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ASYMPTOTIC STABILITY FOR TWO NONLINEAR MATHEMATICAL MODELS STEMMING FROM CELL POPULATIONS

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Abstract. In this paper, we are concerned with two nonlinear mathematical models, which stem from two nonlinear systems of partial differential equations describing cell populations dynamics. We obtain some new results about the behaviors, including the global asymptotic stability, of solutions of these nonlinear systems, which lead to the corresponding results given in previous work as special cases. Moreover, an application with simulation is presented to illustrate the general result.

1. Introduction

Inspired by the works [1, 2, 3, 4, 5], we investigate in this paper the global asymptotic stability for two nonlinear mathematical models, which stem from two systems of partial differential equations describing cell populations dynamics (see (1.4) and (1.6) below) and are more general than the mathematical models considered in [5, 1].

The first one is the following differential system,

$$\left\{\begin{aligned} &\frac{d}{dt}P(t)=d(t)q(P(t))h(S(t))+(b-\mu_P-kZ(t))P(t),\\ &\frac{d}{dt}Z(t)=-\mu_Z Z(t)+kZ(t)P(t),\\ &\frac{d}{dt}S(t)=2(1-d(t-\tau))q(P(t-\tau))h(S(t-\tau))e^{-\mu_S\tau}-d(t)q(P(t))h(S(t)),\end{aligned}\right. \tag{1.1}$$

where $\mu_Z > 0$, b, k, μ_P, μ_S and τ are nonnegative constants, $d(t)$ is a uniformly Lipschitz continuous with $0 < d(t) < 1$, $q(\cdot)$ is a continuous and strictly decreasing function with

$$\lim_{x\to+\infty} q(x) = 0, \tag{1.2}$$

and $h(\cdot)$ is a continuous function satisfying

$$0 \le h(x) \le Lx \quad (\forall\ x \ge 0), \qquad h(x) > 0 \quad (\forall\ x > 0) \tag{1.3}$$

(L is a positive constant). This system originates from a model of cell population with three cell compartments (the precursor cell compartment partly in the bone morrow and partly in the blood fluid, the red blood cell compartment in the blood fluid, and the stem cell compartment in the bone morrow), where $P(t)$, $Z(t)$ and $S(t)$ are the total number of precursor cells, red blood cells, and stem cells at time t respectively, μ_P, μ_Z and μ_S are the lost rates of precursor cells, red blood cells, and stem cells respectively, $d(t)$ is the proportion of cells entering the precursor

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cell stage with a maturity level zero at time t, b is the division rate of cells with all maturation level, and τ is the time duration of the cell division process. More precisely, the model (1.1) can be transformed from the structured model of Grabosh and Heijmans [2]

(1.4)
$$\begin{cases} \dfrac{\partial}{\partial t}p(t,x) + \overline{\psi}(E(t))\dfrac{\partial}{\partial x}(g(x)p(t,x)) = b(x)p(t,x) - \overline{\psi}(E(t))a(x)p(t,x) - \mu_P p(t,x), \\ \dfrac{d}{dt}Z(t) = -\mu_Z Z(t) + \overline{\psi}(E(t))\displaystyle\int_0^{+\infty} a(x)p(t,x)dx, \end{cases}$$

under some conditions including some boundary conditions, where $p(t,x)$ is the density of the precursor cells at time t and maturation x (x is the level of maturation), $E(t)$ is the number of proteins acting between the red blood cell compartment $Z(t)$ and the precursor cell stage $P(t)$ $(= \int_0^{+\infty} p(t,x)dx)$ at time t, $\overline{\psi}(E(t))$ is a decreasing function in E, $a(x)$, $b(x)$ and $g(x)$ are real functions.

The second one is the following nonlinear system,

(1.5)
$$\begin{cases} N'(t) = -[\mu_N + r_N + q(M(t))]h(N(t)) + 2(1-r_P)e^{-\mu_P\tau}q(M(t-\tau))h(N(t-\tau)), \\ M'(t) = -\mu_M M(t) + r_N h(N(t)) + 2r_P e^{-\mu_P\tau}q(M(t-\tau))h(N(t-\tau)), \end{cases}$$

where μ_M is a positive constant, μ_N, μ_P, r_N, r_P and τ are nonnegative constants, $q(\cdot)$ and $h(\cdot)$ are given functions as in the model (1.1). This model originates from a transport system with three cell compartments also, where $N(t)$ and $M(t)$ are the total number of nonproliferating cells and maturing cells at time t respectively, μ_N, μ_P and μ_M are the lost rates of nonproliferating cells, proliferating cells and maturing cells respectively, r_N and r_P are the rates of nonproliferating cells and proliferating cells differentiating in mature cells respectively, q is the rate of nonproliferating cells becoming proliferating cells, and τ is the time duration of the cell division process. Actually, the model (1.5) can be transformed from the partial differential equation

