{6} \lambda_i I_i S f(N)$, where $N = S + \sum_{i=1}^{6} I_i$ is the total active population. Here we assume that the density dependence of the incidence is given by a function $f(N)$ which will be specified below (see also [18]). Average death rate for susceptible compartment is d_0, d_i for the compartment I_i, which may include death due to infection, and d_T for the active disease compartment. It is assumed that the inflow to susceptible is a constant Λ. The population transfer among compartments are schematically depicted in the transfer diagram in Fig. 1. All parameters in the model are assumed to be positive. We remark that if $\lambda_i = 0$ for some i, then the compartment I_i will be regarded as a latent compartment. Thus, our model includes, as a special case, models of $SE_1 \cdots E_m I_1 \cdots I_k R$ type, for $m + k = 6$. Obviously this 6-stage model can be extended to any finite n-stage model, and $SE_1 \cdots E_m I_1 \cdots I_k R$ type models as a special case, for $m + k = n$.

Based on the preceding assumptions and the transfer diagram, the following system of ordinary differential equations is derived for the SP model with variable amelioration

$$\begin{cases} S' = \Lambda - d_0 S - \lambda S, \\ I_1' = \lambda S - (d_1 + \delta_{21}) I_1 + \delta_{12} I_2 + \delta_{13} I_3 + \delta_{14} I_4 + \delta_{15} I_5 + \delta_{16} I_6, \\ I_2' = \delta_{21} I_1 - (d_2 + \delta_{12} + \delta_{32}) I_2 + \delta_{23} I_3 + \delta_{24} I_4 + \delta_{25} I_5 + \delta_{26} I_6, \\ I_3' = \delta_{32} I_2 - (d_3 + \delta_{13} + \delta_{23} + \delta_{43}) I_3 + \delta_{34} I_4 + \delta_{35} I_5 + \delta_{36} I_6, \\ I_4' = \delta_{43} I_3 - (d_4 + \delta_{14} + \delta_{24} + \delta_{34} + \delta_{54}) I_4 + \delta_{45} I_5 + \delta_{46} I_6, \\ I_5' = \delta_{54} I_4 - (d_5 + \delta_{15} + \delta_{25} + \delta_{35} + \delta_{45} + \delta_{65}) I_5 + \delta_{56} I_6, \\ I_6' = \delta_{65} I_5 - (d_6 + \delta_{16} + \delta_{26} + \delta_{36} + \delta_{46} + \delta_{56} + \delta_{76}) I_6, \end{cases} \tag{1}$$

and $T' = \delta_{76} I_6 - d_T T$. The incidence form is λS, where the force of infection

$$\lambda = f(N) \sum_{i=1}^{6} \lambda_i I_i \tag{2}$$

is density dependent. We assume that the function $f(N)$ satisfies the following assumptions.

$$\text{(H)}\, f(N) > 0, \qquad f'(N) \leq 0, \quad \text{and} \quad |Nf'(N)| \leq f(N), \quad \text{for } N > 0.$$

The assumptions that $f(N) > 0$ and $f'(N) \leq 0$ are biologically motivated (see [18]). It can be verified that the class $f(N) = N^{-\alpha}$, $0 \leq \alpha \leq 1$, satisfies (H). This class contains the standard incidence ($\alpha = 1$) and the bilinear incidence ($\alpha = 0$).

Adding the equations in (1) we obtain

$$N' = \Lambda - d_0 S - d_1 I_1 - \cdots - d_6 I_6 - \delta_{76} I_6 \leq \Lambda - \mathrm{d}N,$$

where $d = \min\{d_0, d_1, \ldots, d_6\}$. It follows that $\lim_{t\to\infty}\sup N(t) \leq \Lambda/d$. Similarly, from the first equation of (1) we obtain $S' \leq \Lambda - d_0 S$, and thus $\lim_{t\to\infty}\sup S(t) \leq \Lambda/d_0$. The feasible region for (1) can be chosen as the closed set

$$\Gamma = \left\{(S, I_1, \ldots, I_6) \in \mathbb{R}^7_+ : 0 \leq S \leq \frac{\Lambda}{d_0},\ 0 \leq S + I_1 + \cdots + I_6 \leq \frac{\Lambda}{d}\right\},$$

which can be verified to be positively invariant with respect to (1).

3. Equilibria and stability

For notation convenience, define

$$\delta_{ii} \doteq d_i + \sum_{k=1,k\neq i}^{i+1} \delta_{ki} = d_i + \sum_{k=1}^{i-1} \delta_{ki} + \delta_{i+1,i}, \quad i = 1, \ldots, 6. \tag{3}$$

We rewrite the model (1) in compact form

$$\begin{aligned} S' &= \Lambda - d_0 S - \sum_{i=1}^{6} \lambda_i I_i S f(N), \\ I_1' &= \sum_{i=1}^{6} \lambda_i I_i S f(N) + \sum_{i=2}^{6} \delta_{1i} I_i - \delta_{11} I_1, \\ I_i' &= \sum_{k=i+1}^{6} \delta_{ik} I_k + \delta_{i,i-1} I_{i-1} - \delta_{ii} I_i, \quad i = 2, \ldots, 6. \end{aligned} \tag{4}$$

An equilibrium $(S, I_1, \ldots, I_6)$ of (4) satisfies

$$\begin{aligned} 0 &= \Lambda - d_0 S - \sum_{i=1}^{6} \lambda_i I_i S f(N), \\ 0 &= \sum_{i=1}^{6} \lambda_i I_i S f(N) + \sum_{i=2}^{6} \delta_{1i} I_i - \delta_{11} I_1, \\ 0 &= \sum_{k=i+1}^{6} \delta_{ik} I_k + \delta_{i,i-1} I_{i-1} - \delta_{ii} I_i, \quad i = 2, \ldots, 6. \end{aligned} \tag{5}$$

The disease-free equilibrium $P_0 = (\Lambda/d_0, 0, \ldots, 0)$ always exists for all non-negative parameter values. An endemic equilibria $P^* = (S^*, I_1^*, \ldots, I_6^*)$ satisfies $S^* > 0,\ I_i^* > 0,\ i = 1, \ldots, 6$. Let

$$B = \begin{bmatrix} -\delta_{11} & \delta_{12} & \delta_{13} & \delta_{14} & \delta_{15} & \delta_{16} \\ \delta_{21} & -\delta_{22} & \delta_{23} & \delta_{24} & \delta_{25} & \delta_{26} \\ & \delta_{32} & -\delta_{33} & \delta_{34} & \delta_{35} & \delta_{36} \\ & & \delta_{43} & -\delta_{44} & \delta_{45} & \delta_{46} \\ & & & \delta_{54} & -\delta_{55} & \delta_{56} \\ & & & & \delta_{65} & -\delta_{66} \end{bmatrix}, \tag{6}$$

where δ_{ii} is denoted in (3) and all other entries in B are zeros. Then $-B$ is an M-matrix. Thus $-B^{-1}$ exists and is non-negative. Furthermore, there exists $\alpha > 0$ such that $-B^{-1}x \geq \alpha\, x$ for $x \geq 0$ (see Appendix). It follows that

$$\beta \doteq -(\lambda_1, \ldots, \lambda_6) B^{-1} (1, 0, \ldots, 0)^T > 0, \tag{7}$$

where superscript T denotes the transposition. Define the basic reproduction number of (4) as

$$R_0 = \beta \frac{\Lambda}{d_0} f\left(\frac{\Lambda}{d_0}\right). \tag{8}$$

We have the following results on the existence of endemic equilibrium and stability of disease-free equilibrium.

