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Effect of Educational Programs on Illicit Drug Epidemics

Reza Memarbashi[1], Malek Pourhosseini[2]
Department of Mathematics,
Semnan University, Semnan, Iran.
Email: r memarbashi@semnan.ac.ir

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Abstract. In this paper, we propose and analyze an epidemic model considering the effect of educational programs on the control of illicit drug uses. We compute the threshold quantity R_0 and determine the number of equilibrium points. By applying the center manifold theory, we show that backward bifurcation occurs in the model, further more the global stability of the equilibrium points of the model investigated using Lyapunov functions and geometric approach to stability.

AMS (MOS) Subject Classification Codes: 92D30; 34D23; 34C23
Key Words: Backward bifurcation; Global stability; Illicit drugs; Epidemic models.

1. Introduction

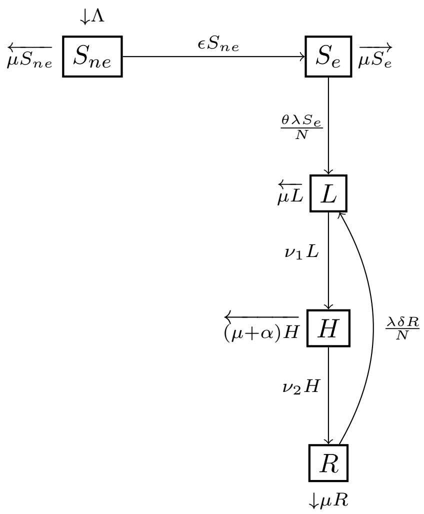
Illicit drug use is an important social and public health problem all over the world. Police records, hospital and rehabilitation centers and prisons records show the increase in harmful drug uses.
Among various drug users, individuals using heroin have a high risk of addiction. White and Comiskey, [26] study the dynamics of heroin users, by using the following system of equations.

$$\begin{cases} \dfrac{dS}{dt} = \Lambda - \frac{\beta_1 S U_1}{N} - \mu S \\ \dfrac{dU_1}{dt} = \frac{\beta_1 S U_1}{N} + \frac{\beta_3 U_1 U_2}{N} - (\mu + \delta_1 + p) U_1 \\ \dfrac{dU_2}{dt} = p U_1 - \frac{\beta_3 U_1 U_2}{N} - (\mu + \delta_2) U_2 \end{cases} \qquad (1.\ 1)$$

After White and Comiskey paper, the epidemiology of drugs has been studied by several authors, see [9, 13, 17, 19, 20, 21, 22].
In general, there exist three strategies to restrict the consumption of illicit drugs in all countries: legal strategies, educational-training, and treatment strategies. The most important educational-training activities are the increasing of awareness among peoples about the

physical, mental and social dangers of drug use. On the other hand, the treatment of drug abuse is challenging, costly and requires a comprehensive treatment and rehabilitation system. Therefore, prevention is a useful solution for the mental and physical safety of drug users. The basic presumption of preventive strategies is that prevention is remarkably easy and more effective than inappropriate drug consumption.
Nyabadza et al., in [21], introduced a modified version of White Comiskey model by dividing the drug users into two compartment, light drug users and hard drug users.
We propose and analyze a modified version of White-Comiskey model by considering the effect of education activities on the drug users and the approach of Nyabadza, et al. We study dynamical behaviors of the model such as steady states, backward bifurcation and local and global stability of steady states. In section 2 we compute the basic reproduction number. In section 3 we study the existence and number of endemic equilibriums, and backward bifurcation of our model is then verified, and in section 4 we study the global stability of equilibriums by using Lyapunov functions and geometric method.

2. Model formulation and basic properties



For the mathematical formulation of our model we suppose that the given community separates to five compartments: S_{ne} noneducated suceptibles, S_e educated suceptibles, L light drug users, H is hard drug users and R drug users in treatment and rehabilitation.
As indicated in [24], school-age and teenage years are critical regarding the experimentation with drugs and the development of behaviors that can lead to dependence and abuse in adulthood. The earlier young people start to use psychoactive substances, the more likely they are to develop drug abuse disorders in later life, [25]. Hence we assume that almost all of the education/prevention activities are concentrated on school age and teenage years, all recruited populations take the educational programs, and we can neglect the flow from S_{ne} to L.
The evolution of the life of an individual in various stages can be represented by the above

diagram, and the parameters are defined as the following.
Λ: Recruitment of susceptible individuals.
ϵ: Uptake rate into education programs.
μ: Natural death rate.
α: Drug-related death rate.
β: Probability of becoming a drug user.
ν_1: Progression rate for addiction.
ν_2: Uptake rate into treatment programs.
η: The infection rate of hard drug users compared to light drug users.
θ: The overall effectiveness of the educational programs.
δ: Level of relapse to hard drug users.
Based on the flow diagram of model depicted in the above figure, we obtain the following ODE system:

$$\begin{cases} \dfrac{dS_{ne}}{dt} = \Lambda - \epsilon S_{ne} - \mu S_{ne} \\ \dfrac{dS_e}{dt} = \epsilon S_{ne} - \dfrac{\theta\lambda S_e}{N} - \mu S_e \\ \dfrac{dL}{dt} = \dfrac{\theta\lambda S_e}{N} + \dfrac{\lambda\delta R}{N} - \nu_1 L - \mu L \\ \dfrac{dH}{dt} = \nu_1 L - \nu_2 H - (\mu+\alpha)H \\ \dfrac{dR}{dt} = \nu_2 H - \dfrac{\lambda\delta R}{N} - \mu R \end{cases} \tag{2. 2}$$

in which $\lambda = \beta(L + \eta H)$ is the force of infection. We consider the total population of the community to be constant. Let $N(t)$ be the total population, $\frac{dN}{dt} = \Lambda - \mu N(t) - \alpha H(t)$ hence $\Lambda = \mu S_{ne} + \mu S_e + \mu L + \mu H + \alpha H + \mu R$. Now we replace Λ in (2. 2), and then use the substitutions $s_{ne} = \dfrac{S_{ne}}{N}$, $s_e = \dfrac{S_e}{N}$, $l = \dfrac{L}{N}$, $h = \dfrac{H}{N}$ and $r = \dfrac{R}{N}$, which yields the following final form of our system:

$$\begin{cases} \dfrac{ds_{ne}}{dt} = \mu + \alpha h - \epsilon s_{ne} - \mu s_{ne} \\ \dfrac{ds_e}{dt} = \epsilon s_{ne} - \theta\beta(l+\eta h)s_e - \mu s_e \\ \dfrac{dl}{dt} = \theta\beta(l+\eta h)s_e + \beta\delta l - \beta\delta l s_{ne} - \beta\delta l s_e - \beta\delta l^2 - \beta\delta l h + \beta\eta\delta h \\ \qquad -\beta\eta\delta h s_{ne} - \beta\eta\delta h s_e - \beta\eta\delta l h - \beta\eta\delta h^2 - \nu_1 l - \mu l \\ \dfrac{dh}{dt} = \nu_1 l - \nu_2 h - (\mu+\alpha)h \end{cases} \tag{2. 3}$$

This system has a unique drug-free equilibrium $P_0 = (\dfrac{\mu}{\epsilon+\mu}, \dfrac{\epsilon}{(\epsilon+\mu)}, 0, 0)$. Using $X = [s_{ne}, s_e, l, h]^T$, we rewrite (2. 3) as $\frac{dX}{dt} = \mathcal{F}(X) - \mathcal{V}(X)$ where,

$$\mathcal{F}(X) = \begin{bmatrix} \theta\lambda s_e \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \mathcal{V}(X) = \begin{bmatrix} -\beta\delta lr - \beta\eta\delta hr + \nu_1 L + \mu L \\ -\nu_1 l + (\mu+\alpha)h + \nu_2 h \\ -\mu s_e - \mu l - \mu h - \alpha h - \mu r + \epsilon s_{ne} \\ -\epsilon s_{ne} + \theta\beta l s_e + \theta\beta\eta h s_e + \mu s_e \\ -\nu_2 h + \beta\delta lr + \beta\eta\delta hr + \mu r \end{bmatrix}$$

We can obtain the following linearizations F and V, at the steady state P_0:

$$F = \begin{bmatrix} \theta\beta s_e^* & \theta\beta\eta s_e^* \\ 0 & 0 \end{bmatrix}, V = \begin{bmatrix} \nu_1+\mu & 0 \\ -\nu_1 & \mu+\alpha+\nu_2 \end{bmatrix}$$

giving:

$$V^{-1} = \begin{bmatrix} \dfrac{1}{\nu_1+\mu} & 0 \\ \dfrac{\nu_1}{(\nu_1+\mu)(\nu_2+\alpha+\mu)} & \dfrac{1}{\mu+\alpha+\nu_2} \end{bmatrix}$$

hence, the next-generation matrix for the model (2. 3) has the following form,

$$FV^{-1} = \begin{bmatrix} \dfrac{\theta\beta s_e^*}{\nu_1+\mu} + \dfrac{\theta\beta\eta\nu_1 s_e^*}{(\nu_1+\mu)(\nu_2+\alpha+\mu)} & \dfrac{\theta\beta\eta s_e^*}{\nu_2+\alpha+\mu} \\ 0 & 0 \end{bmatrix}$$

and Theorem 2 in [7], imply that the basic reproduction number for (2. 3) has the following form, $R_0 = \rho(FV^{-1}) = \dfrac{\theta\beta s_e^*(\nu_2+\mu+\alpha+\eta\nu_1)}{(\nu_1+\mu)(\nu_2+\mu+\alpha)}$.