(1.6)
$$\begin{cases} \dfrac{\partial}{\partial t}n(t,x) + \dfrac{\partial}{\partial x}n(t,x) &= -\left(\mu_N + r_N + q\left(\displaystyle\int_0^{+\infty} m(t,x)dx\right)\right)n(t,x), \\ \dfrac{\partial}{\partial t}m(t,x) + \dfrac{\partial}{\partial x}m(t,x) &= -\mu_M m(t,x), \\ \dfrac{\partial}{\partial t}p(t,x) + \dfrac{\partial}{\partial x}p(t,x) &= -\mu_P p(t,x) \end{cases}$$

under some boundary conditions, where $n(t,x)$, $m(t,x)$ and $p(t,x)$ are the cell population densities of nonproliferating, proliferating and maturing cells at time t and age x respectively.

For the special case of

$$h(x) = x, \quad x \geq 0,$$

the model (1.1) with

$$d(t) \text{ is independent of } t\text{, that is, } d(t) \equiv d \ (d \text{ is a constant}),$$

and

$$q(x) = c\frac{\theta^n}{\theta^n + x^n} \qquad \text{for } c,\ \theta > 0 \text{ and } n \in \mathbb{N},$$

was studied in [5] in terms of the characteristic equations and Rouches theorem. Moreover, for the special case of $h(x) = x$ $(x \geq 0)$, the model (1.5) was studied in [1] in terms of the characteristic equations and Lyapunov functions respectively. From [2, 5], we see that a decreased number of red blood cells leads to a decreased amount hemoglobin, thus to a decrease in the arterial oxygen tension. Then, the proteins cause an increased influx of red blood cells into the blood. Moreover, it is known that the increased influx flow could also be led also by a sudden release of nearly mature precursor cells, a higher division rate of stem cells, an increased flow from the stem cell compartment to the precursor cell compartment, or a sudden change of the number of nonproliferating cells. Therefore, the models (1.1) (the rate $d(t)$ is dependent on t) and (1.5) with nonlinear $h(\cdot)$ would be more suitable for describing the cell population. As one can see, under our setting, we not only allow $h(x) = x$, but also allow

$$h(x) = \sqrt{x^2 + \mu} - \sqrt{\mu}, \quad \text{or} \quad h(x) = k|\sin x|; \quad x \geq 0,$$

$$\text{or} \quad h(x) = \frac{\mu x}{k + x^\nu}, \quad \text{or} \quad h(x) = \frac{\mu |\sin x|}{k + x^\nu}; \quad x \geq 0,$$

($\mu > 0$, $k > 0$, and $\nu > 1$ are constants). Furthermore, h could be other nonlinear functions with (1.3).

The rest of this paper is organized as follows. Section 2 is devoted to the study of behaviors of the solutions of the mathematical model (1.1). In Section 3, we investigate behaviors of the mathematical model (1.5). Finally, an application with simulation is presented to illustrate the criterion in Section 4.

2. On the mathematical model (1.1)

Theorem 2.1. *For any positive initial data, the unique solution* $(S(t),\ P(t),\ Z(t))$ *of (1.1) is positive.*

Proof. Since the initial data is positive, we have

$$S(t) > 0, \quad P(t) > 0, \quad Z(t) > 0, \quad \text{for all } t \in [-\tau, 0]. \tag{2.1}$$

Our strategy next is as follows.

(1) We prove that it is impossible that neither $S(t)$ nor $P(t)$ is positive.
(2) We prove that it is impossible that $P(t)$ is positive but not $S(t)$.
(3) We prove that it is impossible that $S(t)$ is positive but not $P(t)$.
(4) We prove that $Z(t)$ is positive.

Firstly, let's prove (1).

