



## Asymptotic behavior for a cellular replication and maturation model

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### ABSTRACT

We consider a nonlocal first order partial differential equation with time delay that models simultaneous cell replication and maturation processes. We establish a comparison principle and construct monotone sequences to show the existence and uniqueness of the solution to the equation. We then analyze the asymptotic behavior of the solution via upper–lower solution technique.

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### 1. Introduction

In recent years, intensive studies have been devoted to time-age-maturation population models. One important area in which such models have been developed is that of cell replication and maturation (see [2,3,5–7,9,10,12–14] and the references cited therein). In this paper, we consider the following delayed nonlocal transport equation

$$\frac{\partial u}{\partial t} + g(x) \frac{\partial u}{\partial x} = f(t, u, u_\tau) \quad \text{for } 0 < x < 1, \quad t > 0, \quad (1.1)$$

where  $g$  is nonnegative,  $u_\tau = u(h(x), t - \tau)$ ,  $\tau > 0$  with nonnegative  $h$ , and subject to the initial condition

$$u(x, t) = \varphi(x, t) \quad \text{for } 0 \leq x \leq 1, \quad -\tau \leq t \leq 0. \quad (1.2)$$

Eq. (1.1) was introduced by Mackey and Rudnicki [9] to model the biological process of hematological cell development in bone marrow. They assumed that the cell cycle consists of two distinct phases: resting phase and proliferating phase.  $u$  is the total density of cells in the resting phase and  $x$  is the maturation variable. They showed that not only the dynamics of the population are dependent on the behavior of the cell population numbers some time in the past, but also the population behavior at a given maturation level is dependent on the behavior at a previous maturation level. Thus, they obtained Eq. (1.1) with a discrete time delay  $\tau$  and a nonlocal maturation argument  $h(x)$ , both due to cell replication. For a detailed biological background to the model, see Mackey and Rudnicki [9,10].

In order to study the global stability of (1.1), Mackey and Rudnicki [10] introduced an associated delay differential equation by ignoring the maturation variable and thus connected the global solution behavior of this associated differential equation with the local and global solution behavior of (1.1). However, they only considered the special case when the term  $f$  does not depend on  $t$ . Moreover, the nonlocal function  $h(x)$  is restricted by the condition  $h(x) < x$ . Later, He and Luo [7] investigated the long-time behavior of (1.1) by making use of the characteristic theory of first order partial differential equations and the iteration method under the assumptions that  $f$  does not depend on  $t$  and  $h(x)$  takes a special form  $h(x) = \alpha x$ .

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To relax such restrictions on the parameters, in this paper we adopt a new approach to establish the existence–uniqueness result for problem (1.1)–(1.2) and analyze the asymptotic behavior of the solution. This approach is based on the development of a comparison principle and the construction of a monotone approximation. As is well known, over the past several years, many authors have successfully applied the monotone approximation to nonlinear differential equations (see [4,8,11] and the references cited therein). Furthermore, nonnegativity of dependence on the delay term in a differential equation plays a crucial role in establishing a comparison principle. For Eq. (1.1) such nonnegativity requires that  $\partial f / \partial u_\tau \geq 0$ , which is not satisfied in general. To overcome this difficulty, here we introduce a new definition of coupled upper and lower solutions. With such a definition, we are able to establish a comparison principle and thus construct monotone sequences of upper and lower solutions which will lead to the existence of the solution by passing to the limit. We are also able to establish asymptotic behavior results for the model (1.1) by suitable pairs of upper and lower solutions.

The paper is organized as follows. In Section 2, we define a pair of coupled upper and lower solutions and establish a comparison principle. In Section 3, we construct two monotone sequences of lower and upper solutions and show their convergence to the unique local solution of (1.1)–(1.2). In Section 4, we analyze the asymptotic behavior of the model (1.1).

## 2. Comparison principle

Throughout the discussion we assume that the parameters in (1.1)–(1.2) satisfy the following:

- (H1)  $g(x)$  is continuously differentiable on  $[0, 1]$  with  $g(0) = 0$  and  $g(x) > 0$  for  $0 < x \leq 1$ .
- (H2)  $h(x)$  is continuous on  $[0, 1]$  with  $0 \leq h(x) \leq 1$  for  $0 \leq x \leq 1$ .
- (H3)  $f(t, u, u_\tau)$  is continuous with respect to  $t$  and continuously differentiable with respect to  $u$  and  $u_\tau$  on  $[0, \infty) \times (-\infty, \infty) \times (-\infty, \infty)$ . Furthermore, there exists a constant  $M \geq 0$  such that  $\partial f / \partial u_\tau(t, u, u_\tau) + M \geq 0$ .
- (H4)  $\varphi \in L^\infty([0, 1] \times [-\tau, 0])$ .

For simplicity, let  $D_T = (0, 1) \times (0, T)$ . We first introduce the definition of a weak solution of problem (1.1)–(1.2).

**Definition 2.1.** A function  $u(x, t)$  is called a weak solution of (1.1)–(1.2) on  $D_T$  if  $u$  satisfies the following:

- (i)  $u \in L^\infty(D_T)$ .
- (ii)  $u(x, t) = \varphi(x, t)$  a.e. in  $[0, 1] \times [-\tau, 0]$ .
- (iii) For each  $t \in (0, T)$  and every  $\xi \in C^1(\overline{D}_T)$  with  $\xi(\cdot, t)$  having compact support in  $(0, 1)$ ,

$$\begin{aligned} \int_0^1 u(x, t) \xi(x, t) dx &= \int_0^1 u(x, 0) \xi(x, 0) dx + \int_0^t \int_0^1 \left[ \frac{\partial \xi}{\partial s} + \frac{\partial(g\xi)}{\partial x} \right] u(x, s) dx ds \\ &\quad + \int_0^t \int_0^1 \xi(x, s) f(s, u, u_\tau) dx ds. \end{aligned} \quad (2.1)$$

Such a weak solution definition can be formally derived from multiplying (1.1) by  $\xi$  and integrating the resulting equation by parts. Conversely, if a weak solution with enough regularity exists, then one can show that it also satisfies (1.1) in the classical sense.