Theorem 2.1. *The drug-free equilibrium point P_0 of (2. 3) has asymptotic stability when $R_0 < 1$ and instability when $R_0 > 1$.*

3. Endemic equilibrium and backward bifurcation

The endemic equilibrium points of (2. 3) satisfy the following system,

$$\begin{cases} \mu + \alpha h^* - \epsilon s_{ne}^* - \mu s_{ne}^* = 0 \\ \epsilon s_{ne}^* - \theta\beta(l^* + \eta h^*)s_e^* - \mu s_e^* = 0 \\ \theta\beta(l^*+\eta h^*)s_e^* + \beta\delta l^* - \beta\delta l^* s_{ne}^* - \beta\delta l^* s_e^* - \beta\delta(l^*)^2 - \beta\delta l^* h^* + \beta\eta\delta h^* \\ \qquad -\beta\eta\delta h^* s_{ne}^* - \beta\eta\delta h^* s_e^* - \beta\eta\delta l^* h^* - \beta\eta\delta(h^*)^2 - \nu_1 l^* - \mu l^* = 0 \\ \nu_1 l^* - \nu_2 h^* - (\mu+\alpha)h^* = 0 \end{cases}$$

which yields that, l^* is the positive root of

$$A(l^*)^3 + B(l^*)^2 + Cl^* + D = 0 \qquad (3.\ 4)$$

where

$$A = -\beta^2\delta\theta(1+q_1+q_3)(1+\eta q_1)^2,$$

$$B = \beta(1+\eta q_1)(\theta(\beta\delta(1-q_2)(1+\eta q_1)-\mu(1+q_1+q_3)(\theta+\delta)-\nu_2 q_1)-\beta\delta(\alpha q_1-\mu(1+q_1))),$$

$$C = \mu(\nu_1+\mu)R_0 - \mu(\frac{\alpha\nu_1-\mu(\mu+\nu_1)-\nu_2(\mu+\nu_1)-\mu\alpha}{\mu+\alpha+\nu_2})$$

$$D = \mu^2 - \mu^2 q_2 - \mu\epsilon q_2 = 0,$$

in which $q_1 = \dfrac{\nu_1}{\mu+\alpha+\nu_2}$, $q_2 = \dfrac{\mu}{\epsilon+\mu}$ and $q_3 = \dfrac{\alpha q_1}{\epsilon+\mu}$.
The endemic steady state exists when roots of (3. 4) are positive real numbers. Now since $A < 0$, we must have $B \geq 0, \Delta > 0$. Consider the discriminant, $\Delta = B^2 - 4AC$, solving $\Delta = 0$ in terms of R_0, we obtain:

$$R_0^c = \frac{\alpha\nu_1-\mu(\mu+\nu_1)-\nu_2(\mu+\nu_1)-\mu\alpha}{(\nu_1+\mu)(\mu+\alpha+\nu_2)} - \frac{B^2}{4\beta^2\delta\theta(1+q_1+q_3)(1+\eta q_1)^2\mu(\mu+\nu_1)}$$

We note the following relation: if $R_0 \geq 1$ then

$$C \geq \mu(\frac{(\mu+\alpha+\nu_2)(\nu_1+\mu)-\alpha\nu_1+\mu(\mu+\nu_1)+\nu_2(\mu+\nu_1)+\mu\alpha}{\mu+\alpha+\nu_2}) > 0.$$

The above arguments imply the following theorem about the endemic equilibrium points.

Theorem 3.1. *If $R_0 > 1$, system (2. 3) has a unique endemic equilibrium point, and when $R_0^c < R_0 < 1$ it has two endemic equilibrium points.*

Above theorem demonstrates that at $R_0 = 1$ bifurcation occurs. In fact, when the quantity R_0 cross $R_0 = 1$, P_0 changes its stability property.
Now we study the bifurcation of drug-free equilibrium point P_0 when $R_0 = 1$. For this study, we use the Castillo-Chavez and Song theorem which has been obtained in [5], based on center manifold theory, see also [2, 3, 4, 10, 19, 20, 21, 28, 29] for demonstration and application of this theorem.
We consider a system of ODEs,

$$\frac{dX}{dt} = f(X,\phi); f: \mathbb{R}^n \times \mathbb{R} \to \mathbb{R}^n, f \in C^2(\mathbb{R}^n \times \mathbb{R}) \qquad (3.\ 5)$$

with a parameter ϕ, and assume that 0 is a steady state of this system for all ϕ, i.e. $f(0,\phi) = 0$. Let $\mathcal{Q} = D_X f(0,0) = (\frac{\partial f_i}{\partial x_j}(0,0)$ be the Jacobian matrix of $f(X,\phi)$ at $(0,0)$.

Theorem 3.2. *Assume the following:*
(H1): 0 is a simple eigenvalue of $\mathcal{Q}$, further more the other eigenvalues of $\mathcal{Q}$ have negative real parts.
(H2): $\mathcal{Q}$ has a (non-negative) right eigenvector of the form $\mathbf{w} = (w_1, w_2, ..., w_n)^T$ and a left eigenvector of the form $\mathbf{v} = (v_1, v_2, ..., v_n)$ corresponding to the zero eigenvalue. Suppose $f_k(X,\phi)$ denote the k-th component of $f(X,\phi)$ and

$$\mathbf{a} = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0), \mathbf{b} = \sum_{k,i=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \phi}(0,0).$$

Then the quantities a and b determine the local dynamics of (3. 5) around $X = 0$ as follows:
(1): When $\mathbf{a} > 0$ and $\mathbf{b} > 0$, if $\phi < 0$ with $|\phi| \ll 1$, $X = 0$ has asymptotic stability property and also there is a positive and unstable equilibrium point, and if $0 < \phi \ll 1$, $X = 0$ is an unstable equilibrium point and also there is a negative equilibrium point which is asymptotically stable.
(2): When $\mathbf{a} < 0$ and $\mathbf{b} < 0$, if $\phi < 0$ with $|\phi| \ll 1$, $X = 0$ is an unstable equilibrium point, and if $0 < \phi \ll 1$, $X = 0$ is asymptotically stable, and there is a positive equilibrium which is unstable.
(3): When $\mathbf{a} > 0$ and $\mathbf{b} < 0$, if $\phi < 0$ with $|\phi| \ll 1$, $X = 0$ is an unstable equilibrium point and there is a negative equilibrium which is asymptotically stable. If $0 < \phi \ll 1$, $X = 0$ is asymptotically stable and there is a positive and unstable equilibrium point.
(4): When $\mathbf{a} < 0$ and $\mathbf{b} > 0$, if the sign of ϕ varies from negative to positive, then the nature of $x = 0$ varies from stability to instability. Further more, a negative and unstable steady state becomes a positive steady state which is asymptotically stable.

Nonnegativity of $\mathbf{w}$ is unnecessary, see [5].
Introducing $x_1 = s_{ne}$, $x_2 = s_e$, $x_3 = l$ and $x_4 = h$, system (2. 3) becomes,

$$\begin{cases} \dfrac{dx_1}{dt} = \mu + \alpha x_4 - \epsilon x_1 - \mu x_1 \\ \dfrac{dx_2}{dt} = \epsilon x_1 - \theta\beta x_2(x_3 + \eta x_4) - \mu x_2 \\ \dfrac{dx_3}{dt} = \theta\beta x_3 x_2 + \theta\beta\eta x_4 x_2 + \beta\delta x_3 - \beta\delta x_3 x_1 - \beta\delta x_3 x_2 - \beta\delta x_3^2 \\ \qquad -\beta\delta x_3 x_4 + \beta\eta\delta x_4 - \beta\eta\delta x_4 x_1 - \beta\eta\delta x_4 x_2 - \beta\eta\delta x_3 x_4 \\ \qquad -\beta\eta\delta x_4^2 - \nu_1 x_3 - \mu x_3 \\ \dfrac{dx_4}{dt} = \nu_1 x_3 - (\mu + \alpha) x_4 - \nu_2 x_4 \end{cases} \tag{3. 6}$$

Now we apply Th. 3.2. to show that in (3. 6) backward bifurcation occurs when $R_0 = 1$. The relation $R_0 = 1$ can be transformed to the parameter β as $\beta = \beta^* = \dfrac{(\nu_1 + \mu)(\nu_2 + \mu + \alpha)}{\theta s_e^*(\nu_2 + \mu + \alpha + \eta\nu_1)}$. The eigen values of the Jacobian matrix,

$$A = J(P_0, \beta^*) = \begin{bmatrix} -\epsilon - \mu & 0 & 0 & \alpha \\ \epsilon & -\mu & -\theta\beta^* s_e^* & -\theta\beta^*\eta s_e^* \\ 0 & 0 & \theta\beta^* s_e^* - \nu_1 - \mu & \theta\beta^*\eta s_e^* \\ 0 & 0 & \nu_1 & -\mu - \alpha - \nu_2 \end{bmatrix}$$

are $\lambda_1 = -\mu$, $\lambda_2 = -\epsilon - \mu$, $\lambda_3 = -\eta\nu_1(\nu_1 + \mu) - (\nu_2 + \mu + \alpha)(\nu_2 + \mu + \alpha + \eta\nu_1)$ and $\lambda_4 = 0$. Now since 0 is simple and nonzero eigenvalues are nonnegative real numbers, when $\beta = \beta^*$ (or $R_0 = 1$) the assumption (1) of Theorem 3.2., is verified.

Let $w = (w_1, w_2, w_3, w_4, w_5)^T$, be the right eigenvector of $J(P_0, \beta^*)$ associated with eigenvalue $\lambda_4 = 0$, founded by:

$$\begin{cases} (-\epsilon - \mu)w_1 + \alpha w_4 = 0 \\ \epsilon w_1 - \mu w_2 - \theta\beta^* s_e^* w_3 - \theta\beta^* \eta s_e^* w_4 = 0 \\ (\theta\beta^* s_e^* - \nu_1 - \mu)w_3 + (\theta\beta^* \eta s_e^*)w_4 = 0 \\ \nu_1 w_3 - (\mu + \alpha + \nu_2)w_4 = 0 \end{cases}$$

A simple computation implies, $w_1 = \dfrac{\alpha\nu_1}{\epsilon + \mu}$, $w_3 = \mu + \alpha + \nu_2$, $w_4 = \nu_1$ and
$w_2 = -\dfrac{(\nu_2 + \mu + \alpha)(\nu_1 + \mu(1 + \epsilon + \nu_1 + \mu)) + \epsilon\nu_1(\nu_2 + \mu)}{\mu(\epsilon + \mu)}$.
On the other hand, $v = (v_1, v_2, v_3, v_4, v_5)$, the left eigenvector associated with zero eigenvalue is founded by $vA = 0$, and has the following form

$$v = (0, 0, \mu + \alpha + \nu_2 - \eta\nu_1, -\eta(\nu_1 + \mu))$$

Now we compute the quantities $\mathbf{a}$ and $\mathbf{b}$ of theorem 3.2., that is ,

$$\mathbf{a} = \sum_{k,i,j=1}^{4} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(P_0, \beta^*) = -2v_3\beta(\delta_1((w_3 + \eta w_4)(w_1 + w_2) + \\ + w_4 w_3(1 + \eta) + w_3 w_3 + w_4 w_4 \eta) - \theta w_2(w_3 + \eta w_4))$$

and

$$\mathbf{b} = \sum_{k,i=1}^{4} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \phi}(P_0, \beta^*) = v_3 \theta s_e^*(w_3 + \eta w_4)$$

We observe that $\mathbf{b}$ is positive, so that, it is the sign of $\mathbf{a}$ which determines the behaviour of system around $\beta = \beta^*$. We consider

$$X_1 = \delta_1(w_4 w_3(1 + \eta) + w_3 w_3 + w_4 w_4 \eta) - \theta w_2(w_3 + \eta w_4)$$

and

$$X_2 = \delta_1(w_3 + \eta w_4)(w_1 + w_2).$$

Hence if $X_2 > X_1$, $\mathbf{a} > 0$ and $\mathbf{a} < 0$ if $X_2 < X_1$. Now theorem 3.2., imply the following result.