If this is not true, i.e., if neither $S(t)$ nor $P(t)$ is positive, then

$$t_S := \min\{t \in [0, +\infty);\ \ S(t) = 0\} > 0, \quad \text{and} \quad t_S < +\infty,$$

$$t_P := \min\{t \in [0, +\infty);\ \ P(t) = 0\} > 0, \quad \text{and} \quad t_P < +\infty.$$

So,

$$S(t) > 0 \ \ (\forall\ t \in [0, t_S)), \quad S(t_S) = 0, \tag{2.2}$$

$$S'(t_S) = \lim_{t \to t_S^-} \frac{S(t) - S(t_S)}{t - t_S} \le 0, \tag{2.3}$$

and

$$P(t) > 0 \ \ (\forall\, t \in [0, t_P)), \quad P(t_P) = 0, \quad \text{and } P'(t_P) \le 0.$$

Case 1: $t_S \le t_P$.
In this case, we have

$$P(t) > 0 \ \ (\forall\, t \in [0, t_S)).$$

Hence, in view of (1.1), (2.1) and (2.2), we obtain

$$\begin{aligned} S'(t_S) &= 2(1 - d(t_S - \tau))q(P(t_S - \tau))h(S(t_S - \tau))e^{-\mu_S \tau} - d(t_S)q(P(t_S))h(S(t_S)), \\ &= 2(1 - d(t_S - \tau))q(P(t_S - \tau))h(S(t_S - \tau))e^{-\mu_S \tau} \\ &> 0, \end{aligned} \tag{2.4}$$

This contradicts (2.3).

Case 2: $t_P < t_S$.
In this case,

$$S(t) > 0 \ \ (\forall\, t \in [0, t_P]).$$

Therefore, by (1.1) and (1.3), we see that

$$P'(t_P) = d(t)q(P(t_P))h(S(t_P)) + (b - \mu_P - kZ(t_P))P(t_P) = d(t)q(P(t_P))h(S(t_P)) > 0, \tag{2.5}$$

which contradicts that $P'(t_P) \le 0$.
Consequently, we know that (1) is true.

Now, let's prove (2).
If this is false, i.e., if $N(t)$ is positive but not $S(t)$, then $0 < t_S < +\infty$ and (2.3) is true. Moreover, by the positivity of $P(t)$, we get (2.4) from (1.1), (2.1) and (2.2), which contradicts (2.3). Hence, (2) is true.

Next, let's prove (3).
If this does not hold, i.e., if $S(t)$ is positive but not $P(t)$. Then, then $0 < t_P < +\infty$ and $P'(t_P) \le 0$. Thus, it follows from the positivity of $S(t)$, (1.1) and (1.3) that (2.5), which contradicts that $P'(t_P) \le 0$. Therefore, (3) holds.

In conclusion, both $S(t)$ and $P(t)$ are positive.
Finally, in view of (1.1) and the positivity of $P(t)$, we obtain

$$Z(t) = Z(0)e^{-\mu_z t + k\int_0^t P(s)ds} > 0, \quad t \ge 0.$$

This means that (4) holds. □

Theorem 2.2. *Let $(S(t),\ P(t),\ Z(t))$ be a solution of (1.1) for a positive initial data, and $b < \mu_p$. Then*

(1) $\lim_{t\to+\infty} S(t) = 0$ *implies that*

$$\lim_{t\to+\infty} P(t) = 0, \quad \lim_{t\to+\infty} Z(t) = 0;$$

(2) *the boundedness of $S(t)$ for $t \geq 0$ implies that $P(t)$ and $Z(t)$ are bounded for $t \geq 0$.*

Proof. It follows from Theorem 2.1 that

$$S(t) > 0, \quad P(t) > 0, \quad Z(t) > 0, \qquad \text{for } \ t \geq 0. \tag{2.6}$$

We divide the case of $b < \mu_p$ into two cases: $b < \mu_p$ with $b - \mu_p + \mu_Z \geq 0$ and $b < \mu_p$ with $b - \mu_p + \mu_Z < 0$.

<u>Case 1:</u> $b < \mu_p$ with $b - \mu_p + \mu_Z \geq 0$.

By (1.1), we have

$$\begin{aligned}
\left(e^{(\mu_P - b)t}(P(t) + Z(t))\right)' &= e^{(\mu_P - b)t}(P'(t) + Z'(t)) \\
&\quad + (\mu_P - b)e^{(\mu_P - b)t}(P(t) + Z(t)) \\
&= d(t)q(P(t))h(S(t))e^{(\mu_P - b)t} \\
&\quad + (b - \mu_P)P(t)e^{(\mu_P - b)t} - \mu_Z Z(t)e^{(\mu_P - b)t} \\
&\quad + (\mu_P - b)e^{(\mu_P - b)t}(P(t) + Z(t)) \\
&= d(t)q(P(t))h(S(t))e^{(\mu_P - b)t} \\
&\quad - (b - \mu_P + \mu_Z)Z(t)e^{(\mu_P - b)t}, \quad t \geq 0.
\end{aligned}$$