Theorem 3.1. *Assume that f satisfies* (H). *If $R_0 \leq 1$, then P_0 is the only equilibrium in Γ and is globally asymptotically stable. If $R_0 > 1$, then P_0 is unstable, and a unique endemic equilibrium P^* exists in the interior of Γ.*

For the proof, we refer the reader to Theorems 3.1 and 4.1 in [18].

4. The basic reproduction number R_0

Theorem 3.1 establishes R_0 as a sharp threshold parameter. If $R_0 \leq 1$, the disease dies out irrespective of the initial number of cases. If $R_0 > 1$, then the disease persists in the feasible region and there is a unique endemic equilibrium. Such a role of threshold parameter is expected of the basic reproduction number, the average number of infections caused by a single infective in a population at the disease-free equilibrium [20–22]. It is then reasonable to regard the parameter R_0 defined in (8) as the basic reproduction number. Next we derive the basic reproduction number by the method of next generation matrix [22].

Set $y = (I_1, \dots, I_6, S)^T$. Then model (4) can be written as

$$y' = \mathcal{F}(y) + \mathcal{V}(y),$$

where

$$\mathcal{F}(y) = \begin{bmatrix} \lambda S \\ 0 \\ \vdots \\ 0 \end{bmatrix}, \qquad \mathcal{V}(y) = \begin{bmatrix} \displaystyle\sum_{i=2}^{6} \delta_{1i} I_i - \delta_{11} I_1 \\ \displaystyle\delta_{21} I_1 + \sum_{i=3}^{6} \delta_{2i} I_i - \delta_{22} I_2 \\ \vdots \\ \delta_{65} I_5 - \delta_{66} I_6 \\ \Lambda - d_0 S - \lambda S \end{bmatrix}.$$

At the disease-free equilibrium in the new coordinates, $\tilde{P}_0 = (0, 0, \dots, 0, \Lambda/d_0)$,

$$\frac{\partial \mathcal{F}}{\partial y}(\tilde{P}_0) = \begin{bmatrix} F_{6\times 6} & 0 \\ 0 & 0 \end{bmatrix},$$

where

$$F_{6\times 6} = \begin{bmatrix} -\lambda_1 & -\lambda_2 & \cdots & -\lambda_6 \\ 0 & \cdots & \cdots & 0 \\ \vdots & & & \vdots \\ 0 & \cdots & \cdots & 0 \end{bmatrix} g\left(\frac{\Lambda}{d_0}\right),$$

and $g(N) = Nf(N)$. Moreover,

$$\frac{\partial \mathcal{V}}{\partial y}(\tilde{P}_0) = \begin{bmatrix} & & & 0 \\ & V_{6\times 6} & & \vdots \\ & & & 0 \\ -\lambda_1 g\left(\frac{\Lambda}{d_0}\right) & \cdots & -\lambda_n g\left(\frac{\Lambda}{d_0}\right) & -d_0 \end{bmatrix}.$$

Here $V_{6\times 6} = B$, where B is defined in (6). Therefore, the next generation matrix is

$$FV^{-1} = \begin{bmatrix} c_1 & c_2 & \cdots & c_6 \\ 0 & \cdots & \cdots & 0 \\ \vdots & & & \vdots \\ 0 & \cdots & \cdots & 0 \end{bmatrix} g\left(\frac{\Lambda}{d_0}\right),$$

where

$$(c_1, c_2, \dots, c_6) = -(\lambda_1, \lambda_2, \dots, \lambda_6) B^{-1}. \tag{9}$$

Thus

$$c_1 = -(\lambda_1, \lambda_2, \dots, \lambda_6) B^{-1} (1, 0, \cdots, 0)^T = \beta > 0.$$

The basic reproduction number is defined in [22] as the spectral radius, $\rho(FV^{-1})$, of the matrix FV^{-1}. It is easy to see that

$$\rho(FV^{-1}) = c_1 g\left(\frac{\Lambda}{d_0}\right) = \beta \frac{\Lambda}{d_0} f\left(\frac{\Lambda}{d_0}\right).$$

5. Stability of the endemic equilibrium P^*

In this section, for $f(N) \equiv 1$, i.e., the bilinear incidence, we prove the global stability of the endemic equilibrium P^* when $R_0 > 1$. The proof utilizes a global Lyapunov function. The following equilibrium equations are useful for the proof of propositions.

The equilibrium equations (5) for $P^* = (S^*, I_1^*, \ldots, I_6^*)$ are

$$\left[\begin{aligned}
&d_0 S^* + \sum_{i=1}^{6} \lambda_i^* S^* I^* = \Lambda,\\
&\sum_{i=1}^{6} \lambda_i^* S^* I^* + \delta_{12} I_2^* + \delta_{13} I_3^* + \delta_{14} I_4^* + \delta_{15} I_5^* + \delta_{16} I_6^* = \delta_{11} I_1^*,\\
&\delta_{21} I_1^* + \delta_{23} I_3^* + \delta_{24} I_4^* + \delta_{25} I_5^* + \delta_{26} I_6^* = \delta_{22} I_2^*,\\
&\delta_{32} I_2^* + \delta_{34} I_4^* + \delta_{35} I_5^* + \delta_{36} I_6^* = \delta_{33} I_3^*,\\
&\delta_{43} I_3^* + \delta_{45} I_5^* + \delta_{46} I_6^* = \delta_{44} I_4^*,\\
&\delta_{54} I_4^* + \delta_{56} I_6^* = \delta_{55} I_5^*,\\
&\delta_{65} I_5^* = \delta_{66} I_6^*,
\end{aligned}\right. \tag{10}$$

where δ_{ii} is defined in (3).

Theorem 5.1. *Assume that $f(N) \equiv 1$ and $R_0 > 1$. Then the endemic equilibrium P^* is asymptotically stable. Furthermore, all solutions in the interior of Γ converge to P^*.*

Set $x = (S, I_1, I_2, \ldots, I_6) \in \Gamma \subset \mathbb{R}_7^+$. Consider a Lyapunov function

$$W = W(x) = \left(S - S^* - S^* \ln \frac{S}{S^*}\right) + \sum_{i=1}^{6} A_i \left(I_i - I_i^* - I_i^* \ln \frac{I_i}{I_i^*}\right),$$

where $x^* = P^* = (S^*, I_1^*, \ldots, I_6^*)$ and $A_i > 0$ are constants to be determined later. We note that $W(x) \geq 0$, for $x \in \mathrm{Int}\Gamma$, the interior of Γ, and $W(x) = 0 \Longleftrightarrow x = x^*$. So function W is positive definite with respect to the endemic equilibrium $x^* = P^*$. Computing the derivative of W along solutions of system (1), we obtain

$$\frac{\mathrm{d}W}{\mathrm{d}t} = \left(1 - \frac{S^*}{S}\right) S' + \sum_{i=1}^{6} A_i \left(1 - \frac{I_i^*}{I_i}\right) I_i'. \tag{11}$$