Theorem 3.3. *If $X_2 < X_1$, in the ODE system (3. 6), backward bifurcation occurs when $R_0 = 1$. Further more endemic equilibrium has asymptotic stability when $R_0 > 1$ and close to one.*

4. GLOBAL STABILITY OF EQUILIBRIUM POINTS

In this section, we study the global stability of steady states, both drug-free and endemic one in some cases. At first, we consider the drug-free point.

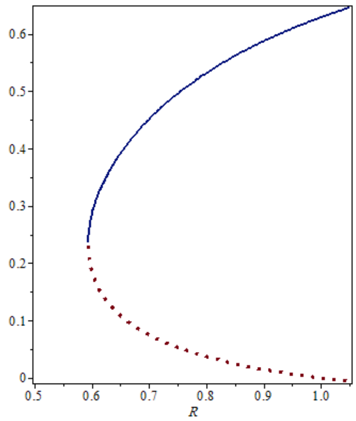


FIGURE 1. The occurence of backward bifurcation when, $\theta = \beta = \nu_1 = 0.1$, $\delta = 0.08, \nu_2 = 0.09, \mu = 0.2$, $\alpha = \eta = 0.04$ and $\epsilon = 0.4$

Lemma 4.1. *The drug-free equilibrium P_0 of the system is globally asymptotically stable if $R_0 \leq R_0^* = \dfrac{\theta s_e^*}{\theta + \delta}$.*

Proof. We consider $V(t) = a_1 l + a_2 h$ as a Lyapunov function with non-negative real numbers a and b. Then the derivative of V along the solution curves of (2. 3) has the following form,

$$\begin{aligned}\frac{dV}{dt} =& a_1\frac{dl}{dt} + a_2\frac{dh}{dt} \leq (a_1(\beta(\theta+\delta) - (\nu_1+\mu)) + a_2\nu_1)l \\ &+ (a_1(\beta\eta(\theta+\delta)) - a_2(\nu_2+\mu+\alpha))h.\end{aligned}$$

Now we choose the coefficients a_1, a_2, with the zero coefficient of h. Hence we obtain

$$a_1 = \nu_2 + \mu + \alpha, a_2 = \beta\eta(\theta+\delta).$$

By substituting these values, the derivative of V can be expressed as:

$$\begin{aligned}\frac{dV}{dt} \leq& (\beta(\theta+\delta)(\nu_2+\mu+\alpha) - (\nu_1+\mu)(\nu_2+\mu+\alpha) + \beta\eta(\theta+\delta)\nu_1)l \\ =& (\beta(\theta+\delta)(\nu_2+\mu+\alpha+\eta\nu_1) - (\nu_1+\mu)(\nu_2+\mu+\alpha))l \\ =& (\nu_1+\mu)(\nu_2+\mu+\alpha)(\frac{R_0(\theta+\delta)}{\theta s_e^*} - 1)l\end{aligned}$$

Clearly, $\dfrac{dV}{dt} \leq 0$ when $R_0 \leq R_0^* = \dfrac{\theta s_e^*}{\theta+\delta}$. Furthermore, $\dfrac{dV}{dt} = 0$ if and only if $L = H = 0$.

Now we present the geometric method for the global stability problem, see [1, 3, 4, 10, 14, 15, 29]. Let us denote unit ball of $\mathbb{R}^2$ and its boundary and clousure by, $\mathcal{B}$, $\partial\mathcal{B}$, and

$\bar{\mathcal{B}}$ respectively. We also denote the collection of all Lipschitzian functions from X to Y, by $Lip(X \to Y)$. We consider a function $\phi \in Lip(\bar{\mathcal{B}} \to \Omega)$ as a simply connected and rectifiable surface in $\Omega \subseteq \mathbb{R}^n$. A closed and rectifiable curve in Ω, can be described as a function $\phi \in Lip(\partial\mathcal{B} \to \Omega)$ and called simple if it is one to one. Suppose $\Sigma(\psi, \Omega) = \{\psi \in Lip(\bar{\mathcal{B}} \to \Omega) : \phi|_{\partial\mathcal{B}} = \psi\}$. Let Ω be an open domain which is simply connected, then $\Sigma(\psi, \Omega)$ is a nonvoid set, for any simple, closed and rectifiable curve ψ in Ω. Consider a norm $\|.\|$ on $\mathbb{R}^{\binom{n}{2}}$. We define a functional $\mathcal{S}$ on the surfaces in Ω by the following relation:

$$\mathcal{S}\phi = \int_{\bar{\mathcal{B}}} \|P \cdot (\frac{\partial \phi}{\partial u_1} \wedge \frac{\partial \phi}{\partial u_2})\| du, \tag{4. 7}$$

in which the mapping $u \mapsto \phi(u)$ is Lipschitzian on $\bar{\mathcal{B}}$, and $\frac{\partial \phi}{\partial u_1} \wedge \frac{\partial \phi}{\partial u_2}$ is the wedge product in $\mathbb{R}^{\binom{n}{2}}$. Further more the $\binom{n}{2} \times \binom{n}{2}$ matrix function P, is invertible and $\|P^{-1}\|$ is a bounded function on $\phi(\bar{\mathcal{B}})$. The following result is stated in [14].

Lemma 4.2. *For an arbitrary simple, closed and rectifiable curve ψ, in $\mathbb{R}^n$, there is $\delta > 0$ with $\mathcal{S}\psi \geq \delta$ for all $\phi \in \Sigma(\psi, \Omega)$.*

Consider the vector field $x \mapsto f(x) \in \mathbb{R}^n$, which is a C^1 function on the set $\Omega \subset \mathbb{R}^n$, and the following ODE system,

$$\frac{dx}{dt} = f(x). \tag{4. 8}$$

We consider the function $\phi_t(u) = x(t, \phi(u))$ as the solution of (4. 8) passing through $(0, \phi(u))$, for any ϕ. We define the right-hand derivative of $\mathcal{S}\phi_t$, by the following relation,

$$D_+\mathcal{S}\phi_t = \int_{\bar{\mathcal{B}}} \lim_{h \to 0^+} \frac{1}{h}(\|z + hQ(\phi_t(u))z\| - \|z\|)du, \tag{4. 9}$$

in which $Q = P_f P^{-1} + P\frac{\partial f^{[2]}}{\partial x}P^{-1}$, P_f represents the directional derivative of P in the direction of the vector field f, and $\frac{\partial f^{[2]}}{\partial x}$ denotes the second additive compound matrix of $\frac{\partial f}{\partial x}$. Furthere more we consider the following differential equation,

$$\frac{dz}{dt} = Q(\phi_t(u))z \tag{4. 10}$$

for which the solution is of the form $z = P \cdot (\frac{\partial \phi}{\partial u_1} \wedge \frac{\partial \phi}{\partial u_2})$. The formula $D_+\mathcal{S}\phi_t$ can be expressed as,

$$D_+\mathcal{S}\phi_t = \int_{\bar{\mathcal{B}}} D_+\|z\|du. \tag{4. 11}$$

The Jacobian matrix at the point (s_{ne}, s_e, l, h) is given by

$$\frac{\partial f}{\partial x} = \begin{bmatrix} a_{11} & a_{12} & a_{13} & a_{14} \\ a_{21} & a_{22} & a_{23} & a_{24} \\ a_{31} & a_{32} & a_{33} & a_{34} \\ a_{41} & a_{42} & a_{43} & a_{44} \end{bmatrix}$$

in which,
$a_{11} = -\epsilon - \mu, a_{12} = 0, a_{13} = 0, a_{14} = \alpha, a_{21} = \epsilon$

$a_{22} = -\theta\beta l - \theta\beta\eta h - \mu, a_{23} = -\theta\beta s_e, a_{24} = -\theta\beta\eta s_e$
$a_{31} = -\beta\delta l - \beta\eta\delta h, a_{32} = \theta\beta l + \theta\beta\eta h - \beta\delta l - \beta\eta\delta h$
$a_{33} = \theta\beta s_e + \beta\delta - \beta\delta s_{ne} - \beta\delta s_e - 2\beta\delta l - \beta\delta h - \beta\eta\delta h - \nu_1 - \mu$
$a_{34} = \theta\beta\eta s_e - \beta\delta l + \beta\eta\delta - \beta\eta\delta s_{ne} - \beta\eta\delta s_e - \beta\eta\delta l - 2\beta\eta\delta h$
$a_{41} = 0, a_{42} = 0, a_{43} = \nu_1, a_{44} = -\nu_2 - \mu - \alpha.$
And the second additive compound matrix of $\frac{\partial f}{\partial x}$ has the following components:

$$M = \frac{\partial f^{[2]}}{\partial x} = \begin{bmatrix} M_{11} & M_{12} & M_{13} & 0 & M_{15} & 0 \\ M_{21} & M_{22} & M_{23} & 0 & 0 & M_{26} \\ 0 & M_{32} & M_{33} & 0 & 0 & 0 \\ M_{41} & M_{42} & 0 & M_{44} & M_{45} & M_{46} \\ 0 & 0 & M_{53} & M_{54} & M_{55} & M_{56} \\ 0 & 0 & M_{63} & 0 & M_{65} & M_{66} \end{bmatrix}$$

with the following components,
$M_{11} = -\epsilon - 2\mu - \theta\beta l - \theta\beta\eta h, M_{12} = -\theta\beta s_e, M_{13} = -\theta\beta\eta s_e$
$M_{14} = 0, M_{15} = \alpha, M_{16} = 0, M_{21} = \theta\beta l + \theta\beta\eta h - \beta\delta l - \beta\eta\delta h$
$M_{22} = -\epsilon - 2\mu + \theta\beta s_e + \beta\delta - \beta\delta s_{ne} - \beta\delta s_e - 2\beta\delta l - \beta\delta h - \beta\eta\delta h - \nu_1$
$M_{23} = \theta\beta\eta s_e - \beta\delta l + \beta\eta\delta - \beta\eta\delta s_{ne} - \beta\eta\delta s_e - \beta\eta\delta l - 2\beta\eta\delta h$
$M_{24} = 0, M_{25} = 0, M_{26} = \alpha, M_{31} = 0, M_{32} = \nu_1$
$M_{33} = -\epsilon - 2\mu - \nu_2 - \alpha, M_{34} = 0, M_{35} = 0, M_{36} = 0$
$M_{41} = \beta\delta l + \beta\eta\delta h, M_{42} = \epsilon, M_{43} = 0$
$M_{44} = -\theta\beta l - \theta\beta\eta h - 2\mu + \theta\beta s_e + \beta\delta - \beta\delta s_{ne} - \beta\delta s_e - 2\beta\delta l - \beta\delta h - \beta\eta\delta h - \nu_1$
$M_{45} = \theta\beta\eta s_e - \beta\delta l + \beta\eta\delta - \beta\eta\delta s_{ne} - \beta\eta\delta s_e - \beta\eta\delta l - 2\beta\eta\delta h$
$M_{46} = \theta\beta\eta s_e, M_{51} = 0, M_{52} = 0, M_{53} = \epsilon, M_{54} = \nu_1$
$M_{55} = -\theta\beta l - \theta\beta\eta h - 2\mu - \nu_2 - \alpha, M_{56} = -\theta\beta s_e, M_{61} = 0, M_{62} = 0$
$M_{63} = -\beta\delta l - \beta\eta\delta h, M_{64} = 0, M_{65} = \theta\beta l + \theta\beta\eta h - \beta\delta l - \beta\eta\delta h$
$M_{66} = \theta\beta s_e + \beta\delta - \beta\delta s_{ne} - \beta\delta s_e - 2\beta\delta l - \beta\delta h - \beta\eta\delta h - \nu_1 - 2\mu - \nu_2 - \alpha$
Let P be the following matrix,

$$P = \begin{bmatrix} \frac{1}{l} & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{1}{l} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{1}{l} & 0 & 0 \\ 0 & 0 & \frac{1}{h} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{1}{h} & 0 \\ 0 & 0 & 0 & 0 & 0 & \frac{1}{h} \end{bmatrix}$$