Since $b - \mu_p + \mu_Z \geq 0$, $q(\cdot)$ is a continuous, positive and decreasing function, we see by (2.6) and (1.3) that for $t \geq 0$,

$$\begin{aligned}
P(t) + Z(t) &\leq (P(0) + Z(0))e^{(b - \mu_P)t} + e^{(b - \mu_P)t} \int_0^t d(s)q(P(s))h(S(s))e^{(\mu_P - b)s} ds \\
&\leq (P(0) + Z(0))e^{(b - \mu_P)t} + Lq(P(0))e^{(b - \mu_P)t} \int_0^t S(s)e^{(\mu_P - b)s} ds \\
&\leq (P(0) + Z(0))e^{(b - \mu_P)t} + Lq(P(0))e^{(b - \mu_P)t} \int_0^{\frac{t}{3}} S(s)e^{(\mu_P - b)s} ds \\
&\quad + Lq(P(0))e^{(b - \mu_P)t} \int_{\frac{t}{3}}^t S(s)e^{(\mu_P - b)s} ds.
\end{aligned} \tag{2.7}$$

Clearly, $\lim_{t \to +\infty} S(t) = 0$ implies that $S(t)$ is bounded, that is, there is a constant $C > 0$ such that

$$S(t) \leq C \qquad (\forall\ t \geq 0). \tag{2.8}$$

Therefore, if $b < \mu_p$, then by (2.7) and the Mean Value Theorem, we know that there is a $\xi \in [\frac{t}{3}, t]$ such that,

$$\begin{aligned}
P(t) + Z(t) &\leq (P(0) + Z(0))e^{(b - \mu_P)t} + CLq(P(0))e^{(b - \mu_P)t} \frac{e^{\frac{(\mu_P - b)t}{3}} - 1}{\mu_P - b} \\
&\quad + Lq(P(0))e^{(b - \mu_P)t} S(\xi) \int_{\frac{t}{3}}^t e^{(\mu_P - b)s} ds
\end{aligned}$$

$$\leq \quad (P(0)+Z(0))e^{(b-\mu_P)t} + CLq(P(0))\frac{e^{\frac{2(b-\mu_P)t}{3}} - e^{(b-\mu_P)t}}{\mu_P - b}$$

$$+Lq(P(0))S(\xi)\frac{1-e^{\frac{2(b-\mu_P)t}{3}}}{\mu_P - b}, \tag{2.9}$$

which goes to 0 as $t \to +\infty$ since $\lim_{t\to+\infty} S(t) = 0$. Hence, by (2.6) we get

$$\lim_{t\to+\infty}(P(t)+Z(t)) = 0.$$

Consequently,

$$\lim_{t\to+\infty} P(t) = 0, \quad \lim_{t\to+\infty} Z(t) = 0.$$

__**Case 2:**__ $b < \mu_p$ with $b - \mu_p + \mu_Z < 0$.

By (1.1), we have

$$\begin{aligned}
\left(e^{\mu_Z t}(P(t)+Z(t))\right)' &= e^{\mu_Z t}(P'(t)+Z'(t)) + \mu_Z e^{\mu_Z t}(P(t)+Z(t)) \\
&= d(t)q(P(t))h(S(t))e^{\mu_Z t} + (b-\mu_P)P(t)e^{\mu_Z t} \\
&\quad -\mu_Z Z(t)e^{\mu_Z t} + \mu_Z e^{\mu_Z t}(P(t)+Z(t)) \\
&= d(t)q(P(t))h(S(t))e^{\mu_Z t} \\
&\quad +(b-\mu_P+\mu_Z)P(t)e^{(\mu_P-b)t}, \quad t \geq 0.
\end{aligned}$$

So,

$$\begin{aligned}
P(t)+Z(t) &\leq (P(0)+Z(0))e^{\mu_Z t} + e^{-\mu_Z t}\int_0^t d(s)q(P(s))h(S(s))e^{\mu_Z s}ds \\
&\leq (P(0)+Z(0))e^{-\mu_Z t} + Lq(P(0))e^{-\mu_Z t}\int_0^t S(s)e^{\mu_Z s}ds \\
&\leq (P(0)+Z(0))e^{-\mu_Z t} + Lq(P(0))e^{-\mu_Z t}\int_0^{\frac{t}{3}} S(s)e^{\mu_Z s}ds
\end{aligned}$$

$$+Lq(P(0))e^{-\mu_Z t}\int_{\frac{t}{3}}^t S(s)e^{\mu_Z s}ds. \tag{2.10}$$

By the similar arguments as those in **Case 1** above, we obtain

$$\lim_{t\to+\infty} P(t) = 0, \quad \lim_{t\to+\infty} Z(t) = 0.$$

Consequently, (1) is true.