Using (4) and the first equation of (10), we have

$$\begin{aligned}
\left(1 - \frac{S^*}{S}\right) S' &= \Lambda - d_0 S - \sum_{i=1}^{6} \lambda_i I_i S - \frac{\Lambda S^*}{S} + d_0 S^* + \sum_{i=1}^{6} \lambda_i I_i S^*\\
&= d_0 S^* + \sum_{i=1}^{6} \lambda_i I_i^* S^* - d_0 S - \sum_{i=1}^{6} \lambda_i I_i S - \frac{d_0 S^{*2}}{S} - \sum_{i=1}^{6} \lambda_i I_i^* \frac{S^{*2}}{S} + d_0 S^* + \sum_{i=1}^{6} \lambda_i I_i S^*\\
&= d_0 S^* \left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) - \sum_{i=1}^{6} \lambda_i I_i S + \sum_{i=1}^{6} \lambda_i I_i S^* + \sum_{i=1}^{6} \lambda_i I_i^* S^* - \sum_{i=1}^{6} \lambda_i I_i^* \frac{S^{*2}}{S}.
\end{aligned} \tag{12}$$

Similarly, using (4), for $i = 1, \ldots, 6$, we obtain

$$\begin{aligned}
A_1 \left(1 - \frac{I_1^*}{I_1}\right) I_1' &= A_1 \left[\sum_{i=1}^{6} \lambda_i I_i S - \delta_{11} I_1 + \sum_{i=2}^{6} \delta_{1i} I_i - \sum_{i=1}^{6} \lambda_i I_i S \frac{I_1^*}{I_1} + \delta_{11} I_1^* - \sum_{i=2}^{6} \delta_{1i} I_i \frac{I_1^*}{I_1}\right],\\
A_i \left(1 - \frac{I_i^*}{I_i}\right) I_i' &= A_i \left[\sum_{k=i+1}^{6} \delta_{ik} I_k + \delta_{i,i-1} I_{i-1} - \delta_{ii} I_i - \sum_{k=i+1}^{6} \delta_{ik} I_k \frac{I_i^*}{I_i} - \delta_{i,i-1} I_{i-1} \frac{I_i^*}{I_i} + \delta_{ii} I_i^*\right].
\end{aligned} \tag{13}$$

Substituting (12), (13) into (11) and rearranging terms we obtain

$$\begin{aligned}
\frac{\mathrm{d}W}{\mathrm{d}t} = {} & d_0 S^* \left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) + \left[-\sum_{i=1}^{6} \lambda_i I_i S + \sum_{i=1}^{6} \lambda_i I_i S^* + \sum_{i=1}^{6} \lambda_i I_i^* S^* - \sum_{i=1}^{6} \lambda_i I_i^* \frac{S^{*2}}{S}\right]\\
& + A_1 \left[\sum_{i=1}^{6} \lambda_i I_i S - \delta_{11} I_1 + \sum_{i=2}^{6} \delta_{1i} I_i - \sum_{i=1}^{6} \lambda_i I_i S \frac{I_1^*}{I_1} + \delta_{11} I_1^* - \sum_{i=2}^{6} \delta_{1i} I_i \frac{I_1^*}{I_1}\right]
\end{aligned}$$

$$\begin{aligned}
&+\sum_{i=2}^{6} A_i \left[\sum_{k=i+1}^{6}\delta_{ik}I_k + \delta_{i,i-1}I_{i-1} - \delta_{ii}I_i - \sum_{k=i+1}^{6}\delta_{ik}I_k\frac{I_i^*}{I_i} - \delta_{i,i-1}I_{i-1}\frac{I_i^*}{I_i} + \delta_{ii}I_i^*\right]\\
&= d_0S^*\left(2-\frac{S}{S^*}-\frac{S^*}{S}\right) + \left(-\sum_{i=1}^{6}\lambda_iI_iS + A_1\sum_{i=1}^{6}\lambda_iI_iS\right) + \left(\sum_{i=1}^{6}\lambda_iI_i^*S^* + A_1\delta_{11}I_1^* + \sum_{i=2}^{6}A_i\delta_{ii}I_i^*\right)\\
&\quad + \left(\sum_{i=1}^{6}\lambda_iI_iS^* + A_1\sum_{i=2}^{6}\delta_{1i}I_i + \sum_{i=2}^{6}A_i\delta_{i,i-1}I_{i-1} + \sum_{i=2}^{6}A_i\sum_{k=i+1}^{6}\delta_{ik}I_k - \sum_{i=1}^{6}A_i\delta_{ii}I_i\right)\\
&\quad + \left(-\sum_{i=1}^{6}\lambda_iI_i^*\frac{S^{*2}}{S} - A_1\sum_{i=1}^{6}\lambda_iI_iS\frac{I_1^*}{I_1} - \sum_{i=2}^{6}A_i\delta_{i,i-1}I_{i-1}\frac{I_i^*}{I_i} - \sum_{i=1}^{6}A_i\sum_{k=i+1}^{6}\delta_{ik}I_k\frac{I_i^*}{I_i}\right)\\
&\doteq W_0 + W_1 + W_2 + W_3 + W_4. \qquad (14)
\end{aligned}$$

In the last step, we have used the following relation

$$-\sum_{i=1}^{6}A_i\sum_{k=i+1}^{6}\delta_{ik}I_k\frac{I_i^*}{I_i} = -A_1\sum_{i=2}^{6}\delta_{1i}I_i\frac{I_1^*}{I_1} - \sum_{i=2}^{6}A_i\sum_{k=i+1}^{6}\delta_{ik}I_k\frac{I_i^*}{I_i}.$$

Note that W_2 in (14) contains all constant terms and W_4 all negative nonlinear terms. W_3 contains all linear terms of I_i. Next we will show that W_1 and W_3 disappear with appropriate choice of A_i. The following proposition determines the coefficients A_i of the Lyapunov function.

Proposition 5.2. *Let* $(A_1, \dots, A_6)$ *be the unique solution to the linear system*

$$\begin{aligned}
&\lambda_1S^* + A_2\delta_{21} - A_1\delta_{11} = 0,\\
&\lambda_2S^* + A_3\delta_{32} + A_1\delta_{12} - A_2\delta_{22} = 0,\\
&\lambda_3S^* + A_4\delta_{43} + A_1\delta_{13} + A_2\delta_{23} - A_3\delta_{33} = 0,\\
&\lambda_4S^* + A_5\delta_{54} + A_1\delta_{14} + A_2\delta_{24} + A_3\delta_{34} - A_4\delta_{44} = 0,\\
&\lambda_5S^* + A_6\delta_{65} + A_1\delta_{15} + A_2\delta_{25} + A_3\delta_{35} + A_4\delta_{45} - A_5\delta_{55} = 0,\\
&\lambda_6S^* + A_1\delta_{16} + A_2\delta_{26} + A_3\delta_{36} + A_4\delta_{46} + A_5\delta_{56} - A_6\delta_{66} = 0.
\end{aligned} \qquad (15)$$

Then $A_i > 0$, $i = 1, \dots, 6$. *In particular,* $A_1 = 1$. *Furthermore, with these choices of* A_i, $W_1 = 0$, $W_3 \equiv 0$ *for all* $(I_1, \dots, I_6) \in \mathbb{R}_6^+$.