We then introduce the definition of coupled upper and lower solutions of problem (1.1)–(1.2).

**Definition 2.2.** A pair of functions  $\bar{u}(x, t)$  and  $\underline{u}(x, t)$  are called an upper and a lower solution of (1.1)–(1.2) on  $D_T$ , respectively, if all the following hold.

- (i)  $\bar{u}, \underline{u} \in L^\infty(D_T)$ .
- (ii)  $\bar{u}(x, t) \geq \varphi(x, t) \geq \underline{u}(x, t)$  a.e. in  $[0, 1] \times [-\tau, 0]$ .
- (iii) For each  $t \in (0, T)$  and every nonnegative  $\xi \in C^1(\overline{D}_T)$  with  $\xi(\cdot, t)$  having compact support in  $(0, 1)$ ,

$$\begin{aligned} \int_0^1 \bar{u}(x, t) \xi(x, t) dx &\geq \int_0^1 \bar{u}(x, 0) \xi(x, 0) dx + \int_0^t \int_0^1 \left[ \frac{\partial \xi}{\partial s} + \frac{\partial(g\xi)}{\partial x} \right] \bar{u}(x, s) dx ds \\ &\quad + \int_0^t \int_0^1 \xi(x, s) [f(s, \bar{u}, \bar{u}_\tau) + M(\bar{u}_\tau - \underline{u}_\tau)] dx ds, \end{aligned} \quad (2.2)$$

$$\begin{aligned}
\int_0^1 \underline{u}(x, t) \xi(x, t) dx &\leq \int_0^1 \underline{u}(x, 0) \xi(x, 0) dx + \int_0^t \int_0^1 \left[ \frac{\partial \xi}{\partial s} + \frac{\partial (g\xi)}{\partial x} \right] \underline{u}(x, s) dx ds \\
&\quad + \int_0^t \int_0^1 \xi(x, s) [f(s, \underline{u}, \underline{u}_\tau) + M(\underline{u}_\tau - \bar{u}_\tau)] dx ds.
\end{aligned} \tag{2.3}$$

Based on Definition 2.2, the following comparison principle can be established.

**Theorem 2.3.** Suppose that (H1)–(H4) hold. Let  $\bar{u}$  and  $\underline{u}$  be an upper solution and a lower solution of (1.1)–(1.2), respectively. Then  $\bar{u} \geq \underline{u}$  a.e. in  $D_T$ .

**Proof.** Let  $w(x, t) = \underline{u}(x, t) - \bar{u}(x, t)$  and  $w_\tau = \underline{u}_\tau - \bar{u}_\tau$ . Then we have

$$w(x, 0) \leq 0 \quad \text{a.e. in } (0, 1), \quad w_\tau \leq 0 \quad \text{a.e. in } [0, 1] \times [0, \tau], \tag{2.4}$$

and

$$\begin{aligned}
\int_0^1 w(x, t) \xi(x, t) dx &\leq \int_0^1 w(x, 0) \xi(x, 0) dx + \int_0^t \int_0^1 \left[ \frac{\partial \xi}{\partial s} + \frac{\partial (g\xi)}{\partial x} \right] w(x, s) dx ds \\
&\quad + \int_0^t \int_0^1 \xi \frac{\partial f}{\partial u}(s, \theta_1, \underline{u}_\tau) w dx ds \\
&\quad + \int_0^t \int_0^1 \xi \left[ \frac{\partial f}{\partial u_\tau}(s, \bar{u}, \theta_2) + 2M \right] w_\tau dx ds,
\end{aligned} \tag{2.5}$$

where  $\theta_1$  is between  $\underline{u}$  and  $\bar{u}$ , and  $\theta_2$  is between  $\underline{u}_\tau$  and  $\bar{u}_\tau$ .

Let  $\xi(x, t) = e^{\lambda t} \zeta(x, t)$ , where  $\zeta \in C^1(\bar{D}_T)$  and  $\lambda (> 0)$  is chosen so that  $\lambda + \partial f / \partial u \geq 0$  on  $[0, T] \times [c, d] \times [c_\tau, d_\tau]$ , where  $c = \min\{\inf_{D_T} \underline{u}, \inf_{D_T} \bar{u}\}$ ,  $d = \max\{\sup_{D_T} \underline{u}, \sup_{D_T} \bar{u}\}$ ,  $c_\tau = \min\{\inf_{D_T} \underline{u}_\tau, \inf_{D_T} \bar{u}_\tau\}$ , and  $d_\tau = \max\{\sup_{D_T} \underline{u}_\tau, \sup_{D_T} \bar{u}_\tau\}$ . Then we find

$$\begin{aligned}
e^{\lambda t} \int_0^1 w(x, t) \zeta(x, t) dx &\leq \int_0^1 w(x, 0) \zeta(x, 0) dx \\
&\quad + \int_0^t \int_0^1 e^{\lambda s} \left[ \frac{\partial \zeta}{\partial s} + \frac{\partial (g\zeta)}{\partial x} \right] w(x, s) dx ds \\
&\quad + \int_0^t \int_0^1 e^{\lambda s} \zeta \left[ \lambda + \frac{\partial f}{\partial u}(s, \theta_1, \underline{u}_\tau) \right] w dx ds \\
&\quad + \int_0^t \int_0^1 e^{\lambda s} \zeta \left[ \frac{\partial f}{\partial u_\tau}(s, \bar{u}, \theta_2) + 2M \right] w_\tau dx ds.
\end{aligned} \tag{2.6}$$

We now set up a backward problem as follows:

$$\begin{aligned}
\frac{\partial \zeta}{\partial s} + \frac{\partial (g\zeta)}{\partial x} &= 0, \quad 0 < s < t, \quad 0 < x < 1, \\
\zeta(x, t) &= \chi(x), \quad 0 \leq x \leq 1.
\end{aligned} \tag{2.7}$$

Here  $\chi \in C_0^\infty(0, 1)$ ,  $0 \leq \chi \leq 1$ . Since the equation in (2.7) is linear, it can be solved by the characteristic method. Note that  $0 \leq \zeta \leq \exp(\sup_{[0,1]} |g'(x)|T)$ .