Moreover, if (2.8) holds, then by (2.7) (or (2.9)) and (2.10) we see that $P(t)+Z(t)$ is bounded for $t \geq 0$, so does $P(t)$ and $Z(t)$ respectively due to (2.6). Thus, (2) is also true. □

Theorem 2.3. *Assume that $d(t) \equiv d$. Then*

(1) $(0,0,0)$ *is a steady state (equilibrium) of (1.1).*

(2) *If $b < \mu_p$ and $d \neq \left(1 + \frac{1}{2}e^{\mu_S \tau}\right)^{-1}$, then $(0,0,0)$ is the only steady state of (1.1).*

(3) *If* $b > \mu_p$ *and* $d \neq \left(1 + \frac{1}{2}e^{\mu_S \tau}\right)^{-1}$, *then (1.1) has only one non-trivial steady state* $(0, \frac{\mu_z}{k}, \frac{b-\mu_P}{k})$.

Proof. Recall that a steady state (equilibrium) of (1.1), is a stationary solution $(S^*,\ P^*,\ Z^*)$, that is, $(S^*,\ P^*,\ Z^*)$, satisfies

$$dq(P^*)h(S^*) = (\mu_P - b + kZ^*)P^*, \tag{2.11}$$

$$\mu_Z Z^* = kZ^*P^*, \tag{2.12}$$

$$2(1-d)q(P^*)h(S^*)e^{-\mu_S\tau} = dq(P^*)h(S^*). \tag{2.13}$$

Clearly, $(0,0,0)$ is a steady state of (1.1). So (1) is true.

From (2.13), we see that

$$[2(1-d)e^{-\mu_S\tau} - d]h(S^*) = 0.$$

This means that $S^* = 0$ if $d \neq \left(1 + \frac{1}{2}e^{\mu_S\tau}\right)^{-1}$. Therefore, if

$$b < \mu_P \quad \text{and} \quad d \neq \left(1 + \frac{1}{2}e^{\mu_S\tau}\right)^{-1},$$

then by (2.11), we get $P^* = 0$. Moreover, we know that $Z^* = 0$ from (2.12). So (2) holds.

Furthermore, if

$$d \neq \left(1 + \frac{1}{2}e^{\mu_S\tau}\right)^{-1} \quad \text{and} \quad b > \mu_P,$$

then by (2.11) and (2.12), we see that (3) is true. □

Theorem 2.4. *Let* $b < \mu_P$ *and*

$$\left(1 + \frac{1}{2}e^{\mu_S\tau}\right)^{-1} < d(t), \quad t \geq 0.$$

Then for any positive initial data, the solution $(S(t),\ P(t),\ Z(t))$ *of (1.1) tends to (0,0,0).*

Proof. In view of Theorem 2.1, (2.6) holds.

Set

$$W(t) = S(t) + 2e^{-\mu_S\tau}\int_{t-\tau}^{t}(1-d(s))q(P(s))h(S(s))ds, \quad t \geq \tau.$$

Then

$$W(t) > 0, \qquad t \geq \tau,$$

and by (1.1),

$$\begin{aligned} W'(t) &= S'(t) - 2(1-d(t-\tau))e^{-\mu_S\tau}q(P(t-\tau))h(S(t-\tau)) \\ &\qquad + 2(1-d(t))e^{-\mu_S\tau}q(P(t))h(S(t)) \\ &= [2(1-d(t))e^{-\mu_S\tau} - d(t)]q(P(t))h(S(t)). \end{aligned} \tag{2.14}$$

Since

$$\left(1 + \frac{1}{2}e^{\mu_S\tau}\right)^{-1} < d(t) < 1, \quad t \geq 0,$$

we have

$$2(1-d(t))e^{-\mu_S\tau}-d(t)<0,\quad t\geq 0.$$

This, together with (2.14), (2.6), (1.3) and the properties of the function q, implies that

$$W'(t)<0,\qquad t\geq\tau.$$

This means that $W(t)$ is strictly decreasing. Hence, $W(t)$ is bounded on $[\tau,+\infty)$. So $S(t)$ is bounded for $t\geq 0$. By (2) of Theorem 2.2, we know that $P(t)$ and $Z(t)$ are bounded for $t\geq 0$. Therefore, we see by (1.1) that $P'(t)$ and $S'(t)$ are bounded on for $t\geq 0$. This means that $P(t)$ and $S(t)$ are uniformly Lipschitz continuous on $[0,+\infty)$. Consequently,

- $W'(t)$ is uniformly continuous on $[\tau,+\infty)$.
- $\lim\limits_{t\to+\infty} W(t)=\inf\limits_{t\geq\tau} W(t)$.