Proof. Let B be the matrix in (6) and B^T be its transposition. Then system (15) can be written as

$$-B^T\begin{bmatrix}A_1\\ \vdots\\ A_6\end{bmatrix} = \begin{bmatrix}\lambda_1S^*\\ \vdots\\ \lambda_6S^*\end{bmatrix}.$$

Since $-(B^T)^{-1}$ is a M-matrix, and hence system (15) has a unique positive solution

$$\begin{bmatrix}A_1\\ \vdots\\ A_6\end{bmatrix} = -(B^T)^{-1}\begin{bmatrix}\lambda_1S^*\\ \vdots\\ \lambda_6S^*\end{bmatrix}.$$

In particular, using the definition of β in (7) and the relation $\beta S^* = 1$ (see proof of Theorem 3.1 in [18]) with $f \equiv 1$, we obtain

$$1 = \beta S^* = -(\lambda_1S^*, \dots, \lambda_6S^*)B^{-1}\begin{bmatrix}1\\0\\ \vdots\\0\end{bmatrix} = -(1, 0, \dots, 0)(B^T)^{-1}\begin{bmatrix}\lambda_1S^*\\ \vdots\\ \lambda_6S^*\end{bmatrix} = A_1.$$

Furthermore, in W_3, we observe that the coefficients for each I_i sum up to zero, by (15). □

In order to simplify W_2, we need the following lemma.

Lemma 5.3. *For any* $i = 2, \dots, 5$, *we have the relation*

$$A_i\delta_{ii}I_i^* = \sum_{k=i}^{6}\lambda_kI_k^*S^* + \sum_{k=1}^{i-1}A_k\sum_{j=i}^{6}\delta_{kj}I_j^* + A_i\sum_{k=i+1}^{6}\delta_{ik}I_k^*. \qquad (16)$$

Proof. It follows from (15) that

$$\begin{aligned}
&\lambda_1 I_1^* S^* + A_2\delta_{21} I_1^* = A_1\delta_{11} I_1^*,\\
&\lambda_2 I_2^* S^* + A_3\delta_{32} I_2^* + A_1\delta_{12} I_2^* = A_2\delta_{22} I_2^*,\\
&\lambda_3 I_3^* S^* + A_4\delta_{43} I_3^* + A_1\delta_{13} I_3^* + A_2\delta_{23} I_3^* = A_3\delta_{33} I_3^*,\\
&\lambda_4 I_4^* S^* + A_5\delta_{54} I_4^* + A_1\delta_{14} I_4^* + A_2\delta_{24} I_4^* + A_3\delta_{34} I_4^* = A_4\delta_{44} I_4^*,\\
&\lambda_5 I_5^* S^* + A_6\delta_{65} I_5^* + A_1\delta_{15} I_5^* + A_2\delta_{25} I_5^* + A_3\delta_{35} I_5^* + A_4\delta_{45} I_5^* = A_5\delta_{55} I_5^*,\\
&\lambda_6 I_6^* S^* + A_1\delta_{16} I_6^* + A_2\delta_{26} I_6^* + A_3\delta_{36} I_6^* + A_4\delta_{46} I_6^* + A_5\delta_{56} I_6^* = A_6\delta_{66} I_6^*.
\end{aligned} \tag{17}$$

Multiplying both sides by A_i for each equation in (10) except the first one and $A_1 = 1$, we get

$$\begin{aligned}
&\sum_{i=1}^{6} \lambda_i I^* S^* + A_1\delta_{12} I_2^* + A_1\delta_{13} I_3^* + A_1\delta_{14} I_4^* + A_1\delta_{15} I_5^* + A_1\delta_{16} I_6^* = A_1\delta_{11} I_1^*,\\
&A_2\delta_{21} I_1^* + A_2\delta_{23} I_3^* + A_2\delta_{24} I_4^* + A_2\delta_{25} I_5^* + A_2\delta_{26} I_6^* = A_2\delta_{22} I_2^*,\\
&A_3\delta_{32} I_2^* + A_3\delta_{34} I_4^* + A_3\delta_{35} I_5^* + A_3\delta_{36} I_6^* = A_3\delta_{33} I_3^*,\\
&A_4\delta_{43} I_3^* + A_4\delta_{45} I_5^* + A_4\delta_{46} I_6^* = A_4\delta_{44} I_4^*,\\
&A_5\delta_{54} I_4^* + A_5\delta_{56} I_6^* = A_5\delta_{55} I_5^*,\\
&A_6\delta_{65} I_5^* = A_6\delta_{66} I_6^*.
\end{aligned} \tag{18}$$

For any i ($i = 2, \ldots, 5$), adding all equations in (17) except the first $i-1$ equations and substracting the sum of all equations in (18) except the first i equations, we have

$$\begin{aligned}
A_i\delta_{ii} I_i^* &= \sum_{k=i}^{6} A_k\delta_{kk} I_k^* - \sum_{k=i+1}^{6} A_k\delta_{kk} I_k^*\\
&= \sum_{k=i}^{6} \lambda_k I_k^* S^* + \sum_{k=1}^{i-1} A_k \sum_{j=i}^{6} \delta_{kj} I_j^* + A_i \sum_{k=i+1}^{6} \delta_{ik} I_k^*.
\end{aligned} \tag{19}$$

This finishes the proof. □

Proposition 5.4. *W_2 in (14) can be simplified as*

$$\begin{aligned}
W_2 = {} & 2\lambda_1 I_1^* S^* + 3\lambda_2 I_2^* S^* + 4\lambda_3 I_3^* S^* + 5\lambda_4 I_4^* S^* + 6\lambda_5 I_5^* S^* + 7\lambda_6 I_6^* S^*\\
& + 2A_1\delta_{12} I_2^* + 3A_1\delta_{13} I_3^* + 4A_1\delta_{14} I_4^* + 5A_1\delta_{15} I_5^* + 6A_1\delta_{16} I_6^*\\
& + 2A_2\delta_{23} I_3^* + 3A_2\delta_{24} I_4^* + 4A_2\delta_{25} I_5^* + 5A_2\delta_{26} I_6^*\\
& + 2A_3\delta_{34} I_4^* + 3A_3\delta_{35} I_5^* + 4A_3\delta_{36} I_6^*\\
& + 2A_4\delta_{45} I_5^* + 3A_4\delta_{46} I_6^*\\
& + 2A_5\delta_{56} I_6^*.
\end{aligned} \tag{20}$$

Proof. Substituting the first equation of (18) into W_2 we have

$$W_2 = 2\sum_{i=1}^{6} \lambda_i I_i^* S^* + A_1 \sum_{i=2}^{6} \delta_{1i} I_i^* + \sum_{i=2}^{5} A_i\delta_{ii} I_i^* + A_6\delta_{66} I_6^*. \tag{21}$$