Hence we have the matrix $P_f P^{-1} = -diag(\frac{l'}{l}, \frac{l'}{l}, \frac{l'}{l}, \frac{h'}{h}, \frac{h'}{h}, \frac{h'}{h})$, thus,

$$Q = P_f P^{-1} + PMP^{-1} = \begin{bmatrix} A_{11} & A_{12} & 0 & A_{14} & A_{15} & 0 \\ A_{21} & A_{22} & 0 & A_{24} & 0 & A_{26} \\ A_{31} & A_{32} & A_{33} & 0 & A_{35} & A_{36} \\ 0 & A_{42} & 0 & A_{44} & 0 & 0 \\ 0 & 0 & A_{53} & A_{54} & A_{55} & A_{56} \\ 0 & 0 & 0 & A_{64} & A_{65} & A_{66} \end{bmatrix}$$

in which

$$\begin{aligned} A_{11} =& -\epsilon - \mu - \theta\beta l - \theta\beta\eta h - \theta\beta s_e - \frac{\theta\beta\eta h s_e}{l} - \beta\delta + \beta\delta s_{ne} + \beta\delta s_e \\ &+ \beta\delta l + \beta\delta h - \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta h s_{ne}}{l} + \frac{\beta\eta\delta h s_e}{l} + \beta\eta\delta h + \frac{\beta\eta\delta h^2}{l} + \nu_1 \end{aligned}$$

$$A_{12} = -\theta\beta s_e, A_{14} = \frac{-\theta\beta\eta s_e h}{l}, A_{15} = \frac{\alpha h}{l}$$

$$A_{21} = \theta\beta l + \theta\beta\eta h - \beta\delta l - \beta\eta\delta h$$

$$A_{22} = -\epsilon - \mu - \beta\delta l - \frac{\theta\beta\eta h s_e}{l} - \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta h s_{ne}}{l} + \frac{\beta\eta\delta h s_e}{l} + \frac{\beta\eta\delta h^2}{l}$$

$$A_{24} = \frac{\theta\beta\eta s_e h}{l} - \beta\delta h + \frac{\beta\eta\delta h}{l} - \frac{\beta\eta\delta s_{ne} h}{l} - \frac{\beta\eta\delta s_e h}{l} - \beta\eta\delta h - \frac{2\beta\eta\delta h^2}{l}$$

$$A_{26} = \frac{\alpha h}{l}, A_{31} = \beta\delta l + \beta\eta\delta h, A_{32} = \epsilon$$

$$A_{33} = -\theta\beta l - \theta\beta\eta h - \beta\delta l - \frac{\theta\beta\eta h s_e}{l} - \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta h s_{ne}}{l} + \frac{\beta\eta\delta h s_e}{l} + \frac{\beta\eta\delta h^2}{l} - \mu$$

$$A_{35} = \frac{\theta\beta\eta s_e h}{l} - \beta\delta h + \frac{\beta\eta\delta h}{l} - \frac{\beta\eta\delta s_{ne} h}{l} - \frac{\beta\eta\delta s_e h}{l} - \beta\eta\delta h - \frac{2\beta\eta\delta h^2}{l}$$

$$A_{36} = \frac{\theta\beta\eta s_e h}{l}, A_{42} = \frac{\nu_1 l}{h}, A_{44} = -\epsilon - \mu - \frac{\nu_1 l}{h}, A_{53} = \frac{\nu_1 l}{h}, A_{54} = \epsilon$$

$$A_{55} = -\theta\beta l - \theta\beta\eta h - \mu - \frac{\nu_1 l}{h}, A_{56} = -\theta\beta s_e, A_{64} = -\beta\delta l - \beta\eta\delta h$$

$$A_{65} = \theta\beta l + \theta\beta\eta h - \beta\delta l - \beta\eta\delta h$$

$$A_{66} = \theta\beta s_e + \beta\delta - \beta\delta s_{ne} - \beta\delta s_e - 2\beta\delta l - \beta\delta h - \beta\eta\delta h - \nu_1 - \mu - \frac{\nu_1 l}{h}$$

Now we use the following norm introduced in [11], for $z = (z_1, z_2, z_3, z_4, z_5, z_6) \in \mathbb{R}^6$, $||z|| = max\{U_1, U_2\}$, where $U_1(z_1, z_2, z_3)$ has the following form:

$$\begin{cases} max\{|z_1|, |z_2| + |z_3|\} & \text{if } sgn(z_1) = sgn(z_2) = sgn(z_3) \\ max\{|z_2|, |z_1| + |z_3|\} & \text{if } sgn(z_1) = sgn(z_2) = -sgn(z_3) \\ max\{|z_1|, |z_2|, |z_3|\} & \text{if } sgn(z_1) = -sgn(z_2) = sgn(z_3) \\ max\{|z_1| + |z_3|, |z_2| + |z_3|\} & \text{if } -sgn(z_1) = sgn(z_2) = sgn(z_3) \end{cases}$$

and $U_2(z_4, z_5, z_6)$ has the following form:

$$\begin{cases} |z_4|+|z_5|+|z_6| & \text{if } \begin{array}{l} sgn(z_4)=sgn(z_5) \\ =sgn(z_6) \end{array} \\ max\{|z_4|+|z_5|,|z_4|+|z_6|\} & \text{if } \begin{array}{l} sgn(z_4)=sgn(z_5) \\ =-sgn(z_6) \end{array} \\ max\{|z_5|,|z_4|+|z_6|\} & \text{if } \begin{array}{l} sgn(z_4)=-sgn(z_5) \\ =sgn(z_6) \end{array} \\ max\{|z_4|+|z_6|,|z_5|+|z_6|\} & \text{if } \begin{array}{l} -sgn(z_4)=sgn(z_5) \\ =sgn(z_6) \end{array} \end{cases}$$

Furthere more we use the following relations:

$$|z_2| < U_1, |z_3| < U_1, |z_2+z_3| < U_1$$

and

$$|z_i|, |z_i+z_j|, |z_4+z_5+z_6| \le U_2(z) \qquad i=4,5,6; i \neq j$$

We use this inequalities in the estimation of $D_+||z||$.

Lemma 4.3. *There is a constant $\tau > 0$, for which $D_+\|z\| \le -\tau\|z\|$ for all $z \in \mathbb{R}^6$ and $s_{ne}, s_e, l, h > 0$, where z is the solution of (4. 10), provided that $\epsilon > 3\theta\beta$, $\mu > \theta\beta$ and*

$$max\{-2\theta\beta l - 2\theta\beta\eta h - \beta\delta r - 2\beta\delta l - \frac{4\beta\eta\delta hr}{l} - \mu + \nu_1 + 3\beta\delta + \frac{\alpha h}{l} + \frac{\theta\beta\eta s_e h}{l} + \frac{4\beta\eta\delta h}{l} + \frac{2\beta\eta\delta h^2}{l}\} < -\tau.$$

Proof. We prove the existence of a $\tau > 0$ for which $D_+\|z\| \le -\tau\|z\|$, for the solution z of the equation (4. 10). The full calculation to demonstrate this relation contains sixteen cases related to the different orthants and the above norm, see [2].
Case 1: $U_1 > U_2$, $z_1, z_2, z_3 > 0$ and $|z_1| > |z_2| + |z_3|$. In this case, $||z|| = |z_1|$ and

$$\begin{aligned} D_+||z|| =& z_1' = A_{11}z_1 + A_{12}z_2 + A_{14}z_4 + A_{15}z_5 \le (-\epsilon - \mu - \theta\beta l - \theta\beta\eta h \\ & - \theta\beta s_e - \frac{\theta\beta\eta h s_e}{l} - \beta\delta + \beta\delta s_{ne} + \beta\delta s_e + \beta\delta l + \beta\delta h - \frac{\beta\eta\delta h}{l} \\ & + \frac{\beta\eta\delta h s_{ne}}{l} + \frac{\beta\eta\delta h s_e}{l} + \beta\eta\delta h + \frac{\beta\eta\delta h^2}{l} + \nu_1)|z_1| + (-\theta\beta s_e)|z_2| \\ & + (\frac{\theta\beta\eta s_e h}{l})|z_4| + (\frac{\alpha h}{l})|z_5| \end{aligned}$$

thus

$$\begin{aligned} D_+||z|| <& (-\epsilon - \mu - \theta\beta l - \theta\beta\eta h - \theta\beta s_e - \frac{\theta\beta\eta h s_e}{l} - \beta\delta r - \frac{\beta\eta\delta hr}{l} + \nu_1 \\ & + \frac{\alpha h}{l})||z|| \le D||z|| \end{aligned}$$

Case 2: $U_1 > U_2$, $z_1, z_2, z_3 > 0$ and $|z_1| < |z_2| + |z_3|$. In this case, $||z|| = |z_2| + |z_3|$ and

$$\begin{aligned}D_+||z|| =& z_2' + z_3' = A_{21}z_1 + A_{22}z_2 + A_{24}z_4 + A_{26}z_6 + A_{31}z_1 + A_{32}z_2 \\ &+ A_{33}z_3 + A_{35}z_5 + A_{36}z_6 \leq (\theta\beta l + \theta\beta\eta h - \beta\delta l - \beta\eta\delta h)|z_1| \\ &+ (-\epsilon - \mu - \beta\delta l - \frac{\theta\beta\eta h s_e}{l} - \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta h s_{ne}}{l} + \frac{\beta\eta\delta h s_e}{l} \\ &+ \frac{\beta\eta\delta h^2}{l})|z_2| + (\frac{\theta\beta\eta s_e h}{l} + \beta\delta h + \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta s_{ne} h}{l} + \frac{\beta\eta\delta s_e h}{l} \\ &+ \beta\eta\delta h + \frac{2\beta\eta\delta h^2}{l})|z_4| + (\frac{\alpha h}{l})|z_6| + (\beta\delta l + \beta\eta\delta h)|z_1| + (\epsilon)|z_2| \\ &+ (-\theta\beta l - \theta\beta\eta h - \beta\delta l - \frac{\theta\beta\eta h s_e}{l} - \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta h s_{ne}}{l} + \frac{\beta\eta\delta h s_e}{l} \\ &+ \frac{\beta\eta\delta h^2}{l} - \mu)|z_3| + (\frac{\theta\beta\eta s_e h}{l} + \beta\delta h + \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta s_{ne} h}{l} \\ &+ \frac{\beta\eta\delta s_e h}{l} + \beta\eta\delta h + \frac{2\beta\eta\delta h^2}{l})|z_5| + (\frac{\theta\beta\eta s_e h}{l})|z_6|\end{aligned}$$

thus

$$\begin{aligned}D_+||z|| <& (-2\beta\delta l - 2\mu - \frac{4\beta\eta\delta h r}{l} - 2\beta\eta\delta h + \frac{\theta\beta\eta s_e h}{l} + 2\beta\delta h + \frac{4\beta\eta\delta h}{l} \\ &+ \frac{2\beta\eta\delta h^2}{l} + \frac{\alpha h}{l})||z|| \leq D||z||\end{aligned}$$