By virtue of the well-known Barbalat's Lemma, we have

$$\lim_{t\to+\infty} W'(t)=0.$$

This, together with (2.14), the boundedness of $P(t)$ and (1.3), shows that

$$\lim_{t\to+\infty} S(t)=0.$$

Thus, by (1) of Theorem 2.2,

$$\lim_{t\to+\infty} P(t)=0,\quad \lim_{t\to+\infty} Z(t)=0.$$

□

The following result is a direct consequence of Theorem 2.4

Corollary 2.5. *Let $b<\mu_P$ and $d(t)\equiv d$ with*

$$\left(1+\frac{1}{2}e^{\mu_S\tau}\right)^{-1}<d.$$

Then the steady state for (1.1) is global asymptotically stable.

3. On the mathematical model (1.5)

Theorem 3.1. *For any positive initial data, the unique solution $(M(t),\ N(t))$ of (1.5) is positive.*

Proof. It is directly conclusion of a similar argument as that of proving that $S(t)$ is positive in Theorem 2.1. □

Theorem 3.2. *Let $(M(t),\ N(t))$ be a solution of (1.5) for a positive initial data.*

(1) *If $N(t)$ is bounded, then $M(t)$ is bounded.*
(2) *If $\lim_{t\to+\infty} N(t)=0$, then $\lim_{t\to+\infty} M(t)=0$.*

Proof. In view of Theorem 3.1,

$$M(t) > 0, \quad N(t) > 0, \qquad \text{for} \;\; t \geq 0. \tag{3.1}$$

By (1.5), we have

$$\left(e^{\mu_M t} M(t)\right)' = e^{\mu_M t} r_N h(N(t)) + 2r_P e^{\mu_M t - \mu_P \tau} q(M(t-\tau))h(N(t-\tau)), \quad t \geq 0.$$

Therefore, for $t \geq \tau$,

$$\begin{aligned} M(t) &= e^{-\mu_M (t-\tau)} M(\tau) + r_N \int_\tau^t e^{\mu_M (s-t)} h(N(s)) ds \\ &\quad + 2r_P e^{-\mu_P \tau} \int_\tau^t e^{\mu_M (s-t)} q(M(s-\tau))h(N(s-\tau)) ds. \end{aligned} \tag{3.2}$$

Noting that β is decreasing and $N(t)$ is bounded, it is easy to show by (3.2) and (1.3) that (1) is true.

Next, we prove (2).

Since $\lim_{t\to+\infty} N(t) = 0$, $N(t)$ is bounded. From (1) we know that $M(t)$ is also bounded. Hence, there is a constant $C_1 > 0$ such that

$$N(t) \leq C_1, \quad M(t) \leq C_1, \qquad (\forall \; t \geq 0).$$

Thus, by (3.2) and (1.3), we obtain, for $t \geq \tau$,

$$\begin{aligned} M(t) = \;& e^{-\mu_M t} \Bigg(e^{\mu_M \tau} M(\tau) \\ & + \int_\tau^{\frac{2(t+\tau)}{3}} (r_N h(N(s)) + 2r_P e^{-\mu_P \tau}) e^{\mu_M (s-\tau)} q(M(s-\tau))h(N(s-\tau)) ds \Bigg) \\ & + e^{-\mu_M t} \int_{\frac{2(t+\tau)}{3}}^t (r_N h(N(s)) + 2r_P e^{-\mu_P \tau}) e^{\mu_M (s-\tau)} q(M(s-\tau))h(N(s-\tau)) ds \\ \leq \;& e^{-\mu_M t} \left(e^{\mu_M \tau} C_1 + [r_N + 2r_P e^{-\mu_P \tau} q(0)] L C_1 e^{\mu_M (\frac{2t-\tau}{3})} \frac{2t-\tau}{3} \right) \\ & + e^{-\mu_M t} [r_N + 2r_P e^{-\mu_P \tau} q(0)] L \int_{\frac{2(t+\tau)}{3}}^t e^{\mu_M (s-\tau)} N(s-\tau) ds. \end{aligned} \tag{3.3}$$

It is clear that

$$\lim_{t\to+\infty} e^{-\mu_M t} e^{\mu_M (\frac{2t-\tau}{3})} \frac{2t-\tau}{3} = \lim_{t\to+\infty} e^{-\mu_M (\frac{t+\tau}{3})} \frac{2t-\tau}{3} = 0. \tag{3.4}$$