Substituting such a  $\zeta$  in (2.6) yields

$$\begin{aligned} \int_0^1 w(x, t) \chi(x) dx &\leq \int_0^1 w(x, 0) \zeta(x, 0) dx + \nu \int_0^t \int_0^1 w^+(x, s) dx ds \\ &\quad + \int_0^t \int_0^1 \left[ \frac{\partial f}{\partial u_\tau}(s, \bar{u}, \theta_2) + 2M \right] w_\tau dx ds, \end{aligned} \quad (2.8)$$

where  $w^+(x, t) = \max\{w(x, t), 0\}$  and  $\nu = \max_{\bar{D}_T} \zeta[\lambda + \partial f / \partial u(t, \theta_1, \underline{u}_\tau)]$ . If  $0 < t \leq \tau$ , by (2.4) and (H3), we then have

$$\int_0^1 w(x, t) \chi(x) dx \leq \nu \int_0^t \int_0^1 w^+(x, s) dx ds.$$

Since this inequality holds for every  $\chi \in C_0^\infty(0, 1)$  with  $0 \leq \chi \leq 1$ , we can choose a sequence  $\{\chi_n\}$  on  $(0, 1)$  converging a.e. to

$$\chi(x) = \begin{cases} 1 & \text{if } w(x, t) > 0, \\ 0 & \text{otherwise.} \end{cases}$$

Consequently, we find that

$$\int_0^1 w^+(x, t) dx \leq \nu \int_0^t \int_0^1 w^+(x, s) dx ds,$$

which by Gronwall's inequality leads to

$$\int_0^1 w^+(x, t) dx = 0. \quad (2.9)$$

If  $\tau < t \leq T$ , proceeding as above, we still have (2.9). Thus, the proof is completed.  $\square$

We then establish the following uniqueness result.

**Theorem 2.4.** Suppose that (H1), (H2), (H4) hold, and  $f(t, u, u_\tau)$  is continuous with respect to  $t$  and continuously differentiable with respect to  $u$  and  $u_\tau$  on  $[0, \infty) \times (-\infty, \infty) \times (-\infty, \infty)$ . Then problem (1.1)–(1.2) has at most one solution.

**Proof.** Suppose that  $\hat{u}$  and  $\tilde{u}$  are two solutions of (1.1)–(1.2). Let  $v(x, t) = \hat{u}(x, t) - \tilde{u}(x, t)$ . Then for each  $t \in (0, T)$  and every  $\zeta \in C^{2,1}(\bar{D}_T)$  with  $\zeta(\cdot, t)$  having compact support in  $(0, 1)$ ,  $v$  satisfies

$$\begin{aligned} \int_0^1 v(x, t) \zeta(x, t) dx &= \int_0^t \int_0^1 \left[ \frac{\partial \zeta}{\partial s} + \frac{\partial(g\zeta)}{\partial x} \right] v(x, s) dx ds \\ &\quad + \int_0^t \int_0^1 \zeta \frac{\partial f}{\partial u}(s, \theta_3, \hat{u}_\tau) v dx ds \\ &\quad + \int_0^t \int_0^1 \zeta \left[ \frac{\partial f}{\partial u_\tau}(s, \tilde{u}, \theta_4) \right] v_\tau dx ds, \end{aligned} \quad (2.10)$$

where  $\theta_3$  is between  $\hat{u}$  and  $\tilde{u}$ , and  $\theta_4$  is between  $\hat{u}_\tau$  and  $\tilde{u}_\tau$ .

Let  $\zeta$  satisfy the following backward problem

$$\begin{aligned} \frac{\partial \zeta}{\partial s} + \frac{\partial(g\zeta)}{\partial x} &= 0, \quad 0 < s < t, \quad 0 < x < 1, \\ \zeta(x, t) &= \tilde{\chi}(x), \quad 0 \leq x \leq 1. \end{aligned} \quad (2.11)$$

Here  $\tilde{\chi} \in C_0^\infty(0, 1)$ ,  $-1 \leq \tilde{\chi} \leq 1$ .

Substituting such a  $\zeta$  in (2.10), we find

$$\int_0^1 v(x, t) \tilde{\chi}(x) dx \leq \tilde{v} \int_0^t \int_0^1 |v(x, s)| dx ds + \int_0^t \int_0^1 \zeta \left[ \frac{\partial f}{\partial u_\tau}(s, \tilde{u}, \theta_4) \right] v_\tau dx ds, \quad (2.12)$$

where  $\tilde{v} = \max_{\overline{D}_T} |\zeta \partial f / \partial u(t, \theta_3, \hat{u}_\tau)|$ .

If  $0 < t \leq T \leq \tau$ , since  $v_\tau = \hat{u}_\tau - \tilde{u}_\tau = 0$ , we then have

$$\int_0^1 v(x, t) \tilde{\chi}(x) dx \leq \tilde{v} \int_0^t \int_0^1 |v(x, s)| dx ds. \quad (2.13)$$

Because inequality (2.13) holds for every  $\tilde{\chi}$ , we can choose a sequence  $\{\tilde{\chi}_n\}$  on  $(0, 1)$  converging a.e. to

$$\tilde{\chi}(x) = \begin{cases} 1 & \text{if } v(x, t) > 0, \\ 0 & \text{if } v(x, t) = 0, \\ -1 & \text{if } v(x, t) < 0. \end{cases}$$

Consequently, we have

$$\int_0^1 |v(x, t)| dx \leq \tilde{v} \int_0^t \int_0^1 |v(x, s)| dx ds,$$

which upon application of Gronwall's inequality implies  $v(x, t) = 0$  on  $D_T$ .