Case 3: $U_1 > U_2$, $z_1 < 0$, $z_2, z_3 > 0$ and $|z_1| > |z_2|$. In this case, $||z|| = |z_1| + |z_3|$ and

$$\begin{aligned}D_+||z|| =& - z_1' + z_3' = -(A_{11}z_1 + A_{12}z_2 + A_{14}z_4 + A_{15}z_5) + A_{31}z_1 + A_{32}z_2 \\ &+ A_{33}z_3 + A_{35}z_5 + A_{36}z_6 \leq (-\epsilon - \mu - \theta\beta l - \theta\beta\eta h - \theta\beta s_e \\ &- \frac{\theta\beta\eta h s_e}{l} - \beta\delta + \beta\delta s_{ne} + \beta\delta s_e + \beta\delta l + \beta\delta h - \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta h s_{ne}}{l} \\ &+ \frac{\beta\eta\delta h s_e}{l} + \beta\eta\delta h + \frac{\beta\eta\delta h^2}{l} + \nu_1)|z_1| + (\theta\beta s_e)|z_2| + (\frac{\theta\beta\eta s_e h}{l})|z_4| \\ &+ (\frac{\alpha h}{l})|z_5| - (\beta\delta l + \beta\eta\delta h)|z_1| + (\epsilon)|z_2| + (-\theta\beta l - \theta\beta\eta h - \beta\delta l \\ &- \frac{\theta\beta\eta h s_e}{l} - \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta h s_{ne}}{l} + \frac{\beta\eta\delta h s_e}{l} + \frac{\beta\eta\delta h^2}{l} - \mu)|z_3| \\ &+ (\frac{\theta\beta\eta s_e h}{l} + \beta\delta h + \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta s_{ne} h}{l} + \frac{\beta\eta\delta s_e h}{l} + \beta\eta\delta h \\ &+ \frac{2\beta\eta\delta h^2}{l})|z_5| + (\frac{\theta\beta\eta s_e h}{l})|z_6|\end{aligned}$$

thus

$$\begin{aligned}D_+||z|| <& (-2\mu - 2\theta\beta l - 2\theta\beta\eta h - \beta\delta r - 2\beta\delta l - \frac{4\beta\eta\delta h r}{l} + \nu_1 + \frac{\alpha h}{l} + \beta\eta\delta h \\ &+ \frac{\theta\beta\eta s_e h}{l} + \beta\delta h + \frac{2\beta\eta\delta h}{l} + \frac{\beta\eta\delta h^2}{l})||z|| \leq D||z||\end{aligned}$$

Case 4: $U_1 > U_2$, $z_1 < 0$, $z_2, z_3 > 0$ and $|z_1| < |z_2|$. In this case, $||z|| = |z_2| + |z_3|$ and

$$\begin{aligned}D_+||z|| =& z_2' + z_3' = A_{21}z_1 + A_{22}z_2 + A_{24}z_4 + A_{26}z_6 + A_{31}z_1 + A_{32}z_2 \\ &+ A_{33}z_3 + A_{35}z_5 + A_{36}z_6 \leq -(\theta\beta l + \theta\beta\eta h - \beta\delta l - \beta\eta\delta h)|z_1| \\ &+ (-\epsilon - \mu - \beta\delta l - \frac{\theta\beta\eta h s_e}{l} - \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta h s_{ne}}{l} + \frac{\beta\eta\delta h s_e}{l} \\ &+ \frac{\beta\eta\delta h^2}{l})|z_2| + (\frac{\theta\beta\eta s_e h}{l} + \beta\delta h + \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta s_{ne} h}{l} + \frac{\beta\eta\delta s_e h}{l} \\ &+ \beta\eta\delta h + \frac{2\beta\eta\delta h^2}{l})|z_4| + (\frac{\alpha h}{l})|z_6| - (\beta\delta l + \beta\eta\delta h)|z_1| + (\epsilon)|z_2| \\ &+ (-\theta\beta l - \theta\beta\eta h - \beta\delta l - \frac{\theta\beta\eta h s_e}{l} - \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta h s_{ne}}{l} + \frac{\beta\eta\delta h s_e}{l} \\ &+ \frac{\beta\eta\delta h^2}{l} - \mu)|z_3| + (\frac{\theta\beta\eta s_e h}{l} + \beta\delta h + \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta s_{ne} h}{l} \\ &+ \frac{\beta\eta\delta s_e h}{l} + \beta\eta\delta h + \frac{2\beta\eta\delta h^2}{l})|z_5| + (\frac{\theta\beta\eta s_e h}{l})|z_6|\end{aligned}$$

thus

$$\begin{aligned}D_+||z|| <& (-2\theta\beta l - 2\theta\beta\eta h - 2\mu - 2\beta\delta l - 2\beta\eta\delta h - \frac{4\beta\eta\delta h r}{l} + 2\beta\delta h + \frac{4\beta\eta\delta h}{l} \\ &+ \frac{\alpha h}{l} + \frac{2\beta\eta\delta h^2}{l} + \frac{\theta\beta\eta s_e h}{l})||z|| \leq D||z||\end{aligned}$$

Case 5: $U_1 > U_2$, $z_1, z_2 > 0$, $z_3 < 0$ and $|z_2| > |z_1| + |z_3|$. In this case, $||z|| = |z_2|$ and

$$\begin{aligned}D_+||z|| =& z_2' = A_{21}z_1 + A_{22}z_2 + A_{24}z_4 + A_{26}z_6 \leq (\theta\beta l + \theta\beta\eta h - \beta\delta l \\ &- \beta\eta\delta h)|z_1| + (-\epsilon - \mu - \beta\delta l - \frac{\theta\beta\eta h s_e}{l} - \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta h s_{ne}}{l} \\ &+ \frac{\beta\eta\delta h s_e}{l} + \frac{\beta\eta\delta h^2}{l})|z_2| + (\frac{\theta\beta\eta s_e h}{l} + \beta\delta h + \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta s_{ne} h}{l} \\ &+ \frac{\beta\eta\delta s_e h}{l} + \beta\eta\delta h + \frac{2\beta\eta\delta h^2}{l})|z_4| + (\frac{\alpha h}{l})|z_6|\end{aligned}$$

thus

$$\begin{aligned}D_+||z|| <& (-2\beta\delta l - 2\beta\eta\delta h - \epsilon - \mu - \frac{2\beta\eta\delta h r}{l} + \theta\beta l + \theta\beta\eta h + \beta\delta h + \frac{2\beta\eta\delta h}{l} \\ &+ \frac{\beta\eta\delta h^2}{l} + \frac{\alpha h}{l})||z|| \leq D||z||\end{aligned}$$

Case 6: $U_1 > U_2$, $z_1, z_2 > 0$, $z_3 < 0$ and $|z_2| < |z_1| + |z_3|$. In this case, $||z|| = |z_1| + |z_3|$ and

$$
\begin{aligned}
D_+||z|| =& z_1' - z_3' = A_{11}z_1 + A_{12}z_2 + A_{14}z_4 + A_{15}z_5 - (A_{31}z_1 + A_{32}z_2 \\
&+ A_{33}z_3 + A_{35}z_5 + A_{36}z_6) \leq (-\epsilon - \mu - \theta\beta l - \theta\beta\eta h - \theta\beta s_e \\
&- \frac{\theta\beta\eta h s_e}{l} - \beta\delta + \beta\delta s_{ne} + \beta\delta s_e + \beta\delta l + \beta\delta h - \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta h s_{ne}}{l} \\
&+ \frac{\beta\eta\delta h s_e}{l} + \beta\eta\delta h + \frac{\beta\eta\delta h^2}{l} + \nu_1)|z_1| + (-\theta\beta s_e)|z_2| \\
&+ (\frac{\theta\beta\eta s_e h}{l})|z_4| + (\frac{\alpha h}{l})|z_5| - (\beta\delta l + \beta\eta\delta h)|z_1| - (\epsilon)|z_2| + (-\theta\beta l \\
&- \theta\beta\eta h - \beta\delta l - \frac{\theta\beta\eta h s_e}{l} - \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta h s_{ne}}{l} + \frac{\beta\eta\delta h s_e}{l} + \frac{\beta\eta\delta h^2}{l} \\
&- \mu)|z_3| + (\frac{\theta\beta\eta s_e h}{l} + \beta\delta h + \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta s_{ne} h}{l} + \frac{\beta\eta\delta s_e h}{l} + \beta\eta\delta h \\
&+ \frac{2\beta\eta\delta h^2}{l})|z_5| + (\frac{\theta\beta\eta s_e h}{l})|z_6|
\end{aligned}
$$

thus

$$
\begin{aligned}
D_+||z|| <& (-2\epsilon - 2\mu - 2\theta\beta l - 2\theta\beta\eta h - 2\theta\beta s_e - \beta\delta r - \frac{3\beta\eta\delta h r}{l} - 2\beta\delta l \\
&- 3\beta\eta\delta h + \nu_1 + \frac{\alpha h}{l} + \beta\delta h + \frac{2\beta\eta\delta h}{l} + \frac{\beta\eta\delta h^2}{l} + \frac{\theta\beta\eta s_e h}{l})||z|| \\
&\leq D||z||
\end{aligned}
$$

