

Traveling Wavefronts of a Diffusive Hematopoiesis Model with Time Delay

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Abstract

In this paper, a reaction-diffusion equation with discrete time delay that describes the dynamics of the blood cell production is analyzed. The existence of the traveling wave front solutions is demonstrated using the technique of upper and lower solutions and the associated monotone iteration.

Keywords

Traveling Wavefronts, Hematopoiesis Model, Time Delay

1. Introduction

It is well known that the traveling wave theory was initiated in 1937 by Kolmogorov, Petrovskii, Piskunov [1] and Fisher [2]. Now, the theory of traveling wave solutions to reaction-diffusion equations is one of the fast developing areas of modern mathematics and has attracted much attention due to its significance in biology, chemistry, epidemiology and physics, see [3] [4] and the reference cited therein. In recent years, the traveling wave problem for reaction-diffusion systems with delay has been widely studied. For example, Gomez and Trofimchuk [5] considered the Fisher-KPP equation and their results showed that each monotone traveling wave could be found via an iteration procedure by using the special monotone integral operators. Schaaf [6] systematically studied two scalar reaction-diffusion equations with a single discrete delay by using the phase plane technique, the maximum principle for parabolic functional differential equations and the general theory of ordinary differential equations. The degree theory has been adopted in [7] [8].

In this paper we consider the following reaction-diffusion equation with a discrete time delay:

$$\frac{\partial N(t, x)}{\partial t} = \Delta N(t, x) - \delta N(t, x) + \frac{\beta N(t - \tau, x)}{1 + N^n(t - \tau, x)}. \quad (1.1)$$

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When N is independent on the spatial variable x , the above equation reduces to the following ordinary differential equation

$$N'(t) = -\delta N(t) + \frac{\beta N(t-\tau)}{1 + N^n(t-\tau)}, \tag{1.2}$$

which was first proposed by Mackey and Glass [9] to describe the dynamics of blood cell production. Here, $N(t)$ denotes the density of mature stem cells in blood circulation and τ is the time delay between the production of immature stem cells in bone marrow and their maturation for release in the circulating blood stream; $\delta, \beta \in (0, +\infty)$ and $n \in (1, +\infty)$ are positive constants that represent some specific meanings in blood circulation. For instance, δ is the lost rate of the cells from the circulation. The term $\frac{\beta N(t-\tau)}{1 + N^n(t-\tau)}$ shows that the

flux of the cells into the circulation from the stem cell compartment depends on the number of cells N at time $t - \tau$. For more details about Hematopoiesis model, we refer the readers to the articles of Mackey [9]-[11] and the references given in them.

Equation (1.2) has been studied by many authors such as in [12]-[14]. Weng and Dai [13] proved that the positive equilibrium to Equation (1.2) could be a global attractor under some conditions. Wu, Li and Zhou [14] derived a sufficient and necessary condition that guarantees the existence of positive periodic solutions of Equation (1.2) with periodic coefficients.

Equation (1.2) can be generalized as the following functional differential equation

$$\frac{\partial u(t, x)}{\partial t} - \Delta u(t, x) = -\delta u(t, x) + f(u(t-\tau, x)). \tag{1.3}$$

Wang [15] investigated the generalized equation with Neumann boundary condition and obtained the oscillatory behavior of solutions about the positive equilibrium of (1.3). Further, they derived the sufficient and necessary conditions for global attractivity of the zero solution. In addition, global attractivity of the positive equilibrium of (1.3) was investigated by Gopalsamy and Kulencic [16]. Cheng and Zhang [17] and Jiang *et al.* [18] (n -dimensional case) instead investigated the existence of positive periodic solutions of Equation (1.3) by using the Krasnosel'skii fixed point theorem.

The aim of this paper is to consider the existence of traveling wave front solutions for (1.1) in the case of one dimensional space.

This paper is outlined as follows. The next section, we will introduce the technique of upper and lower solutions developed by Wu and Zou [19]. The conditions for establishing the positive equilibria and obtaining the existence of traveling waves are derived in Section 2.

To investigate the existence of traveling wave fronts of (1.1), we describe briefly the technique of upper and lower solutions developed by Wu and Zhou [19].

Consider a scalar reaction-diffusion equation with time delay:

$$\frac{\partial u(t, x)}{\partial t} = D \frac{\partial^2 u(t, x)}{\partial x^2} + f(u_t(x)), \tag{1.4}$$

where $t \geq 0, x \in \mathbb{R}, u \in \mathbb{R}$, and $D > 0$ is the diffusion coefficient. The function $f : C([- \tau, 0], \mathbb{R}) \rightarrow \mathbb{R}$ is continuous and $u_t(x)$ is an element in $C([- \tau, 0], \mathbb{R}) \rightarrow \mathbb{R}$ parameterized by $x \in \mathbb{R}$ and given by

$$u_t(x)(s) = u(t + s, x), \quad s \in [- \tau, 0], t \geq 0, x \in \mathbb{R}.$$

Looking for traveling wave solutions of the form $u(t, x) = \phi(x + ct)$ leads to a second-order functional differential Equation

$$D\phi''(t) - c\phi'(t) + f_c(\phi_t) = 0, \quad t \in \mathbb{R}, \tag{1.5}$$

where $f_c : X_c \triangleq C([-c\tau, 0], \mathbb{R}) \rightarrow \mathbb{R}$ is define by

$$f_c(\psi) = f(\psi^c), \quad \psi^c(s) = \psi(cs), \quad s \in [- \tau, 0].$$

Now we assume that

A1. There exists $K > 0$ such that $f_c(\hat{0}) = f_c(\hat{K}) = 0$ and $f_c(\hat{u}) \neq 0$ for $u \in (0, K)$, where \hat{u} denotes the constant function taking the value u on $[-c\tau, 0]$.