If  $\tau < t \leq T$ , arguing analogously, we still have  $v(x, t) = 0$  on  $D_T$ .  $\square$

### 3. Monotone approximation and existence of the solution

We begin this section by constructing monotone sequences of lower and upper solutions. Suppose that  $\underline{u}^0(x, t)$  and  $\bar{u}^0(x, t)$  are a pair of lower and upper solutions of (1.1)–(1.2). Under the hypothesis (H3), we can choose a positive constant  $N$  such that  $\partial f / \partial u(t, u, u_\tau) + N \geq 0$  for  $(x, t) \in \overline{D}_T$ ,  $\underline{u}^0 \leq u \leq \bar{u}^0$ , and  $\underline{u}_\tau^0 \leq u_\tau \leq \bar{u}_\tau^0$ . We then set up two sequences  $\{\underline{u}^k\}_{k=0}^\infty$  and  $\{\bar{u}^k\}_{k=0}^\infty$  by the following procedure:

For  $k = 1, 2, \dots$ , let  $\underline{u}^k$  and  $\bar{u}^k$  satisfy the system

$$\begin{aligned} \frac{\partial \underline{u}^k}{\partial t} + g(x) \frac{\partial \underline{u}^k}{\partial x} &= f(t, \underline{u}^{k-1}, \underline{u}_\tau^{k-1}) + M(\underline{u}_\tau^{k-1} - \bar{u}_\tau^{k-1}) - N(\underline{u}^k - \underline{u}^{k-1}) \quad \text{for } (x, t) \in D_T, \\ \underline{u}^k(x, t) &= \varphi(x, t) \quad \text{for } 0 \leq x \leq 1, -\tau \leq t \leq 0, \end{aligned} \quad (3.1)$$

and

$$\begin{aligned} \frac{\partial \bar{u}^k}{\partial t} + g(x) \frac{\partial \bar{u}^k}{\partial x} &= f(t, \bar{u}^{k-1}, \bar{u}_\tau^{k-1}) + M(\bar{u}_\tau^{k-1} - \underline{u}_\tau^{k-1}) - N(\bar{u}^k - \bar{u}^{k-1}) \quad \text{for } (x, t) \in D_T, \\ \bar{u}^k(x, t) &= \varphi(x, t) \quad \text{for } 0 \leq x \leq 1, -\tau \leq t \leq 0. \end{aligned} \quad (3.2)$$

The existence of solutions to problems (3.1) and (3.2) follows from the fact that (3.1) and (3.2) both are linear problems. We first show that  $\underline{u}^0 \leq \underline{u}^1 \leq \bar{u}^1 \leq \bar{u}^0$ . Let  $w(x, t) = \underline{u}^0 - \underline{u}^1$ . Then  $w$  satisfies

$$\int_0^1 w(x, t) \xi(x, t) dx \leq \int_0^t \int_0^1 \left[ \frac{\partial \xi}{\partial s} + \frac{\partial(g\xi)}{\partial x} \right] w(x, s) dx ds + N \int_0^t \int_0^1 \xi(x, s) w(x, s) dx ds.$$

Thus,  $w(x, t) \leq 0$ , that is,  $\underline{u}^0 \leq \underline{u}^1$ . In a similar manner, it can be shown that  $\bar{u}^1 \leq \bar{u}^0$ .

We now claim that  $\underline{u}^1$  and  $\bar{u}^1$  are a lower solution and an upper solution of (1.1)–(1.2), respectively, and hence by our comparison principle  $\underline{u}^1 \leq \bar{u}^1$ . Since  $\underline{u}^0 \leq \underline{u}^1$  and  $\bar{u}^1 \leq \bar{u}^0$ , on the one hand, the right-hand side of the equation in (3.1) satisfies

$$\begin{aligned} &f(t, \underline{u}^0, \underline{u}_\tau^0) + M(\underline{u}_\tau^0 - \bar{u}_\tau^0) - N(\underline{u}^1 - \underline{u}^0) \\ &= f(t, \underline{u}^1, \underline{u}_\tau^1) - \left[ \frac{\partial f}{\partial u}(t, \theta_5, \underline{u}_\tau^0) + N \right] (\underline{u}^1 - \underline{u}^0) - \left[ \frac{\partial f}{\partial u_\tau}(t, \underline{u}^1, \theta_6) + M \right] (\underline{u}_\tau^1 - \underline{u}_\tau^0) + M(\underline{u}_\tau^1 - \bar{u}_\tau^0) \\ &\leq f(t, \underline{u}^1, \underline{u}_\tau^1) + M(\underline{u}_\tau^1 - \bar{u}_\tau^1) \end{aligned} \quad (3.3)$$

with  $\underline{u}^0 \leq \theta_5 \leq \underline{u}^1$  and  $\underline{u}_\tau^0 \leq \theta_6 \leq \underline{u}_\tau^1$ . On the other hand, the right-hand side of the equation in (3.2) satisfies

$$\begin{aligned} & f(t, \bar{u}^0, \bar{u}_\tau^0) + M(\bar{u}_\tau^0 - \underline{u}_\tau^0) - N(\bar{u}^1 - \bar{u}^0) \\ &= f(t, \bar{u}^1, \bar{u}_\tau^1) + \left[ \frac{\partial f}{\partial u}(t, \theta_7, \bar{u}_\tau^0) + N \right] (\bar{u}^0 - \bar{u}^1) + \left[ \frac{\partial f}{\partial u_\tau}(t, \bar{u}^1, \theta_8) + M \right] (\bar{u}_\tau^0 - \bar{u}_\tau^1) + M(\bar{u}_\tau^1 - \underline{u}_\tau^0) \\ &\geq f(t, \bar{u}^1, \bar{u}_\tau^1) + M(\bar{u}_\tau^1 - \underline{u}_\tau^1) \end{aligned} \quad (3.4)$$

with  $\bar{u}^1 \leq \theta_7 \leq \bar{u}^0$  and  $\bar{u}_\tau^1 \leq \theta_8 \leq \bar{u}_\tau^0$ .