Case 7: $U_1 > U_2$, $z_1, z_3 > 0$, $z_2 < 0$ and $|z_1| > max\{|z_2|, |z_3|\}|$. In this case $||z|| = |z_1|$ and

$$
\begin{aligned}
D_+||z|| =& z_1' = A_{11}z_1 + A_{12}z_2 + A_{14}z_4 + A_{15}z_5 \leq (-\epsilon - \mu - \theta\beta l - \theta\beta\eta h \\
&- \theta\beta s_e - \frac{\theta\beta\eta h s_e}{l} - \beta\delta + \beta\delta s_{ne} + \beta\delta s_e + \beta\delta l + \beta\delta h - \frac{\beta\eta\delta h}{l} \\
&+ \frac{\beta\eta\delta h s_{ne}}{l} + \frac{\beta\eta\delta h s_e}{l} + \beta\eta\delta h + \frac{\beta\eta\delta h^2}{l} + \nu_1)|z_1| - (-\theta\beta s_e)|z_2| \\
&+ (\frac{\theta\beta\eta s_e h}{l})|z_4| + (\frac{\alpha h}{l})|z_5|
\end{aligned}
$$

thus

$$
D_+||z|| < (-\epsilon - \mu - \theta\beta l - \theta\beta\eta h - \beta\delta r - \frac{\beta\eta\delta h r}{l} + \nu_1 + \frac{\alpha h}{l})||z|| \leq D||z||
$$

Case 8: $U_1 > U_2$, $z_1, z_3 > 0$, $z_2 < 0$ and $|z_2| > max\{|z_1|, |z_3|\}$. In this case, $||z|| = |z_2|$ and

$$\begin{aligned}D_+||z|| =& - z_2' = -(A_{21}z_1 + A_{22}z_2 + A_{24}z_4 + A_{26}z_6) \leq -(\theta\beta l + \theta\beta\eta h - \beta\delta l \\ & - \beta\eta\delta h)|z_1| + (-\epsilon - \mu - \beta\delta l - \frac{\theta\beta\eta h s_e}{l} - \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta h s_{ne}}{l} \\ & + \frac{\beta\eta\delta h s_e}{l} + \frac{\beta\eta\delta h^2}{l})|z_2| + (\frac{\theta\beta\eta s_e h}{l} + \beta\delta h + \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta s_{ne} h}{l} \\ & + \frac{\beta\eta\delta s_e h}{l} + \beta\eta\delta h + \frac{2\beta\eta\delta h^2}{l})|z_4| + (\frac{\alpha h}{l})|z_6|\end{aligned}$$

thus

$$\begin{aligned}D_+||z|| <& (-\theta\beta l - \theta\beta\eta h - \epsilon - \mu - \frac{2\beta\eta\delta hr}{l} + \beta\delta h + \frac{2\beta\eta\delta h}{l} + \frac{\beta\eta\delta h^2}{l} \\ & + \frac{\alpha h}{l})||z|| \leq D||z||\end{aligned}$$

Case 9: $U_1 > U_2$, $z_1, z_3 > 0$, $z_2 < 0$ and $|z_3| > max\{|z_1|, |z_2|\}$. In this case $||z|| = |z_3|$ and

$$\begin{aligned}D_+||z|| =& z_3' = A_{31}z_1 + A_{32}z_2 + A_{33}z_3 + A_{35}z_5 + A_{36}z_6 \leq (\beta\delta l + \beta\eta\delta h)|z_1| \\ & - (\epsilon)|z_2| + (-\theta\beta l - \theta\beta\eta h - \beta\delta l - \frac{\theta\beta\eta h s_e}{l} - \frac{\beta\eta\delta h}{l} + \frac{\beta\eta\delta h s_{ne}}{l} \\ & + \frac{\beta\eta\delta h s_e}{l} + \frac{\beta\eta\delta h^2}{l} - \mu)|z_3| + (\frac{\theta\beta\eta s_e h}{l} + \beta\delta h + \frac{\beta\eta\delta h}{l} \\ & + \frac{\beta\eta\delta s_{ne} h}{l} + \frac{\beta\eta\delta s_e h}{l} + \beta\eta\delta h + \frac{2\beta\eta\delta h^2}{l})|z_5| + (\frac{\theta\beta\eta s_e h}{l})|z_6|\end{aligned}$$

thus

$$\begin{aligned}D_+||z|| <& (-\epsilon - \theta\beta l - \theta\beta\eta h - \frac{2\beta\eta\delta hr}{l} - \mu - \beta\eta\delta h + \frac{\theta\beta\eta s_e h}{l} + \beta\delta h \\ & + \frac{2\beta\eta\delta h}{l} + \frac{\beta\eta\delta h^2}{l})||z|| \leq D||z||\end{aligned}$$

Case 10: $U_1 < U_2$ and $z_4, z_5, z_6 > 0$. In this case $||z|| = |z_4| + |z_5| + |z_6|$ and

$$\begin{aligned}D_+||z|| =& z_4' + z_5' + z_6' = A_{42}z_2 + A_{44}z_4 + A_{53}z_3 + A_{54}z_4 + A_{55}z_5 \\ & + A_{56}z_6 + A_{64}z_4 + A_{65}z_5 + A_{66}z_6 \leq (\frac{\nu_1 l}{h})|z_2| + (-\epsilon - \mu \\ & - \frac{\nu_1 l}{h})|z_4| + (\frac{\nu_1 l}{h})|z_3| + (\epsilon)|z_4| + (-\theta\beta l - \theta\beta\eta h - \mu - \frac{\nu_1 l}{h})|z_5| \\ & + (-\theta\beta s_e)|z_6| + (-\beta\delta l - \beta\eta\delta h)|z_4| + (\theta\beta l + \theta\beta\eta h - \beta\delta l \\ & - \beta\eta\delta h)|z_5| + (\theta\beta s_e + \beta\delta - \beta\delta s_{ne} - \beta\delta s_e - 2\beta\delta l - \beta\delta h - \beta\eta\delta h \\ & - \nu_1 - \mu - \frac{\nu_1 l}{h})|z_6|\end{aligned}$$

thus

$$D_+||z|| < (-3\mu - 3\beta\delta l - 3\beta\eta\delta h - \nu_1 - \frac{\nu_1 l}{h} + \beta\delta r)||z|| \le D||z||$$

Case 11: $U_1 < U_2$, $z_4, z_5 > 0$, $z_6 < 0$ and $|z_5| > |z_6|$. In this case $||z|| = |z_4| + |z_5|$ and

$$\begin{aligned} D_+||z|| =& z_4' + z_5' = A_{42}z_2 + A_{44}z_4 + A_{53}z_3 + A_{54}z_4 + A_{55}z_5 + A_{56}z_6 \\ \le& (\frac{\nu_1 l}{h})|z_2| + (-\epsilon - \mu - \frac{\nu_1 l}{h})|z_4| + (\frac{\nu_1 l}{h})|z_3| + (\epsilon)|z_4| + (-\theta\beta l \\ &- \theta\beta\eta h - \mu - \frac{\nu_1 l}{h})|z_5| - (-\theta\beta s_e)|z_6| \end{aligned}$$

thus

$$D_+||z|| < (-2\mu - \theta\beta l - \theta\beta\eta h + \theta\beta s_e)||z|| \le D||z||$$

Case 12: $U_1 < U_2$, $z_4, z_5 > 0$, $z_6 < 0$ and $|z_5| < |z_6|$. In this case $||z|| = |z_4| + |z_6|$ and

$$\begin{aligned} D_+||z|| =& z_4' - z_6' = A_{42}z_2 + A_{44}z_4 - (A_{64}z_4 + A_{65}z_5 + A_{66}z_6) \le (\frac{\nu_1 l}{h})|z_2| \\ &+ (-\epsilon - \mu - \frac{\nu_1 l}{h})|z_4| - (-\beta\delta l - \beta\eta\delta h)|z_4| - (\theta\beta l + \theta\beta\eta h - \beta\delta l \\ &- \beta\eta\delta h)|z_5| + (\theta\beta s_e + \beta\delta - \beta\delta s_{ne} - \beta\delta s_e - 2\beta\delta l - \beta\delta h - \beta\eta\delta h \\ &- \nu_1 - \mu - \frac{\nu_1 l}{h})|z_6| \end{aligned}$$

thus

$$\begin{aligned} D_+||z|| <& (-\epsilon - 2\mu - \theta\beta l - \theta\beta\eta h - \nu_1 - \frac{\nu_1 l}{h} + \beta\delta l + \beta\eta\delta h + \theta\beta s_e \\ &+ \beta\delta r)||z|| \le D||z|| \end{aligned}$$

Case 13: $U_1 < U_2$, $z_4, z_6 > 0$, $z_5 < 0$ and $|z_5| > |z_4| + |z_6|$. In this case $||z|| = |z_5|$ and

$$\begin{aligned} D_+||z|| =& - z_5' = -(A_{53}z_3 + A_{54}z_4 + A_{55}z_5 + A_{56}z_6) \le (\frac{\nu_1 l}{h})|z_3| - (\epsilon)|z_4| \\ &+ (-\theta\beta l - \theta\beta\eta h - \mu - \frac{\nu_1 l}{h})|z_5| - (-\theta\beta s_e)|z_6| \end{aligned}$$

thus

$$D_+||z|| < (-\epsilon - \theta\beta l - \theta\beta\eta l - \mu + \theta\beta s_e)||z|| \le D||z||$$

Case 14: $U_1 < U_2$, $z_4, z_6 > 0$, $z_5 < 0$ and $|z_5| < |z_4| + |z_6|$. In this case $||z|| = |z_4| + |z_6|$ and

$$\begin{aligned} D_+||z|| =& z_4' + z_6' = A_{42}z_2 + A_{44}z_4 + A_{64}z_4 + A_{65}z_5 + A_{66}z_6 \le (\frac{\nu_1 l}{h})|z_2| \\ &+ (-\epsilon - \mu - \frac{\nu_1 l}{h})|z_4| + (-\beta\delta l - \beta\eta\delta h)|z_4| - (\theta\beta l + \theta\beta\eta h - \beta\delta l \\ &- \beta\eta\delta h)|z_5| + (\theta\beta s_e + \beta\delta - \beta\delta s_{ne} - \beta\delta s_e - 2\beta\delta l - \beta\delta h - \beta\eta\delta h \\ &- \nu_1 - \mu - \frac{\nu_1 l}{h})|z_6| \end{aligned}$$

thus

$$D_+||z|| <(-\epsilon - 2\mu - \theta\beta l - \theta\beta\eta h - \beta\delta l - \beta\eta\delta h - \nu_1 - \frac{\nu_1 l}{h} + \theta\beta s_e + \beta\delta r)||z|| \leq D||z||$$

Case 15: $U_1 < U_2$, $z_5, z_6 > 0$, $z_4 < 0$ and $|z_5| < |z_4|$. In this case $||z|| = |z_4| + |z_6|$ and

$$\begin{aligned} D_+||z|| =& - z_4' + z_6' = -(A_{42}z_2 + A_{44}z_4) + A_{64}z_4 + A_{65}z_5 + A_{66}z_6 \\ &\leq (\frac{\nu_1 l}{h})|z_2| + (-\epsilon - \mu - \frac{\nu_1 l}{h})|z_4| - (-\beta\delta l - \beta\eta\delta h)|z_4| + (\theta\beta l + \theta\beta\eta h \\ &- \beta\delta l - \beta\eta\delta h)|z_5| + (\theta\beta s_e + \beta\delta - \beta\delta s_{ne} - \beta\delta s_e - 2\beta\delta l - \beta\delta h \\ &- \beta\eta\delta h - \nu_1 - \mu - \frac{\nu_1 l}{h})|z_6| \end{aligned}$$

thus

$$D_+||z|| <(-\epsilon - 2\mu - \beta\delta l - \beta\eta\delta h - \nu_1 - \frac{\nu_1 l}{h} + \theta\beta l + \theta\beta\eta h + \theta\beta s_e + \beta\delta r)||z|| \leq D||z||$$