By Lemma 5.3,

$$\begin{aligned}
A_2\delta_{22} I_2^* &= \sum_{i=2}^{6} \lambda_i I_i^* S^* + A_1 \sum_{i=2}^{6} \delta_{1i} I_i^* + A_2 \sum_{i=3}^{6} \delta_{2i} I_i^*,\\
A_3\delta_{33} I_3^* &= \sum_{i=3}^{6} \lambda_i I_i^* S^* + A_1 \sum_{i=3}^{6} \delta_{1i} I_i^* + A_2 \sum_{i=3}^{6} \delta_{2i} I_i^* + A_3 \sum_{i=4}^{6} \delta_{3i} I_i^*,\\
A_4\delta_{44} I_4^* &= \sum_{i=4}^{6} \lambda_i I_i^* S^* + A_1 \sum_{i=4}^{6} \delta_{1i} I_i^* + A_2 \sum_{i=4}^{6} \delta_{2i} I_i^* + A_3 \sum_{i=4}^{6} \delta_{3i} I_i^* + A_4 \sum_{i=5}^{6} \delta_{4i} I_i^*,\\
A_5\delta_{55} I_5^* &= \sum_{i=5}^{6} \lambda_i I_i^* S^* + A_1 \sum_{i=5}^{6} \delta_{1i} I_i^* + A_2 \sum_{i=5}^{6} \delta_{2i} I_i^* + A_3 \sum_{i=5}^{6} \delta_{3i} I_i^* + A_4 \sum_{i=5}^{6} \delta_{4i} I_i^* + A_5 \sum_{i=6}^{6} \delta_{5i} I_i^*.
\end{aligned} \tag{22}$$

From the last equation of (17) we obtain

$$A_6\delta_{66}I_6^* = \sum_{i=6}^{6}\lambda_i I_i^* S^* + A_1\sum_{i=6}^{6}\delta_{1i}I_i^* + A_2\sum_{i=6}^{6}\delta_{2i}I_i^* + A_3\sum_{i=6}^{6}\delta_{3i}I_i^* + A_4\sum_{i=6}^{6}\delta_{4i}I_i^* + A_5\sum_{i=6}^{6}\delta_{5i}I_i^*. \tag{23}$$

Substituting (22) and (23) into (21), we have

$$\begin{aligned} W_2 &= 2\sum_{i=1}^{6}\lambda_i I_i^* S^* + A_1\sum_{i=2}^{6}\delta_{1i}I_i^* \\ &\quad + \sum_{i=2}^{6}\lambda_i I_i^* S^* + A_1\sum_{i=2}^{6}\delta_{1i}I_i^* + A_2\sum_{i=3}^{6}\delta_{2i}I_i^* \\ &\quad + \sum_{i=3}^{6}\lambda_i I_i^* S^* + A_1\sum_{i=3}^{6}\delta_{1i}I_i^* + A_2\sum_{i=3}^{6}\delta_{2i}I_i^* + A_3\sum_{i=4}^{6}\delta_{3i}I_i^* \\ &\quad + \sum_{i=4}^{6}\lambda_i I_i^* S^* + A_1\sum_{i=4}^{6}\delta_{1i}I_i^* + A_2\sum_{i=4}^{6}\delta_{2i}I_i^* + A_3\sum_{i=4}^{6}\delta_{3i}I_i^* + A_4\sum_{i=5}^{6}\delta_{4i}I_i^* \\ &\quad + \sum_{i=5}^{6}\lambda_i I_i^* S^* + A_1\sum_{i=5}^{6}\delta_{1i}I_i^* + A_2\sum_{i=5}^{6}\delta_{2i}I_i^* + A_3\sum_{i=5}^{6}\delta_{3i}I_i^* + A_4\sum_{i=5}^{6}\delta_{4i}I_i^* + A_5\sum_{i=6}^{6}\delta_{5i}I_i^* \\ &\quad + \sum_{i=6}^{6}\lambda_i I_i^* S^* + A_1\sum_{i=6}^{6}\delta_{1i}I_i^* + A_2\sum_{i=6}^{6}\delta_{2i}I_i^* + A_3\sum_{i=6}^{6}\delta_{3i}I_i^* + A_4\sum_{i=6}^{6}\delta_{4i}I_i^* + A_5\sum_{i=6}^{6}\delta_{5i}I_i^*. \end{aligned} \tag{24}$$

Simplifying W_2 in (24), we obtain

$$\begin{aligned} W_2 &= \sum_{i=1}^{6}(i+1)\lambda_i I_i^* S^* + 2A_1\delta_{12}I_2^* + 3A_1\delta_{13}I_3^* + 4A_1\delta_{14}I_4^* + 5A_1\delta_{15}I_5^* + 6A_1\delta_{16}I_6^* \\ &\quad + 2A_2\delta_{23}I_3^* + 3A_2\delta_{24}I_4^* + 4A_2\delta_{25}I_5^* + 5A_2\delta_{26}I_6^* + 2A_3\delta_{34}I_4^* + 3A_3\delta_{35}I_5^* + 4A_3\delta_{36}I_6^* \\ &\quad + 2A_4\delta_{45}I_5^* + 3A_4\delta_{46}I_6^* + 2A_5\delta_{56}I_6^*. \end{aligned}$$

This finishes the proof. □

Proposition 5.5. *The following groups of partition of unity hold:*

$$x_k^{(2)} = \frac{\lambda_{k+1}I_{k+1}^* S^*}{A_2\delta_{21}I_1^*}, \quad (k = 1, \ldots, 5), \qquad x_k^{(2)} = \frac{A_1\delta_{1,k-4}I_{k-4}^*}{A_2\delta_{21}I_1^*}, \quad (k = 6, \ldots, 10),\ x_k^{(2)} > 0,\ \sum_{k=1}^{10} x_k^{(2)} = 1. \tag{25}$$

$$\begin{aligned} x_k^{(3)} &= \frac{\lambda_{k+2}I_{k+2}^* S^*}{A_3\delta_{32}I_2^*}, \quad (k = 1, \ldots, 4), \qquad x_k^{(3)} = \frac{A_1\delta_{1,k-2}I_{k-2}^*}{A_3\delta_{32}I_2^*}, \quad (i = 5, \ldots, 8), \\ x_k^{(3)} &= \frac{A_2\delta_{2,k-6}I_{k-6}^*}{A_3\delta_{32}I_2^*}, \quad (k = 9, \ldots, 12),\ x_k^{(3)} > 0,\ \textit{and}\ \sum_{k=1}^{12} x_k^{(3)} = 1. \end{aligned} \tag{26}$$

$$\begin{aligned} x_k^{(4)} &= \frac{\lambda_{k+3}I_{k+3}^* S^*}{A_4\delta_{43}I_3^*}, \quad (k = 1, 2, 3), \qquad x_k^{(4)} = \frac{A_1\delta_{1,k}I_k^*}{A_4\delta_{43}I_3^*}, \quad (k = 4, 5, 6), \\ x_k^{(4)} &= \frac{A_2\delta_{2,k-3}I_{k-3}^*}{A_4\delta_{43}I_3^*}, \quad (k = 7, 8, 9), \qquad x_k^{(4)} = \frac{A_3\delta_{3,k-6}I_{k-6}^*}{A_4\delta_{43}I_3^*}, \quad (k = 10, 11, 12),\ x_k^{(4)} > 0,\ \textit{and}\ \sum_{k=1}^{12} x_k^{(4)} = 1. \end{aligned} \tag{27}$$