We then assume that for some  $k > 1$ ,  $\underline{u}^k$  and  $\bar{u}^k$  are a lower solution and an upper solution of (1.1)–(1.2), respectively. Proceeding analogously, we can show that  $\underline{u}^k \leq \underline{u}^{k+1} \leq \bar{u}^{k+1} \leq \bar{u}^k$  and that  $\underline{u}^{k+1}$  and  $\bar{u}^{k+1}$  are also a lower solution and an upper solution of (1.1)–(1.2), respectively. Hence by induction, we obtain two monotone sequences that satisfy

$$\underline{u}^0 \leq \underline{u}^1 \leq \dots \leq \underline{u}^k \leq \bar{u}^k \leq \dots \leq \bar{u}^1 \leq \bar{u}^0 \quad \text{in } D_T$$

for each  $k = 0, 1, 2, \dots$ . From the monotonicity of the sequences  $\{\underline{u}^k\}_{k=0}^\infty$  and  $\{\bar{u}^k\}_{k=0}^\infty$ , it follows that there exist functions  $\underline{u}$  and  $\bar{u}$  such that  $\underline{u}^k \rightarrow \underline{u}$  and  $\bar{u}^k \rightarrow \bar{u}$  pointwise on  $D_T$ . Clearly  $\underline{u} \leq \bar{u}$  on  $D_T$ . Furthermore,  $\underline{u}$  and  $\bar{u}$  can be treated as an upper solution and a lower solution of (1.1)–(1.2), respectively, and hence  $\underline{u} = \bar{u}$ . Defining this common limit by  $u$ , we find that  $u$  is a solution of (1.1)–(1.2).

We now construct a pair of lower and upper solutions of (1.1)–(1.2). Let

$$M_0 = \max \left\{ 1, \sup_{[0,1] \times [-\tau,0]} |\varphi(x,t)| \right\}$$

and

$$M_1 = \sup |f(t, u, u_\tau)| \quad \text{for } (t, u, u_\tau) \in [0, 2] \times [-4M_0, 4M_0] \times [-4M_0, 4M_0].$$

We then let  $\underline{u}^0(x, t) = -M_0$  and  $\bar{u}^0(x, t) = M_0$  for  $(x, t) \in [0, 1] \times [-\tau, 0]$ , and let  $\underline{u}^0(x, t) = -M_0 e^{\sigma t}$  and  $\bar{u}^0(x, t) = M_0 e^{\sigma t}$  for  $(x, t) \in [0, 1] \times [0, 2]$ , where  $\sigma$  is a positive constant chosen to be large enough such that  $\sigma \geq M_1 + 2M$ . It can be easily shown that such  $\underline{u}^0$  and  $\bar{u}^0$  are a pair of lower and upper solutions of (1.1)–(1.2) on  $D_T$  with  $T = \min\{2, \ln 4/\sigma\}$ .

In summary, we have the following existence–uniqueness result.

**Theorem 3.1.** Suppose that hypotheses (H1)–(H4) hold. Then there exists  $T$  such that two monotone sequences  $\{\underline{u}^k(x, t)\}$  and  $\{\bar{u}^k(x, t)\}$  converge to the unique weak solution of (1.1)–(1.2) on  $D_T$ .

From the aforementioned process, we also have the following comparison result.

**Corollary 3.2.** Suppose that hypotheses (H1)–(H4) hold. Furthermore, suppose that  $\underline{u}(x, t)$  and  $\bar{u}(x, t)$  are a pair of lower and upper solutions of (1.1)–(1.2). Then the solution  $u(x, t)$  of (1.1)–(1.2) satisfies

$$\underline{u}(x, t) \leq u(x, t) \leq \bar{u}(x, t) \quad \text{on } D_T.$$

**Remark 3.3.** All the results hold if we assume instead of (H3) that  $\partial f / \partial u_\tau - M \leq 0$  and define another pair of coupled upper and lower solutions by replacing Definition 2.2(iii) with the following inequalities:

$$\begin{aligned} \int_0^1 \bar{u}(x, t) \xi(x, t) dx &\geq \int_0^1 \bar{u}(x, 0) \xi(x, 0) dx + \int_0^t \int_0^1 \left[ \frac{\partial \xi}{\partial s} + \frac{\partial(g\xi)}{\partial x} \right] \bar{u}(x, s) dx ds \\ &\quad + \int_0^t \int_0^1 \xi(x, s) [f(s, \bar{u}, \underline{u}_\tau) - M(\underline{u}_\tau - \bar{u}_\tau)] dx ds, \end{aligned} \quad (3.5)$$

$$\begin{aligned} \int_0^1 \underline{u}(x, t) \xi(x, t) dx &\leq \int_0^1 \underline{u}(x, 0) \xi(x, 0) dx + \int_0^t \int_0^1 \left[ \frac{\partial \xi}{\partial s} + \frac{\partial(g\xi)}{\partial x} \right] \underline{u}(x, s) dx ds \\ &\quad + \int_0^t \int_0^1 \xi(x, s) [f(s, \underline{u}, \bar{u}_\tau) - M(\bar{u}_\tau - \underline{u}_\tau)] dx ds. \end{aligned} \quad (3.6)$$

**Remark 3.4.** For certain nonlinearities  $f(t, u, u_\tau)$ , by constructing suitable pairs of upper and lower solutions, the hypothesis (H3) may be relaxed. Suppose that  $\bar{u}(x, t)$  and  $\underline{u}(x, t)$  are a pair of upper and lower solutions of (1.1)–(1.2) on  $D_T$ . If there exist  $A_1(x, t)$  and  $B_1(x, t)$  on  $D_T$  with  $\|A_1\|_{L^\infty} < \infty$  and  $B_1 \geq 0$  such that

$$\begin{aligned} f(t, \underline{u}, \underline{u}_\tau) - f(t, \bar{u}, \bar{u}_\tau) &= [f(t, \underline{u}, \underline{u}_\tau) - f(t, \bar{u}, \underline{u}_\tau)] + [f(t, \bar{u}, \underline{u}_\tau) - f(t, \bar{u}, \bar{u}_\tau)] \\ &= A_1(x, t)(\underline{u} - \bar{u}) + B_1(x, t)(\underline{u}_\tau - \bar{u}_\tau), \end{aligned} \quad (3.7)$$

then the hypothesis  $\partial f / \partial u_\tau + M \geq 0$  is no longer required, and we can set  $M = 0$  in (2.2) and (2.3). On the other hand, taking Remark 3.3 into account, if there exist  $A_2(x, t)$  and  $B_2(x, t)$  on  $D_T$  with  $\|A_2\|_{L^\infty} < \infty$  and  $B_2 \leq 0$  such that

$$\begin{aligned} f(t, \underline{u}, \bar{u}_\tau) - f(t, \bar{u}, \underline{u}_\tau) &= [f(t, \underline{u}, \bar{u}_\tau) - f(t, \bar{u}, \bar{u}_\tau)] + [f(t, \bar{u}, \bar{u}_\tau) - f(t, \bar{u}, \underline{u}_\tau)] \\ &= A_2(x, t)(\underline{u} - \bar{u}) - B_2(x, t)(\underline{u}_\tau - \bar{u}_\tau), \end{aligned} \quad (3.8)$$

then the hypothesis  $\partial f / \partial u_\tau - M \leq 0$  is no more needed, and we can take  $M = 0$  in (3.5) and (3.6).