Case 16: $U_1 < U_2$, $z_5, z_6 > 0$, $z_4 < 0$ and $|z_5| > |z_4|$. In this case $||z|| = |z_5| + |z_6|$ and

$$\begin{aligned} D_+||z|| =& z_5' + z_6' = A_{53}z_3 + A_{54}z_4 + A_{55}z_5 + A_{56}z_6 + A_{64}z_4 + A_{65}z_5 \\ &+ A_{66}z_6 \leq (\frac{\nu_1 l}{h})|z_3| - (\epsilon)|z_4| + (-\theta\beta l - \theta\beta\eta h - \mu - \frac{\nu_1 l}{h})|z_5| \\ &+ (-\theta\beta s_e)|z_6| - (-\beta\delta l - \beta\eta\delta h)|z_4| + (\theta\beta l + \theta\beta\eta h - \beta\delta l \\ &- \beta\eta\delta h)|z_5| + (\theta\beta s_e + \beta\delta - \beta\delta s_{ne} - \beta\delta s_e - 2\beta\delta l - \beta\delta h - \beta\eta\delta h \\ &- \nu_1 - \mu - \frac{\nu_1 l}{h})|z_6| \end{aligned}$$

thus

$$D_+||z|| < (-\epsilon - 2\mu - \beta\delta l - \beta\eta\delta h - \nu_1 - \frac{\nu_1 l}{h} + \beta\delta r)||z|| \leq D||z||$$

Lemma 4.4. *For an arbitrary simple and closed curve ψ in Ω, there is an $\epsilon > 0$ and surfaces φ^k which minimizes $\mathcal{S}$ with respect to $\Sigma(\psi, \Omega)$, in such a way that, for all $k = 2, 3, ...$ and $t \in [0, \epsilon]$, $\varphi_t^k \subseteq \Omega$.*

Proof. Let $\xi = \frac{1}{2} min\{l, h : (s_{ne}, s_e, l, h) \in \psi\}$. It is easy to see that $\psi > 0$. Based on the inequalities $\frac{dl}{dt} \geq -(\nu_1 + \mu)l$, $\frac{dh}{dt} \geq -(\nu_2 + \mu + \alpha)h$ which holds in Ω, there exists $\epsilon > 0$ such that, the solutions with $l(0) \geq \xi$ and $h(0) \geq \xi$, remains in Ω, for $t \in [0, \epsilon]$. Hence we must show the existence of a sequence $\{\varphi^k\}$ which minimizes $\mathcal{S}$ with respect to $\Sigma(\psi, \widetilde{\Omega})$, in which $\widetilde{\Omega} = \{(s_{ne}, s_e, l, h) \in \Omega : l \geq \xi, h \geq \xi\}$. Now for $\varphi(u) = (s_{ne}(u), s_e(u), l(u), h(u)) \in \Sigma(\psi, \Omega)$, we define another surface $\widetilde{\varphi}(u) = (\widetilde{s}_{ne}(u), \widetilde{s}_e(u), \widetilde{l}(u), \widetilde{h}(u))$ by,

$$\begin{cases} \varphi(u) & \text{if } l(u) \geq \xi, h(u) \geq \xi \\ (s_{ne}, s_e, \xi, h) & \text{if } \begin{matrix} l(u) < \xi, h(u) \geq \xi, \\ s_{ne} + s_e + \xi + h \leq \frac{\Lambda}{\mu} \end{matrix} \\ (\frac{s_{ne}}{s_{ne}+s_e}(\frac{\Lambda}{\mu} - 2\xi), \frac{s_e}{s_{ne}+s_e}(\frac{\Lambda}{\mu} - 2\xi), \xi, \xi) & \text{if } \begin{matrix} l(u) < \xi, h(u) \geq \xi, \\ s_{ne} + s_e + \xi + h > \frac{\Lambda}{\mu} \end{matrix} \\ (s_{ne}, s_e, l, \xi) & \text{if } \begin{matrix} l(u) \geq \xi, h(u) < \xi, \\ s_{ne} + s_e + l + \xi \leq \frac{\Lambda}{\mu} \end{matrix} \\ (\frac{s_{ne}}{s_{ne}+s_e}(\frac{\Lambda}{\mu} - 2\xi), \frac{s_e}{s_{ne}+s_e}(\frac{\Lambda}{\mu} - 2\xi), \xi, \xi) & \text{if } \begin{matrix} l(u) \geq \xi, h(u) < \xi, \\ s_{ne} + s_e + l + \xi > \frac{\Lambda}{\mu} \end{matrix} \\ (s_{ne}, s_e, \xi, \xi) & \text{if } \begin{matrix} l(u) < \xi, h(u) < \xi, \\ s_{ne} + s_e + 2\xi \leq \frac{\Lambda}{\mu} \end{matrix} \\ (\frac{s_{ne}}{s_{ne}+s_e}(\frac{\Lambda}{\mu} - 2\xi), \frac{s_e}{s_{ne}+s_e}(\frac{\Lambda}{\mu} - 2\xi), \xi, \xi) & \text{if } \begin{matrix} l(u) < \xi, h(u) < \xi, \\ s_{ne} + s_e + 2\xi > \frac{\Lambda}{\mu} \end{matrix} \end{cases}$$

It is easy to see that $\widetilde{\varphi}(u) \in \Sigma(\psi, \widetilde{\Omega})$. We will prove $\mathcal{S}\widetilde{\varphi} \leq \mathcal{S}\phi$. From the definition of wedge product, we obtain that

$$\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2} = \begin{bmatrix} \frac{\partial s_{ne}}{\partial u_1} \\ \frac{\partial s_e}{\partial u_1} \\ \frac{\partial l}{\partial u_1} \\ \frac{\partial h}{\partial u_1} \end{bmatrix} \wedge \begin{bmatrix} \frac{\partial s_{ne}}{\partial u_2} \\ \frac{\partial s_e}{\partial u_2} \\ \frac{\partial l}{\partial u_2} \\ \frac{\partial h}{\partial u_2} \end{bmatrix} = \begin{bmatrix} det \begin{bmatrix} \frac{\partial s_{ne}}{\partial u_1} & \frac{\partial s_{ne}}{\partial u_2} \\ \frac{\partial s_e}{\partial u_1} & \frac{\partial s_e}{\partial u_2} \end{bmatrix} \\ det \begin{bmatrix} \frac{\partial s_{ne}}{\partial u_1} & \frac{\partial s_{ne}}{\partial u_2} \\ \frac{\partial l}{\partial u_1} & \frac{\partial l}{\partial u_2} \end{bmatrix} \\ det \begin{bmatrix} \frac{\partial s_{ne}}{\partial u_1} & \frac{\partial s_{ne}}{\partial u_2} \\ \frac{\partial h}{\partial u_1} & \frac{\partial h}{\partial u_2} \end{bmatrix} \\ det \begin{bmatrix} \frac{\partial s_e}{\partial u_1} & \frac{\partial s_e}{\partial u_2} \\ \frac{\partial l}{\partial u_1} & \frac{\partial l}{\partial u_2} \end{bmatrix} \\ det \begin{bmatrix} \frac{\partial s_e}{\partial u_1} & \frac{\partial s_e}{\partial u_2} \\ \frac{\partial h}{\partial u_1} & \frac{\partial h}{\partial u_2} \end{bmatrix} \\ det \begin{bmatrix} \frac{\partial l}{\partial u_1} & \frac{\partial l}{\partial u_2} \\ \frac{\partial h}{\partial u_1} & \frac{\partial h}{\partial u_2} \end{bmatrix} \end{bmatrix}$$

is a vector in $\mathbb{R}^6$ for each $u \in \mathcal{B}$. We denote $\frac{\partial \widetilde{\varphi}}{\partial u_1} \wedge \frac{\partial \widetilde{\varphi}}{\partial u_2} = (\widetilde{x}_1, \widetilde{x}_2, \widetilde{x}_3, \widetilde{x}_4, \widetilde{x}_5, \widetilde{x}_6)^T$ and $\frac{\partial \varphi}{\partial u_1} \wedge \frac{\partial \varphi}{\partial u_2} = (x_1, x_2, x_3, x_4, x_5, x_6)^T$. We prove $|\widetilde{x}_i| \le |x_i|$ $(i = 1, 2, \cdots, 6)$ in the possible cases.

Case 1. If $l(u) \ge \xi, h(u) \ge \xi$ then $\widetilde{\varphi} = \varphi$ and therefore, $|\widetilde{x}_i| = |x_i|$ $(i = 1, 2, \cdots, 6)$.

Case 2. If $l(u) < \xi, h(u) \ge \xi$ and $s_{ne}+s_e+\xi+h \le \frac{\Lambda}{\mu}$, then $\widetilde{\varphi}(u) = (s_{ne}(u), s_e(u), \xi, h(u))$. Therefore

$$\frac{\partial \widetilde{\varphi}}{\partial u_1} \wedge \frac{\partial \widetilde{\varphi}}{\partial u_2} = \begin{bmatrix} det \begin{bmatrix} \frac{\partial s_{ne}}{\partial u_1} & \frac{\partial s_{ne}}{\partial u_2} \\ \frac{\partial s_e}{\partial u_1} & \frac{\partial s_e}{\partial u_2} \end{bmatrix} \\ 0 \\ det \begin{bmatrix} \frac{\partial s_{ne}}{\partial u_1} & \frac{\partial s_{ne}}{\partial u_2} \\ \frac{\partial h}{\partial u_1} & \frac{\partial h}{\partial u_2} \end{bmatrix} \\ 0 \\ det \begin{bmatrix} \frac{\partial s_e}{\partial u_1} & \frac{\partial s_e}{\partial u_2} \\ \frac{\partial h}{\partial u_1} & \frac{\partial h}{\partial u_2} \end{bmatrix} \\ 0 \end{bmatrix}$$

almost everywhere. Hence it follows $\widetilde{x}_i = x_i (i = 1, 3, 5)$ and $\widetilde{x}_i = 0 (i = 2, 4, 6)$. Thus $|\widetilde{x}_i| \le |x_i|$.