Moreover, by the Mean Value Theorem, we know that there is a $\xi \in [\frac{2(t+\tau)}{3}, t]$ such that

$$\begin{aligned} e^{-\mu_M t} \int_{\frac{2(t+\tau)}{3}}^t e^{\mu_M (s-\tau)} N(s-\tau) ds &= e^{-\mu_M t} N(\xi - \tau) \int_{\frac{2(t+\tau)}{3}}^t e^{\mu_M (s-\tau)} ds \\ &= N(\xi-\tau) \frac{e^{-\mu_M \tau} - e^{-\mu_M \left(\frac{t+\tau}{3}\right)}}{\mu_M}, \end{aligned}$$

which goes to 0 as $t \to +\infty$ since $\lim_{t\to+\infty} N(t) = 0$. This fact, together with (3.3), (3.4) and (3.1), implies that

$$\lim_{t\to+\infty} M(t) = 0.$$

□

Theorem 3.3. *Let*

$$[2(1-r_P)e^{-\mu_P\tau}L - 1]q(0) < \mu_N + r_N. \tag{3.5}$$

Then

(1) $(0,0)$ *is the only steady state of (1.5);*
(2) *for any positive initial data, the solution* $(M(t),\ N(t))$ *of (1.5) tends to (0,0).*

Proof. The proof of (1) is obvious.

Next, we prove (2).

Let $(M(t),\ N(t))$ be a solution of (1.5) for a positive initial datum. Then (3.1) is true by Theorem 3.1.

Define

$$U(t) = N(t) + 2(1-r_P)e^{-\mu_P\tau}\int_{t-\tau}^{t} q(M(s))h(N(s))ds, \quad t \geq \tau.$$

Then

$$U(t) > 0, \qquad t \geq \tau, \tag{3.6}$$

and by (1.5),

$$\begin{aligned} U'(t) &= N'(t) + 2(1-r_P)e^{-\mu_P\tau}[q(M(t))h(N(t)) - q(M(t-\tau))h(N(t-\tau))] \\ &= -[\mu_N + r_N]N(t) - q(M(t))N(t) + 2(1-r_P)e^{-\mu_P\tau}q(M(t))h(N(t)). \end{aligned} \tag{3.7}$$

(i) If $2(1-r_P)e^{-\mu_P\tau}L - 1 \geq 0$, and (3.5) holds, then by (3.7), (1.3), (3.1), (1.3) and the properties of β, we obtain

$$\begin{aligned} U'(t) &\leq -[\mu_N + r_N]N(t) - q(M(t))N(t) + 2(1-r_P)e^{-\mu_P\tau}Lq(M(t))N(t) \\ &= -[\mu_N + r_N]N(t) + [2(1-r_P)e^{-\mu_P\tau}L - 1]q(M(t))N(t) \\ &\leq -[\mu_N + r_N]N(t) + [2(1-r_P)e^{-\mu_P\tau}L - 1]q(0)N(t) \\ &= \left\{[2(1-r_P)e^{-\mu_P\tau}L - 1]q(0) - [\mu_N + r_N]\right\}N(t) \\ &< 0, \quad t \geq \tau. \end{aligned} \tag{3.8}$$

(ii) If $2(1-r_P)e^{-\mu_P\tau}L - 1 < 0$, then by (3.7), (1.3), (3.1), (1.3) and the properties of β, we have

$$\begin{aligned} U'(t) &\leq -[\mu_N + r_N]N(t) - q(M(t))N(t) + 2(1-r_P)e^{-\mu_P\tau}Lq(M(t))N(t) \\ &= -[\mu_N + r_N]N(t) + [2(1-r_P)e^{-\mu_P\tau}L - 1]q(M(t))N(t) \\ &< 0, \quad t \geq \tau. \end{aligned} \tag{3.9}$$

Consequently we see that if (3.5) holds, then

$$U'(t) < 0, \qquad t \geq \tau.$$

Hence, $U(t)$ is strictly decreasing, which means that $U(t)$ is bounded on $[\tau, +\infty)$. Thus, $N(t)$ is bounded on $[0, +\infty)$. (1) of Theorem 3.2 shows that $M(t)$ is bounded on $[0, +\infty)$. By the same argument as that in the proof Theorem 2.4, we obtain

$$\lim_{t \to +\infty} U'(t) = 0. \tag{3.10}$$

Next, by virtue of the idea and similar arguments given in [3], we can prove that

$$\lim_{t \to +\infty} N(t) = 0. \tag{3.11}$$

For paper's completeness as well as readers' convenience, we present the whole proof as follows.