#### 4. Asymptotic behavior of the model

In this section we analyze the asymptotic behavior of the model (1.1). Specifically, we use the upper–lower solution technique to study two models considered by Rey and Mackey [12], Dyson et al. [6], and Mackey and Rudnicki [10].

##### 4.1. Maturation structured model

We first consider the following equation

$$\frac{\partial u}{\partial t} + g(x) \frac{\partial u}{\partial x} = -[c_1(t) + \beta(u)]u + c_2(t)\beta(u_\tau)u_\tau. \quad (4.1)$$

In [10] under the assumptions that  $c_1$  and  $c_2$  are positive constants, and  $\beta$  is a continuously differentiable, decreasing and positive function, Mackey and Rudnicki established the following stability result:

- (i) If  $c_1 > (c_2 - 1)\beta(0)$ , then every nonnegative solution of (4.1) converges exponentially to zero as  $t \rightarrow \infty$  uniformly for  $x \in [0, 1]$ .
- (ii) If  $c_1 < (c_2 - 1)\beta(0)$ , then all solutions of (4.1) with positive initial data converge exponentially to the positive constant solution  $u_*$  as  $t \rightarrow \infty$  uniformly for  $x \in [0, 1]$ .

For time dependent functions  $c_1(t)$ ,  $c_2(t)$  and a general nonlocal term  $h(x)$ , their arguments appear not applicable, and thus we apply the theory developed in Sections 2 and 3 to (4.1). To this end, we make assumptions on the parameters as follows:

(A1)  $c_1(t)$  and  $c_2(t)$  both are positive and continuous on  $[0, \infty)$ .

(A2)  $\beta(u)$  is continuously differentiable, decreasing and positive on  $[0, \infty)$ , and  $u\beta' + \beta \geq 0$  on  $[0, \infty)$ .

Note that (H3) is satisfied because  $u\beta' + \beta \geq 0$ . We first show the global stability of the trivial solution. For this purpose, we make further assumptions as follows:

(A3)  $\inf_{[0, \infty)} c_1(t) > \sup_{[0, \infty)} (c_2(t) - 1)\beta(0)$ .

(A4) The initial data  $\varphi$  satisfies  $0 \leq \varphi \leq \eta$  on  $[0, 1] \times [-\tau, 0]$ .

Clearly,  $\underline{u} = 0$  is a lower solution. Let  $\bar{u} = \eta e^{-\mu t}$  be a positive function with  $\mu$  a positive constant to be determined. To be an upper solution,  $\bar{u}$  must satisfy the following inequality:

$$-\mu \eta e^{-\mu t} \geq -(c_1(t) + \beta(\eta e^{-\mu t}))\eta e^{-\mu t} + c_2(t)\beta(\eta e^{-\mu t} e^{\mu \tau})\eta e^{-\mu t} e^{\mu \tau}. \quad (4.2)$$

Since  $\beta$  is decreasing, the above inequality holds if we require

$$c_1(t) \geq (e^{\mu \tau} c_2(t) - 1)\beta(\eta e^{-\mu t}) + \mu. \quad (4.3)$$

In view of (A3), (4.3) is valid if we choose  $\mu$  sufficiently small. Thus, we have  $0 \leq u(x, t) \leq \eta e^{-\mu t}$ , which implies that  $u(x, t) \rightarrow 0$  as  $t \rightarrow \infty$  uniformly for  $x \in [0, 1]$ .

On the other hand, if  $c_1$  or  $c_2$  is time dependent, and if the inequality in (A3) is reversed, we may not have a global stability result. For example, if  $c_1(t) = (2t^2 + 7t + 2)/(t + 2)^2(t + 3)$ ,  $c_2 = 4$ ,  $\beta(u) = 1/(u + 1)$ , and  $\tau = 1$ , then (4.1) has the solution  $u = t + 2$ , which diverges as  $t \rightarrow \infty$ . Therefore, to show the global stability of the positive constant solution, we assume the following

(A5)  $c_1, c_2$  are positive constants with  $c_1 < (c_2 - 1)\beta(0)$  and  $\lim_{u \rightarrow \infty} \beta(u) < c_1/(c_2 - 1)$ .

(A6) The initial data  $\varphi$  satisfies  $0 < \varphi \leq \eta$  on  $[0, 1] \times [-\tau, 0]$ .

By (A5), there is a positive constant solution  $u_*$  of (4.1). Let  $\underline{u} = u_* - \delta e^{-\mu t}$  and  $\bar{u} = u_* + \eta e^{-\mu t}$ , where  $\delta$  and  $\mu$  are positive constants to be chosen so that  $0 < u_* - \delta < \varphi$  and  $0 \leq u_* - \delta e^{\mu\tau} \leq \varphi$  on  $[0, 1] \times [-\tau, 0]$ . To be a pair of lower and upper solutions,  $\underline{u}$  and  $\bar{u}$  must satisfy the following inequalities, respectively

$$-(c_1 + \beta(\underline{u}))\underline{u} + c_2\beta(\underline{u}_\tau)\underline{u}_\tau \geq \mu\delta e^{-\mu t} \quad (4.4)$$

and

$$-(c_1 + \beta(\bar{u}))\bar{u} + c_2\beta(\bar{u}_\tau)\bar{u}_\tau \leq -\mu\eta e^{-\mu t}. \quad (4.5)$$