$$\begin{aligned} x_k^{(5)} &= \frac{\lambda_{k+4}I_{k+4}^* S^*}{A_5\delta_{54}I_5^*}, \quad (k = 1, 2), \qquad x_k^{(5)} = \frac{A_1\delta_{1,k+2}I_{k+2}^*}{A_5\delta_{54}I_4^*}, \quad (k = 3, 4), \qquad x_k^{(5)} = \frac{A_2\delta_{2,k}I_k^*}{A_5\delta_{54}I_4^*}, \quad (k = 5, 6), \\ x_k^{(5)} &= \frac{A_3\delta_{3,k-2}I_{k-2}^*}{A_5\delta_{54}I_4^*}, \quad (k = 7, 8), \qquad x_k^{(5)} = \frac{A_4\delta_{4,k-4}I_{k-4}^*}{A_5\delta_{54}I_4^*}, \quad (k = 9, 10),\ x_k^{(5)} > 0,\ \textit{and}\ \sum_{k=1}^{10} x_k^{(5)} = 1. \end{aligned} \tag{28}$$

$$\begin{aligned} &x_1^{(6)} = \frac{\lambda_6 I_6^* S^*}{A_6\delta_{65} I_6^*}, \qquad x_2^{(6)} = \frac{A_1\delta_{16} I_6^*}{A_6\delta_{65} I_6^*}, \qquad x_3^{(6)} = \frac{A_2\delta_{26} I_6^*}{A_6\delta_{65} I_6^*}, \qquad x_4^{(6)} = \frac{A_3\delta_{36} I_6^*}{A_6\delta_{65} I_6^*}, \\ &x_5^{(6)} = \frac{A_4\delta_{46} I_6^*}{A_6\delta_{65} I_6^*}, \qquad x_6^{(6)} = \frac{A_5\delta_{56} I_6^*}{A_6\delta_{65} I_6^*}, \quad x_k^{(6)} > 0, \ \textit{and} \ \sum_{k=1}^{6} x_k^{(6)} = 1. \end{aligned} \tag{29}$$

Proof. Combining (17) and (18) gives a system of equations

$$\begin{aligned} A_2\delta_{21} I_1^* &= \sum_{i=2}^{6} \lambda_i I^* S^* + A_1\delta_{12} I_2^* + A_1\delta_{13} I_3^* + A_1\delta_{14} I_4^* + A_1\delta_{15} I_5^* + A_1\delta_{16} I_6^*, \lambda_2 I_2^* S^* + A_3\delta_{32} I_2^* + A_1\delta_{12} I_2^* \\ &= A_2\delta_{21} I_1^* + A_2\delta_{23} I_3^* + A_2\delta_{24} I_4^* + A_2\delta_{25} I_5^* + A_2\delta_{26} I_6^*, \lambda_3 I_3^* S^* + A_4\delta_{43} I_3^* + A_1\delta_{13} I_3^* + A_2\delta_{23} I_3^* \\ &= A_3\delta_{32} I_2^* + A_3\delta_{34} I_4^* + A_3\delta_{35} I_5^* + A_3\delta_{36} I_6^*, \lambda_4 I_4^* S^* + A_5\delta_{54} I_4^* + A_1\delta_{14} I_4^* + A_2\delta_{24} I_4^* + A_3\delta_{34} I_4^* \\ &= A_4\delta_{43} I_3^* + A_4\delta_{45} I_5^* + A_4\delta_{46} I_6^*, \lambda_5 I_5^* S^* + A_6\delta_{65} I_5^* + A_1\delta_{15} I_5^* + A_2\delta_{25} I_5^* + A_3\delta_{35} I_5^* + A_4\delta_{45} I_5^* \\ &= A_5\delta_{54} I_4^* + A_5\delta_{56} I_6^*, \lambda_6 I_6^* S^* + A_1\delta_{16} I_6^* + A_2\delta_{26} I_6^* + A_3\delta_{36} I_6^* + A_4\delta_{46} I_6^* + A_5\delta_{56} I_6^* \\ &= A_6\delta_{65} I_5^*. \end{aligned} \tag{30}$$

The first equation of (30) gives (25). Adding the first two equations in (30) leads to

$$A_3\delta_{32} I_2^* = \sum_{i=3}^{6} \lambda_i I_i^* S^* + \sum_{i=3}^{6} A_1\delta_{1i} I_i^* + \sum_{i=3}^{6} A_2\delta_{2i} I_i^*,$$

and thus (26) follows. Similarly, adding the first three equations in (30), we get

$$A_4\delta_{43} I_3^* = \sum_{i=4}^{6} \lambda_i I_i^* S^* + \sum_{i=4}^{6} A_1\delta_{1i} I_i^* + \sum_{i=4}^{6} A_2\delta_{2i} I_i^* + \sum_{i=4}^{6} A_3\delta_{3i} I_i^*,$$

which gives (27). Adding the first four equations in (30), we obtain

$$A_5\delta_{54} I_4^* = \sum_{i=5}^{6} \lambda_i I_i^* S^* + \sum_{i=5}^{6} A_1\delta_{1i} I_i^* + \sum_{i=5}^{6} A_2\delta_{2i} I_i^* + \sum_{i=5}^{6} A_3\delta_{3i} I_i^* + \sum_{i=5}^{6} A_4\delta_{4i} I_i^*,$$

and this leads to (28). Adding the first five equations in (30) gives

$$A_6\delta_{65} I_5^* = \lambda_6 I_6^* S^* + A_1\delta_{16} I_6^* + A_2\delta_{26} I_6^* + A_3\delta_{36} I_6^* + A_4\delta_{46} I_6^* + A_5\delta_{56} I_6^*,$$

and we arrive at (29). This finishes the proof. □

Proposition 5.6. *The following partitions of unity hold:*

$$\begin{aligned} \sum_{i=2}^{6} A_i \frac{\delta_{i,i-1} I_{i-1} I_i^*}{I_i} &= \sum_{i=2}^{6} A_i \left(\sum_{k=1}^{7-i} x_k^{(i)}\right) \frac{\delta_{i,i-1} I_{i-1} I_i^*}{I_i} + \sum_{i=2}^{6} A_i \left(\sum_{k=8-i}^{14-2i} x_k^{(i)}\right) \frac{\delta_{i,i-1} I_{i-1} I_i^*}{I_i} \\ &\quad + \sum_{i=3}^{6} A_i \left(\sum_{k=15-2i}^{21-3i} x_k^{(i)}\right) \frac{\delta_{i,i-1} I_{i-1} I_i^*}{I_i} + \sum_{i=4}^{6} A_i \left(\sum_{k=22-3i}^{28-4i} x_k^{(i)}\right) \frac{\delta_{i,i-1} I_{i-1} I_i^*}{I_i} \\ &\quad + \sum_{i=5}^{6} A_i \left(\sum_{k=29-4i}^{35-5i} x_k^{(i)}\right) \frac{\delta_{i,i-1} I_{i-1} I_i^*}{I_i} + A_6 x_6^{(6)} \frac{\delta_{65} I_5 I_6^*}{I_6}. \end{aligned} \tag{31}$$