Case 3. If $l(u) < \xi, h(u) \ge \xi$ and $s_{ne} + s_e + \xi + h > \frac{\Lambda}{\mu}$, then $\widetilde{\varphi}(u) = (\frac{s_{ne}}{s_{ne}+s_e}(\frac{\Lambda}{\mu} - 2\xi), \frac{s_e}{s_{ne}+s_e}(\frac{\Lambda}{\mu} - 2\xi), \xi, \xi)$. Thus,

$$\frac{\partial \widetilde{\varphi}}{\partial u_j} = (\frac{\Lambda}{\mu} - 2\xi) \frac{s_e \frac{\partial s_{ne}}{\partial u_j} - s_{ne} \frac{\partial s_e}{\partial u_j}}{(s_{ne}+s_e)^2} \begin{bmatrix} -1 \\ 1 \\ 0 \\ 0 \end{bmatrix}$$

for $j = 1, 2$. Therefore, $\frac{\partial \widetilde{\varphi}}{\partial u_1}$ and $\frac{\partial \widetilde{\varphi}}{\partial u_2}$ have linear dependence, hence their wedge product is zero. Thus $\widetilde{x}_i = 0 (i = 1, 2, 3, 4, 5, 6)$. Therefore $|\widetilde{x}_i| \le |x_i| (i = 1, 2, \cdots, 6)$.

Case 4. If $l(u) \ge \xi, h(u) < \xi$ and $s_{ne}+s_e+l+\xi \le \frac{\Lambda}{\mu}$, then $\widetilde{\varphi}(u) = (s_{ne}(u), s_e(u), l(u), \xi)$. Hence,

$$\frac{\partial\widetilde{\varphi}}{\partial u_1}\wedge\frac{\partial\widetilde{\varphi}}{\partial u_2}=\begin{bmatrix} det\begin{bmatrix}\frac{\partial s_{ne}}{\partial u_1} & \frac{\partial s_{ne}}{\partial u_2}\\ \frac{\partial s_e}{\partial u_1} & \frac{\partial s_e}{\partial u_2}\end{bmatrix}\\ det\begin{bmatrix}\frac{\partial s_{ne}}{\partial u_1} & \frac{\partial s_{ne}}{\partial u_2}\\ \frac{\partial l}{\partial u_1} & \frac{\partial l}{\partial u_2}\end{bmatrix}\\ 0\\ det\begin{bmatrix}\frac{\partial s_e}{\partial u_1} & \frac{\partial s_e}{\partial u_2}\\ \frac{\partial l}{\partial u_1} & \frac{\partial l}{\partial u_2}\end{bmatrix}\\ 0\\ 0\end{bmatrix}$$

almost everywhere. Therefore, $\widetilde{x}_i = x_i (i = 1, 2, 4)$ and $\widetilde{x}_i = 0$ $(i = 3, 5, 6)$. Thus $|\widetilde{x}_i| \le |x_i|$.

Case 5. If $l(u) \ge \xi, h(u) < \xi$ and $s_{ne} + s_e + l + \xi > \frac{\Lambda}{\mu}$, then $\widetilde{\varphi}(u) = (\frac{s_{ne}}{s_{ne}+s_e}(\frac{\Lambda}{\mu} - 2\xi), \frac{s_e}{s_{ne}+s_e}(\frac{\Lambda}{\mu} - 2\xi), \xi, \xi)$, thus,

$$\frac{\partial\widetilde{\varphi}}{\partial u_j} = (\frac{\Lambda}{\mu} - 2\xi)\frac{s_e\frac{\partial s_{ne}}{\partial u_j} - s_{ne}\frac{\partial s_e}{\partial u_j}}{(s_{ne}+s_e)^2}\begin{bmatrix}1\\-1\\0\\0\end{bmatrix}$$

for $j = 1, 2$. Therefore, $\frac{\partial\widetilde{\varphi}}{\partial u_1}$ and $\frac{\partial\widetilde{\varphi}}{\partial u_2}$ have linear dependence, hence their wedge product is zero. Thus $\widetilde{x}_i = 0 (i = 1, 2, 3, 4, 5, 6)$, and $|\widetilde{x}_i| \le |x_i| (i = 1, 2, \cdots, 6)$.

Case 6. If $l(u) < \xi, h(u) < \xi$ and $s_{ne} + s_e + 2\xi \le \frac{\Lambda}{\mu}$, then $\widetilde{\varphi}(u) = (s_{ne}(u), s_e(u), \xi, \xi)$, hence,

$$\frac{\partial\widetilde{\varphi}}{\partial u_1}\wedge\frac{\partial\widetilde{\varphi}}{\partial u_2}=\begin{bmatrix} det\begin{bmatrix}\frac{\partial s_{ne}}{\partial u_1} & \frac{\partial s_{ne}}{\partial u_2}\\ \frac{\partial s_e}{\partial u_1} & \frac{\partial s_e}{\partial u_2}\end{bmatrix}\\ 0\\ 0\\ 0\\ 0\\ 0\end{bmatrix}$$

almost everywhere. Therefore, $\widetilde{x}_i = x_i (i = 1)$ and $\widetilde{x}_i = 0$ $(i = 2, 3, 4, 5, 6)$, then $|\widetilde{x}_i| \leq |x_i|$.
Case 7. If $l(u) < \xi, h(u) < \xi$ and $s_{ne} + s_e + 2\xi > \frac{\Lambda}{\mu}$, then $\widetilde{\varphi}(u) = (\frac{s_{ne}}{s_{ne}+s_e}(\frac{\Lambda}{\mu} - 2\xi), \frac{s_e}{s_{ne}+s_e}(\frac{\Lambda}{\mu} - 2\xi), \xi, \xi)$, thus,

$$\frac{\partial \widetilde{\varphi}}{\partial u_j} = (\frac{\Lambda}{\mu} - 2\xi) \frac{s_e \frac{\partial s_{ne}}{\partial u_j} - s_{ne}\frac{\partial s_e}{\partial u_j}}{(s_{ne}+s_e)^2} \begin{bmatrix} -1 \\ -1 \\ 0 \\ 0 \end{bmatrix}$$

for $j = 1, 2$. Therefore $\frac{\partial \widetilde{\varphi}}{\partial u_1}$ and $\frac{\partial \widetilde{\varphi}}{\partial u_2}$ have linear dependence, therefore their wedge product is zero. Thus $\widetilde{x}_i = 0 (i = 1, 2, 3, 4, 5, 6)$, and $|\widetilde{x}_i| \leq |x_i| (i = 1, 2, \cdots, 6)$. Furthere more $\widetilde{l}(u) = \max\{l(u), \xi\}$ and $\widetilde{h}(u) = \max\{h(u), \xi\}$, hence $\frac{1}{\widetilde{l}} \leq \frac{1}{l}$ and $\frac{1}{\widetilde{h}} \leq \frac{1}{h}$. Now let

$$\widetilde{P} = \begin{bmatrix} \frac{1}{\widetilde{l}} & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{1}{\widetilde{l}} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{1}{\widetilde{l}} & 0 & 0 \\ 0 & 0 & \frac{1}{\widetilde{h}} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{1}{\widetilde{h}} & 0 \\ 0 & 0 & 0 & 0 & 0 & \frac{1}{\widetilde{h}} \end{bmatrix}$$

Since $|\frac{1}{\widetilde{l}}\widetilde{x}_i| \leq |\frac{1}{l}x_i|$ $(i = 1, 2, 4)$ and $|\frac{1}{\widetilde{h}}\widetilde{x}_i| \leq |\frac{1}{h}x_i|$ $(i = 3, 5, 6)$, by an easy computation

$$\mathcal{S}\widetilde{\phi} = \int_{\bar{\mathcal{B}}} \|\widetilde{P} \cdot (\frac{\partial \widetilde{\phi}}{\partial u_1} \wedge \frac{\partial \widetilde{\phi}}{\partial u_2})\| du \leq \int_{\bar{\mathcal{B}}} \|P \cdot (\frac{\partial \phi}{\partial u_1} \wedge \frac{\partial \phi}{\partial u_2})\| du = \mathcal{S}\phi$$

Using lemma, we can choose $\delta = \inf\{\mathcal{S}\phi : \phi \in \Sigma(\psi, \Omega)\}$. Suppose that $\{\phi^k\}$, minimizes $\mathcal{S}$ with respect to $\Sigma(\psi, \Omega)$, then $\lim_{k\to\infty} \mathcal{S}\phi^k = \delta$. Now consider the sequence $\{\widetilde{\phi}^k\} \subset \Sigma(\psi, \widetilde{\Omega})$ as in the above definition, from the boundedness of $\{\mathcal{S}\widetilde{\phi}^k\}$ and $\mathcal{S}\widetilde{\phi}^k \leq \mathcal{S}\phi^k$, we have $\lim_{k\to\infty} \mathcal{S}\widetilde{\phi}_k \leq \delta$. Furthere more $\widetilde{\phi}^k \in \Sigma(\psi, \Omega)$, hence $\mathcal{S}\widetilde{\phi}^k \geq \delta$, and $\lim_{k\to\infty} \mathcal{S}\widetilde{\phi}_k \geq \delta$, which implies $\lim_{k\to\infty} \mathcal{S}\widetilde{\phi}_k = \delta$. Now

$$\inf\{\mathcal{S}\widetilde{\phi} : \widetilde{\phi} \in \Sigma(\psi, \widetilde{\Omega})\} \leq \inf\{\mathcal{S}\phi : \phi \in \Sigma(\psi, \Omega)\} = \delta$$

and from $\widetilde{\phi} \in \Sigma(\psi, \Omega)$ we have $\inf\{\mathcal{S}\widetilde{\phi} : \widetilde{\phi} \in \Sigma(\psi, \widetilde{\Omega})\} \geq \delta$, which implies $\inf\{\mathcal{S}\widetilde{\phi} : \widetilde{\phi} \in \Sigma(\psi, \widetilde{\Omega})\} = \delta$. At the final we can show that $\lim_{k\to\infty} \mathcal{S}\widetilde{\phi}_k = \delta = \inf\{\mathcal{S}\widetilde{\phi} : \widetilde{\phi} \in \Sigma(\psi, \widetilde{\Omega})\}$, i.e. $\{\widetilde{\phi}^k\}$ minimizes $\mathcal{S}$ relative to $\Sigma(\psi, \widetilde{\Omega})$.
From lemmas (4.3) and (4.4), and as in theorem 4.5 in [10], we have the following result.

Theorem 4.5. *Suppose that the inequalities in Lemma 4.3., is verified, then:*
(1) when the only equilibrium point is the drug-free equilibrium P_0, then all solutions tend to P_0;
(2) when $R_0 > 1$, then all solutions of (2. 2) converge to the unique endemic equilibrium;
(3) when there are two endemic equilibrium points, which occurs when $R_0^c < R_0 < 1$, solutions of the system either go to the drug-free equilibrium P_0 or tend to the upper equilibrium point.

Remark. Epidemic models can be studied numerically or by the discretization shcemes, for example see, [12, 16, 23].

Conflict of interest. The authors declare that there is no conflict of interests regarding the publication of this paper.

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