Since  $\beta$  is decreasing,  $\beta(\underline{u}_\tau) > \beta(\underline{u})$  and  $\beta(\bar{u}_\tau) < \beta(\bar{u})$ . Moreover, by continuity of  $\beta'$  and the mean value theorem, there exist positive constants  $\sigma$  and  $\varepsilon$  ( $\varepsilon \leq \min\{\delta, \eta\}$ ) such that  $\beta(u) \geq \beta(u_*) - \sigma(u - u_*)$  for  $u_* - \varepsilon \leq u \leq u_*$  and  $\beta(u) \leq \beta(u_*) - \sigma(u - u_*)$  for  $u_* \leq u \leq u_* + \varepsilon$ . Thus, by (A5) we find

$$\begin{aligned} & -(c_1 + \beta(\underline{u}))\underline{u} + c_2\beta(\underline{u}_\tau)\underline{u}_\tau \\ & > [-c_1 + (c_2 - 1)\beta(\underline{u})]\underline{u} - \delta c_2\beta(\underline{u})(e^{\mu\tau} - 1)e^{-\mu t} \\ & > [-c_1 + (c_2 - 1)\beta(u_* - \varepsilon e^{-\mu t})]\underline{u} - \delta c_2\beta(0)(e^{\mu\tau} - 1)e^{-\mu t} \\ & > [-c_1 + (c_2 - 1)\beta(u_*)]\underline{u} + (c_2 - 1)\underline{u}\varepsilon\sigma e^{-\mu t} - \delta c_2\beta(0)(e^{\mu\tau} - 1)e^{-\mu t} \\ & \geq (c_2 - 1)(u_* - \delta)\varepsilon\sigma e^{-\mu t} - \delta c_2\beta(0)(e^{\mu\tau} - 1)e^{-\mu t} \end{aligned} \quad (4.6)$$

and

$$\begin{aligned} & -(c_1 + \beta(\bar{u}))\bar{u} + c_2\beta(\bar{u}_\tau)\bar{u}_\tau \\ & < [-c_1 + (c_2 - 1)\beta(\bar{u})]\bar{u} + \eta c_2\beta(\bar{u})(e^{\mu\tau} - 1)e^{-\mu t} \\ & < [-c_1 + (c_2 - 1)\beta(u_* + \varepsilon e^{-\mu t})]\bar{u} + \eta c_2\beta(0)(e^{\mu\tau} - 1)e^{-\mu t} \\ & < [-c_1 + (c_2 - 1)\beta(u_*)]\bar{u} - (c_2 - 1)\bar{u}\varepsilon\sigma e^{-\mu t} + \eta c_2\beta(0)(e^{\mu\tau} - 1)e^{-\mu t} \\ & \leq -(c_2 - 1)u_*\varepsilon\sigma e^{-\mu t} + \eta c_2\beta(0)(e^{\mu\tau} - 1)e^{-\mu t}. \end{aligned} \quad (4.7)$$

Then (4.6) and (4.7) yield the validity of (4.4) and (4.5), respectively, if  $\mu$  is chosen small enough. Hence, we have  $u_* - \delta e^{-\mu t} \leq u \leq u_* + \eta e^{-\mu t}$ , i.e., all solutions of (4.1) with positive initial data converge exponentially to the positive constant solution  $u_*$  as  $t \rightarrow \infty$  uniformly for  $x \in [0, 1]$ .

## 4.2. Blood production system

We then consider the following equation

$$\frac{\partial u}{\partial t} + g(x)\frac{\partial u}{\partial x} = -r(t)u + (a(t) + b(t)u_\tau)u_\tau. \quad (4.8)$$

In [10] under the assumptions that  $r, a, b$  are constants with  $r > 0$  and  $-r < a < r$ , if  $b > 0$  and  $-r/b < \varphi(0, t) < (r - a)/b$  or  $b < 0$  and  $(r - a)/b < \varphi(0, t) < -r/b$  for  $t \in [-\tau, 0]$ , Mackey and Rudnicki proved that every solution of (4.8) converges exponentially to zero as  $t \rightarrow \infty$  uniformly for  $x \in [0, 1]$ . However, for time dependent parameters and a general nonlocal term  $h(x)$ , their analysis seems not amendable, and thus we use the upper-lower solution technique to give conditions on the initial data  $\varphi$  such that all solutions of (4.8) converge exponentially to zero as  $t \rightarrow \infty$  uniformly for  $x \in [0, 1]$ .

We first consider the case that  $a(t) > 0$  and  $b(t) > 0$ . Surely, (H3) is not satisfied because  $\partial f / \partial u_\tau = a + 2bu_\tau$  is not bounded below in general. We then use the idea stated in Remark 3.4. Let  $\underline{u} = -\delta e^{-\mu t}$  and  $\bar{u} = \eta e^{-\mu t}$  with  $\delta, \eta, \mu$  positive constants to be determined.

$$(a(t) + b(t)\underline{u}_\tau)\underline{u}_\tau - (a(t) + b(t)\bar{u}_\tau)\bar{u}_\tau = [a(t) + b(t)(\eta - \delta)e^{-\mu t}e^{\mu\tau}](\underline{u}_\tau - \bar{u}_\tau). \quad (4.9)$$

Since  $a(t) > 0$ , in view of (3.7) we require that  $a(t) + b(t)(\eta - \delta) > 0$ , which is valid if

$$\inf_{(0, \infty)} \left[ \frac{a(t)}{b(t)} \right] > \delta - \eta. \quad (4.10)$$

Then as a pair of lower and upper solutions,  $\underline{u}$  and  $\bar{u}$  must satisfy the following inequalities, respectively

$$r(t)\delta e^{-\mu t} - a(t)\delta e^{-\mu t}e^{\mu\tau} + b(t)\delta^2 e^{-2\mu t}e^{2\mu\tau} \geq \mu\delta e^{-\mu t} \quad (4.11)$$



and

$$-r(t)\eta e^{-\mu t} + a(t)\eta e^{-\mu t} e^{\mu \tau} + b(t)\eta^2 e^{-2\mu t} e^{2\mu \tau} \leq -\mu \eta e^{-\mu t}. \quad (4.12)$$

These inequalities hold if  $\mu$  is sufficiently small and if

$$\inf_{[0, \infty)} [r(t) - a(t)] > 0 \quad (4.13)$$

and

$$\eta < \inf_{[0, \infty)} \left[ \frac{r(t) - a(t)}{b(t)} \right]. \quad (4.14)$$