Suppose (3.11) is false. Then there exists at least an $\epsilon_0 > 0$ such that for every $n \in \mathbb{N}$, there is $t_n > n$ such that

$$N(t_n) > \epsilon_0.$$

The boundedness of $N(t)$ implies that there exists a subsequence $\{t_{n_k}\}$ of $\{t_n\}$ such that

$$t_{n_k} > \tau \quad \text{for all } k > k_0$$

where k_0 is a fixed positive integer, and

$$\lim_{k \to +\infty} N(t_{n_k}) = \alpha \geq \epsilon_0 > 0,$$

where α is a constant.

If $2(1 - r_P)e^{-\mu_P \tau} L - 1 \geq 0$, and (3.5) holds, then by the property of β, (3.1), (1.3) and (3.7), we obtain

$$\begin{aligned} \lim_{k \to +\infty} U'(t_{n_k}) &\leq \lim_{k \to +\infty} \left\{ [2(1 - r_P)e^{-\mu_P \tau} L - 1] q(0) - [\mu_N + r_N] \right\} N((t_{n_k})) \\ &= \alpha \left\{ [2(1 - r_P)e^{-\mu_P \tau} L - 1] q(0) - [\mu_N + r_N] \right\} \\ &< 0, \quad t \geq \tau. \end{aligned}$$

which contradicts (3.10).

Moreover, if $2(1 - r_P)e^{-\mu_P \tau} L - 1 < 0$, then, by (3.9), we have

$$\lim_{k \to +\infty} U'(t_{n_k}) = -\mu_N \lim_{k \to +\infty} N(t_{n_k}) = -\mu_N \alpha < 0,$$

which contradicts with (3.10) also.

Therefore, (3.11) holds. This, together with Theorem 3.1, shows that

$$\lim_{t \to +\infty} M(t) = 0.$$

□

4. An application with simulation

Example 4.1. Consider the following nonlinear differential system, which could be used to model a cell population

(4.1)
$$\begin{cases} N'(t) &= -2\left(1+\dfrac{1}{1+10^{-12}M(t)^{1.25}}\right)\dfrac{N(t)}{[1+4\times 10^{-8}N(t)]} \\ & \quad +\dfrac{1.92N(t-0.05)}{[1+10^{-12}M(t-0.05)^{1.25}][1+4\times 10^{-8}N(t-0.05)]}, \quad t\geq 0, \\ M'(t) &= -\dfrac{M(t)}{2}+\dfrac{0.96N(t)}{1+4\times 10^{-8}N(t)} \\ & \quad +\dfrac{1.92N(t-0.05)}{[1+10^{-12}M(t-0.05)^{1.25}][1+4\times 10^{-8}N(t-0.05)]}, \quad t\geq 0. \end{cases}$$

Take

$$\mu_N = 0.52, \quad r_N = 0.48, \quad q(M) = \frac{1}{1+10^{-12}M^{1.25}},$$
$$h(N) = \frac{2N}{1+4\times 10^{-8}N}, \quad r_P = 0.5, \quad \mu_P = -20\ln 0.96,$$
$$\tau = 0.05, \quad \mu_M = 0.5, \quad L = 2.$$

Then it is easy to see that (3.5) is satisfied for (4.1). Therefore, by virtue of Theorem 3.3, we know that for all positive initial data, the solution $(M(t),\ N(t))$ of (4.1) tends to (0,0). This means that for the model (4.1), the cell population extinct definitely.

On the other hand, solving the problem (4.1) on [0, 20] with history $M(t) = 100$, $N(t) = 100$ for $t \leq 0$, by means of the Matlab package DDE23, we obtain Figure 1 below. This figure illustrates numerically that the conclusion of Theorem 3.3

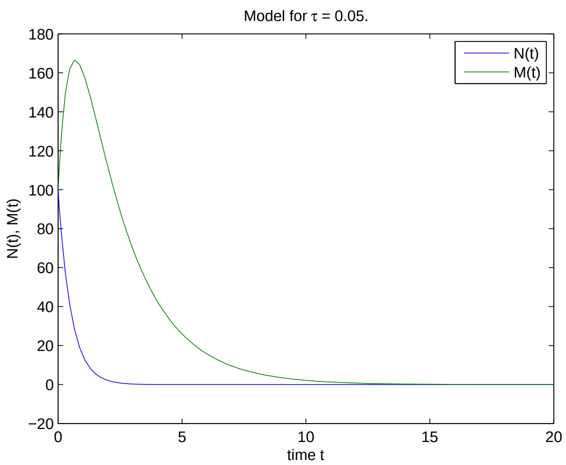

Figure 1

very well, which shows clearly that for the model (4.1), the cell population extinct definitely.

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