Proof. From Proposition 5.5, we have

$$A_2 = A_2 \sum_{k=1}^{10} x_k^{(2)}, \qquad A_3 = A_3 \sum_{k=1}^{12} x_k^{(3)}, \qquad A_4 = A_4 \sum_{k=1}^{12} x_k^{(4)}, \qquad A_5 = A_5 \sum_{k=1}^{10} x_k^{(5)}, \qquad A_6 = A_6 \sum_{k=1}^{6} x_k^{(6)}.$$

Thus

$$\begin{aligned} \sum_{i=2}^{6} A_i \delta_{i,i-1} I_{i-1} \frac{I_i^*}{I_i} &= \sum_{i=2}^{6} A_i \left(\sum_{k} x_k^{(i)}\right) \frac{\delta_{i,i-1} I_{i-1} I_i^*}{I_i} \\ &= A_2 \left(\sum_{k=1}^{10} x_k^{(2)}\right) \frac{\delta_{21} I_1 I_2^*}{I_2} + A_3 \left(\sum_{k=1}^{12} x_k^{(3)}\right) \frac{\delta_{32} I_2 I_3^*}{I_3} + A_4 \left(\sum_{k=1}^{12} x_k^{(4)}\right) \frac{\delta_{43} I_3 I_4^*}{I_4} \end{aligned}$$

$$
\begin{aligned}
&+A_5\left(\sum_{k=1}^{10}x_k^{(5)}\right)\frac{\delta_{54}I_4I_5^*}{I_5}+A_6\left(\sum_{k=1}^{6}x_k^{(6)}\right)\frac{\delta_{65}I_5I_6^*}{I_6}\\
&=\sum_{i=2}^{6}A_i\left(\sum_{k=1}^{7-i}x_k^{(i)}\right)\frac{\delta_{i,i-1}I_{i-1}I_i^*}{I_i}+\sum_{i=2}^{6}A_i\left(\sum_{k=8-i}^{14-2i}x_k^{(i)}\right)\frac{\delta_{i,i-1}I_{i-1}I_i^*}{I_i}\\
&\quad+\sum_{i=3}^{6}A_i\left(\sum_{k=15-2i}^{21-3i}x_k^{(i)}\right)\frac{\delta_{i,i-1}I_{i-1}I_i^*}{I_i}+\sum_{i=4}^{6}A_i\left(\sum_{k=22-3i}^{28-4i}x_k^{(i)}\right)\frac{\delta_{i,i-1}I_{i-1}I_i^*}{I_i}\\
&\quad+\sum_{i=5}^{6}A_i\left(\sum_{k=29-4i}^{35-5i}x_k^{(i)}\right)\frac{\delta_{i,i-1}I_{i-1}I_i^*}{I_i}+A_6x_6^{(6)}\frac{\delta_{65}I_5I_6^*}{I_6}. \qquad (32)
\end{aligned}
$$

This completes the proof. □

Continuing the proof of Theorem 5.1, we want to show that $W_4 \le -W_2$. Noting $A_1 = 1$ and applying Proposition 5.6 to W_4 in (14), we have

$$
\begin{aligned}
W_4 &= -\sum_{i=1}^{6}\lambda_iI_i^*\frac{S^{*2}}{S}-A_1\sum_{i=1}^{6}\lambda_iI_iS\frac{I_1^*}{I_1}-\sum_{i=2}^{6}A_i\delta_{i,i-1}I_{i-1}\frac{I_i^*}{I_i}-\sum_{i=1}^{6}A_i\sum_{k=i+1}^{6}\delta_{ik}I_k\frac{I_i^*}{I_i}\\
&= -\sum_{i=1}^{6}\lambda_iI_i^*\frac{S^{*2}}{S}-\sum_{i=1}^{6}\lambda_iI_iS\frac{I_1^*}{I_1}-\sum_{i=2}^{6}A_i\left(\sum_{k=1}^{7-i}x_k^{(i)}\right)\frac{\delta_{i,i-1}I_{i-1}I_i^*}{I_i}\\
&\quad -A_1\sum_{k=2}^{6}\frac{\delta_{1k}I_kI_1^*}{I_1}-\sum_{i=2}^{6}A_i\left(\sum_{k=8-i}^{14-2i}x_k^{(i)}\right)\frac{\delta_{i,i-1}I_{i-1}I_i^*}{I_i}\\
&\quad -A_2\sum_{k=3}^{6}\frac{\delta_{2k}I_kI_2^*}{I_2}-\sum_{i=3}^{6}A_i\left(\sum_{k=15-2i}^{21-3i}x_k^{(i)}\right)\frac{\delta_{i,i-1}I_{i-1}I_i^*}{I_i}\\
&\quad -A_3\sum_{k=4}^{6}\frac{\delta_{3k}I_kI_3^*}{I_3}-\sum_{i=4}^{6}A_i\left(\sum_{k=22-3i}^{28-4i}x_k^{(i)}\right)\frac{\delta_{i,i-1}I_{i-1}I_i^*}{I_i}\\
&\quad -A_4\sum_{k=5}^{6}\frac{\delta_{4k}I_kI_4^*}{I_4}-\sum_{i=5}^{6}A_i\left(\sum_{k=29-4i}^{35-5i}x_k^{(i)}\right)\frac{\delta_{i,i-1}I_{i-1}I_i^*}{I_i}\\
&\quad -A_5\sum_{k=6}^{6}\frac{\delta_{5k}I_kI_5^*}{I_5}-A_6x_6^{(6)}\frac{\delta_{65}I_5I_6^*}{I_6}\\
&\doteq I_1+I_2+I_3+I_4+I_5+I_6. \qquad (33)
\end{aligned}
$$

Using the inequality $a_1 + a_2 + \cdots + a_n \ge n\sqrt[n]{a_1a_2\cdots a_n}$, for $a_i \ge 0$, $i = 1, \ldots, n$, we obtain

$$
W_0 = d_0S^*\left(2-\frac{S^*}{S}-\frac{S}{S^*}\right)\le 0. \qquad (34)
$$

Similarly, using (25)–(29), we have

$$
I_1 = -\sum_{i=1}^{6}\lambda_iI_i^*\frac{S^{*2}}{S}-\sum_{i=1}^{6}\lambda_iI_iS\frac{I_1^*}{I_1}-\sum_{i=2}^{6}A_i\left(\sum_{k=1}^{7-i}x_k^{(i)}\right)\frac{\delta_{i,i-1}I_{i-1}I_i^*}{I_i}\le-\sum_{i=1}^{6}(i+1)\lambda_iI_i^*S^*. \qquad (35)
$$