A combination of (4.10) and (4.14) then yields

$$\delta < \inf_{[0, \infty)} \left[ \frac{a(t)}{b(t)} \right] + \inf_{[0, \infty)} \left[ \frac{r(t) - a(t)}{b(t)} \right]. \quad (4.15)$$

Since the initial data  $\varphi$  satisfies  $-\delta \leq \varphi \leq \eta$ , we find that

$$-\inf_{[0, \infty)} \left[ \frac{a(t)}{b(t)} \right] - \inf_{[0, \infty)} \left[ \frac{r(t) - a(t)}{b(t)} \right] < \varphi < \inf_{[0, \infty)} \left[ \frac{r(t) - a(t)}{b(t)} \right]. \quad (4.16)$$

**Remark 4.1.** If the condition (4.16) is valid, there exists a positive constant  $\varepsilon$  such that

$$\varepsilon < \inf_{[0, \infty)} \left[ \frac{r(t) - a(t)}{b(t)} \right]$$

and

$$-\inf_{[0, \infty)} \left[ \frac{a(t)}{b(t)} \right] - \inf_{[0, \infty)} \left[ \frac{r(t) - a(t)}{b(t)} \right] + \varepsilon \leq \varphi \leq \inf_{[0, \infty)} \left[ \frac{r(t) - a(t)}{b(t)} \right] - \varepsilon.$$

Then we can take

$$\delta = \inf_{[0, \infty)} \left[ \frac{a(t)}{b(t)} \right] + \inf_{[0, \infty)} \left[ \frac{r(t) - a(t)}{b(t)} \right] - \varepsilon \quad \text{and} \quad \eta = \inf_{[0, \infty)} \left[ \frac{r(t) - a(t)}{b(t)} \right] - \frac{\varepsilon}{2},$$

and it follows that (4.10), (4.14), and (4.15) hold.

In the case that  $a(t) > 0$  and  $b(t) < 0$ , set  $v(x, t) = -u(x, t)$ , then  $v$  satisfies the equation

$$\frac{\partial v}{\partial t} + g(x) \frac{\partial v}{\partial x} = -r(t)v + (a(t) - b(t)v_\tau)v_\tau. \quad (4.17)$$

Thus, we obtain the following condition on the initial data  $\varphi$

$$\sup_{[0, \infty)} \left[ \frac{r(t) - a(t)}{b(t)} \right] < \varphi < -\sup_{[0, \infty)} \left[ \frac{a(t)}{b(t)} \right] - \sup_{[0, \infty)} \left[ \frac{r(t) - a(t)}{b(t)} \right]. \quad (4.18)$$

We then consider the case that  $a(t) < 0$  and  $b(t) > 0$ . Obviously, the hypothesis in Remark 3.3 is not satisfied, and we again use the idea in Remark 3.4. Let  $\underline{u} = -\delta e^{-\mu t}$  and  $\bar{u} = \eta e^{-\mu t}$  with  $\delta, \eta, \mu$  positive constants to be determined.

$$(a(t) + b(t)\bar{u}_\tau)\bar{u}_\tau - (a(t) + b(t)\underline{u}_\tau)\underline{u}_\tau = -[a(t) + b(t)(\eta - \delta)e^{-\mu t}e^{\mu \tau}](\underline{u}_\tau - \bar{u}_\tau). \quad (4.19)$$

Since  $a(t) < 0$ , noticing (3.8) we require that  $a(t) + b(t)(\eta - \delta) < 0$ . Then as a pair of coupled lower and upper solutions,  $\underline{u}$  and  $\bar{u}$  must satisfy the following coupled inequalities, respectively

$$r(t)\delta e^{-\mu t} + a(t)\eta e^{-\mu t} e^{\mu \tau} + b(t)\eta^2 e^{-2\mu t} e^{2\mu \tau} \geq \mu \delta e^{-\mu t} \quad (4.20)$$

and

$$-r(t)\eta e^{-\mu t} - a(t)\delta e^{-\mu t} e^{\mu \tau} + b(t)\delta^2 e^{-2\mu t} e^{2\mu \tau} \leq -\mu \eta e^{-\mu t}. \quad (4.21)$$

Combining (4.20) and (4.21) yields

$$r(t)\delta + a(t)\eta > 0 \quad \text{and} \quad r(t)\eta + a(t)\delta > 0,$$

which further yields  $\delta = \eta$ . Then (4.20) and (4.21) hold if we require

$$\inf_{[0, \infty)} [r(t) + a(t)] > 0 \quad \text{and} \quad \eta < \inf_{[0, \infty)} \left[ \frac{r(t) + a(t)}{b(t)} \right]. \quad (4.22)$$

Hence, the initial data  $\varphi$  satisfies the condition

$$-\inf_{[0, \infty)} \left[ \frac{r(t) + a(t)}{b(t)} \right] < \varphi < \inf_{[0, \infty)} \left[ \frac{r(t) + a(t)}{b(t)} \right]. \quad (4.23)$$

Similarly, in the case that  $a(t) < 0$  and  $b(t) < 0$ , the initial data  $\varphi$  satisfies the condition

$$\sup_{[0, \infty)} \left[ \frac{r(t) + a(t)}{b(t)} \right] < \varphi < -\sup_{[0, \infty)} \left[ \frac{r(t) + a(t)}{b(t)} \right]. \quad (4.24)$$

Conditions (4.23) and (4.24) are not optimal as those obtained in [10], because in the case that  $a(t) < 0$ , a pair of coupled upper and lower solutions are introduced. On the other hand, if  $a(t) > 0$ , upper and lower solutions are uncoupled, and thus application of the upper–lower solution technique can produce satisfactory results.

Finally, it is worth pointing out that the above-mentioned discussion can be extended to the following equation

$$\frac{\partial u}{\partial t} + g(x, t) \frac{\partial u}{\partial x} = f(x, t, u, u_\tau) \quad \text{for } 0 < x < 1, \quad t > 0. \quad (4.25)$$

Furthermore, arguments used in this paper may be applied to first order nonlocal equations with distributed time delay such as the one developed by Adimy and Crauste [1].

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