Similarly,

$$
\begin{aligned}
I_2 &= -A_1\sum_{k=2}^{6}\frac{\delta_{1k}I_kI_1^*}{I_1}-\sum_{i=2}^{6}A_i\left(\sum_{k=8-i}^{14-2i}x_k^{(i)}\right)\frac{\delta_{i,i-1}I_{i-1}I_i^*}{I_i}\\
&= -A_1\frac{\delta_{12}I_2I_1^*}{I_1}-A_2\sum_{k=6}^{10}x_k^{(2)}\frac{\delta_{21}I_1I_2^*}{I_2}-A_1\frac{\delta_{13}I_3I_1^*}{I_1}-A_3\sum_{k=5}^{8}x_k^{(3)}\frac{\delta_{32}I_2I_3^*}{I_3}\\
&\quad -A_1\frac{\delta_{14}I_4I_1^*}{I_1}-A_4\sum_{k=4}^{6}x_k^{(4)}\frac{\delta_{43}I_3I_4^*}{I_4}-A_1\frac{\delta_{15}I_5I_1^*}{I_1}-A_5\sum_{k=3}^{4}x_k^{(5)}\frac{\delta_{54}I_4I_5^*}{I_5}
\end{aligned}
$$

$$
\begin{aligned}
&-A_1\frac{\delta_{16}I_6I_1^*}{I_1}-A_6\sum_{k=2}^{2}x_k^{(2)}\frac{\delta_{65}I_5I_6^*}{I_6}\\
=&\left(-A_1\frac{\delta_{12}I_2I_1^*}{I_1}-A_2x_6^{(2)}\frac{\delta_{21}I_1I_2^*}{I_2}\right)\\
&+\left(-A_1\frac{\delta_{13}I_3I_1^*}{I_1}-A_2x_7^{(2)}\frac{\delta_{21}I_1I_2^*}{I_2}-A_3x_5^{(3)}\frac{\delta_{32}I_2I_3^*}{I_3}\right)\\
&+\left(-A_1\frac{\delta_{14}I_4I_1^*}{I_1}-A_2x_8^{(2)}\frac{\delta_{21}I_1I_2^*}{I_2}-A_3x_6^{(3)}\frac{\delta_{32}I_2I_3^*}{I_3}-A_4x_4^{(4)}\frac{\delta_{43}I_3I_4^*}{I_4}\right)\\
&+\left(-A_1\frac{\delta_{15}I_5I_1^*}{I_1}-A_2x_9^{(2)}\frac{\delta_{21}I_1I_2^*}{I_2}-A_3x_7^{(3)}\frac{\delta_{32}I_2I_3^*}{I_3}-A_4x_5^{(4)}\frac{\delta_{43}I_3I_4^*}{I_4}-A_5x_3^{(5)}\frac{\delta_{54}I_4I_5^*}{I_5}\right)\\
&+\left(-A_1\frac{\delta_{16}I_6I_1^*}{I_1}-A_2x_{10}^{(2)}\frac{\delta_{21}I_1I_2^*}{I_2}-A_3x_8^{(3)}\frac{\delta_{32}I_2I_3^*}{I_3}-A_4x_6^{(4)}\frac{\delta_{43}I_3I_4^*}{I_4}-A_5x_4^{(5)}\frac{\delta_{54}I_4I_5^*}{I_5}-A_6x_2^{(2)}\frac{\delta_{65}I_5I_6^*}{I_6}\right)\\
\le&-\left[2A_1\delta_{12}I_2^*+3A_1\delta_{13}I_3^*+4A_1\delta_{14}I_4^*+5A_1\delta_{15}I_5^*+6A_1\delta_{16}I_6^*\right].
\end{aligned}
\tag{36}
$$

Furthermore,

$$
\begin{aligned}
I_3&=-A_2\sum_{k=3}^{6}\frac{\delta_{2k}I_kI_2^*}{I_2}-\sum_{i=3}^{6}A_i\left(\sum_{k=15-2i}^{21-3i}x_k^{(i)}\right)\frac{\delta_{i,i-1}I_{i-1}I_i^*}{I_i}\\
&\le-\left[2A_2\delta_{23}I_3^*+3A_2\delta_{24}I_4^*+4A_2\delta_{25}I_5^*+5A_2\delta_{26}I_6^*\right],\\
I_4&=-A_3\sum_{k=4}^{6}\frac{\delta_{3k}I_kI_3^*}{I_3}-\sum_{i=4}^{6}A_i\left(\sum_{k=22-3i}^{28-4i}x_k^{(i)}\right)\frac{\delta_{i,i-1}I_{i-1}I_i^*}{I_i}\\
&\le-\left[2A_3\delta_{34}I_4^*+3A_3\delta_{35}I_5^*+4A_3\delta_{36}I_6^*\right],\\
I_5&=-A_4\sum_{k=5}^{6}\frac{\delta_{4k}I_kI_4^*}{I_4}-\sum_{i=5}^{6}A_i\left(\sum_{k=29-4i}^{35-5i}x_k^{(i)}\right)\frac{\delta_{i,i-1}I_{i-1}I_i^*}{I_i}\\
&\le-\left[2A_4\delta_{45}I_5^*+3A_4\delta_{46}I_6^*\right],\\
I_6&=-A_5\frac{\delta_{56}I_6I_5^*}{I_5}-A_6x_6^{(6)}\frac{\delta_{65}I_5I_6^*}{I_6}\\
&\le-2A_5\delta_{56}I_6^*.
\end{aligned}
\tag{37}
$$

By Proposition 5.4 and (34)–(37), we arrive at

$$\frac{\mathrm{d}W}{\mathrm{d}t}\le W_0+W_2+W_4\le 0,$$

for all solution $(S(t),I_1(t),\dots,I_6(t))$ in Int Γ. Furthermore, $\frac{\mathrm{d}W}{\mathrm{d}t}=0$, if and only if equalities hold in (34)–(37). This implies $S=S^*$ and $I_i=aI_i^*,\ i=1,\dots,6$, for some positive a. Substituting $S=S^*$ and $I_i=aI_i^*,\ i=1,\dots,6$ into the first equation of system (4) we obtain

$$\Lambda=d_0S^*+a\sum_{i=1}^{6}\lambda_iI_i^*S^*.$$

Since the right hand side is strictly monotone in a, the equality can only hold at $a=1$, namely, at the endemic equilibrium P^*. This shows that the largest compact invariant set where $\mathrm{d}W/\mathrm{d}t=0$ is the singleton $\{P^*\}$, and thus P^* is globally stable in IntΓ by the LaSalle's Invariance Principle [23]. This completes the proof of Theorem 5.1. □

We note that in the case of no amelioration, namely, $\delta_{ij}=0,\ i<j,\ i=1,\dots,5$, Theorem 5.1 includes a global-stability result in [24] for $n=6$. In the case of partial amelioration, namely, $\delta_{ij}=0,\ j>1+i,\ i=1,\dots,4$, but $\delta_{i,i+1}\neq 0,\ i=1,\dots,5$, Theorem 5.1 includes a global-stability result of [18] for $n=6$. Our global-stability results generalized those in [18,15,25,26]. We remark that the proof of main theorem can be easily extended to an n-stage SP model with amelioration, except for more complicated notations. The form of Lyapunov functions utilized in our proof have been used in the literature of ecological models [27–29], and recently been applied successfully to epidemic models [30,24,18,31,32,3].

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Appendix

The following definition and properties of M-matrices are used in our analysis. They can be found in most of the texts on matrix theory, see e.g. [33].

Definition. $B_{n\times n}$ is a M-matrix if

(1) Off-diagonal entries of B are non-positive, and
(2) B is positively stable, namely, all eigenvalues of B have positive real parts.

Proposition. *Properties of M-matrices*

(1) $B = \alpha I - P,\ P \geq 0,\ \alpha > \rho(P)$, *the spectral radius of* P.
(2) B *is nonsingular and* $B^{-1} \geq 0$.
(3) *There exists* $\beta > 0$ *such that* $B^{-1}x \geq \beta x$ *for* $x \geq 0$.

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