A2. There exists $\alpha \geq 0$ such that

$$f_c(\phi) - f_c(\psi) + \alpha[\phi(0) - \psi(0)] \geq 0$$

for $\phi, \psi \in X_c$ with $0 \leq \psi(s) \leq \phi(s) \leq K, s \in [-c\tau, 0]$.

If for some $c > 0$, (1.5) has a monotone solution ϕ defined on \mathbb{R} such that

$$\lim_{t \rightarrow -\infty} \phi(t) = 0, \quad \lim_{t \rightarrow \infty} \phi(t) = K, \tag{1.6}$$

then $u(t, x) = \phi(x + ct)$ is called a traveling wave front of (1.4) with a wave speed c .

Define a profile set for traveling wave fronts of (1.1) by

$$\Gamma = \left\{ \phi \in C(\mathbb{R}, \mathbb{R}^n) : \begin{array}{l} (i) \ \phi \text{ is nondecreasing in } \mathbb{R}, \\ (ii) \ \lim_{t \rightarrow -\infty} \phi(t) = 0, \ \lim_{t \rightarrow \infty} \phi(t) = K, \end{array} \right\}.$$

The upper and lower solution for (2.1) are defined as follows:

Definition 1 The piecewise smooth functions $\bar{\phi}$ and $\underline{\phi}$ in $C(\mathbb{R}, \mathbb{R})$ are called upper and lower solution of (1.4) if $\bar{\phi} \geq \underline{\phi}$ and if

$$c\bar{\phi}'(t) \geq D\bar{\phi}''(t) + f_c(\bar{\phi}_t), \quad t \in \mathbb{R}$$

and $\underline{\phi}$ satisfies the above differential inequalities in reversed order.

Now we are in the position to state a scalar version of [19] (Theorem 3.6).

Theorem 1 If the conditions (A1) and (A2) hold, suppose that (1.5) has an upper solution $\bar{\phi}$ in Γ and a lower solution $\underline{\phi}$ (which is not necessarily in Γ) with $0 \leq \underline{\phi}(t) \leq \bar{\phi}(t) \leq K$ and $\underline{\phi}(t) \neq 0$ in \mathbb{R} , then the problem (1.4) admits a traveling wave front.

2. Existence of Traveling Wave Fronts

Assume that $\beta > \delta$, and we can get two equilibria of (1.1)

$$k_1 = 0, \quad k_2 = \left(\frac{\beta}{\delta} - 1 \right)^{\frac{1}{n}} > 0.$$

We will tackle the existence of solutions of (3.1) with the asymptotic boundary condition

$$\lim_{t \rightarrow -\infty} \phi(t) = k_1, \quad \lim_{t \rightarrow \infty} \phi(t) = k_2,$$

which corresponds to the traveling wave fronts of (1.2) connecting k_1 and k_2 .

Substituting $u(t, x) = \phi(s)$ into (1.2), and denoting the moving variable s still by t , the resulting wave equation becomes

$$c\phi'(t) - \phi''(t) = -\delta\phi(t) + \frac{\beta\phi(t - c\tau)}{1 + \phi^n(t - c\tau)}. \tag{1.7}$$

Define the function

$$f_c(\phi) = -\delta\phi(0) + \frac{\beta\phi(c\tau)}{1 + \phi^n(c\tau)}.$$

Lemma 1 If $\beta > \delta$, then $f_c(\hat{0}) = f_c(\hat{k}_2) = 0$, and $f_c(\hat{K}) \neq 0$, for any $K \in (k_1, k_2)$, where \hat{K} denotes the constant function taking the value K on $[-c\tau, 0]$.

Next we show that $f_c(\phi)$ satisfies quasi-monotonicity condition with some assumptions.

Lemma 2 If $\frac{n}{n-1} > \frac{\beta}{\delta} > 1$, $n \in (1, \infty)$, then $f_c(\phi)$ satisfies the following quasi-monotonicity condition:

Take $\alpha \geq \delta$, and we have

$$f_c(\phi) - f_c(\psi) + \alpha[\phi(0) - \psi(0)] \geq 0$$

for all $\phi, \psi \in C([-c\tau, 0], \mathbb{R})$ with $k_1 \leq \psi(s) \leq \phi(s) \leq k_2$, $s \in [-c\tau, 0]$.

Proof 1 Consider the function $h(y) = \frac{y}{1+y^n}$, and it is obvious that

$$h'(y) = \frac{1+(1-n)y^n}{(1+y^n)^2} \geq 0, \quad \text{for } 0 \leq y \leq \left(\frac{1}{n-1}\right)^{\frac{1}{n}}.$$

If $\frac{n}{n-1} > \frac{\beta}{\delta} > 1$, then

$$0 \leq \psi(t) \leq \phi(t) \leq k_2 = \left(\frac{\beta}{\delta} - 1\right)^{\frac{1}{n}} \leq \left(\frac{1}{n-1}\right)^{\frac{1}{n}}$$

since $n > 1$.

It demonstrates that the function $h(y)$ is increasing on $[k_1, k_2]$. A direct computation shows that

$$\begin{aligned} f_c(\phi) - f_c(\psi) &= -\delta\phi(0) + \frac{\beta\phi(c\tau)}{1+\phi^n(c\tau)} + \delta\psi(0) - \frac{\beta\psi(c\tau)}{1+\psi^n(c\tau)} \\ &= -\delta(\phi(0) - \psi(0)) + \beta \left(\frac{\phi(c\tau)}{1+\phi^n(c\tau)} - \frac{\psi(c\tau)}{1+\psi^n(c\tau)} \right) \\ &\geq -\delta(\phi(0) - \psi(0)), \end{aligned}$$

and then

$$f_c(\phi) - f_c(\psi) + \alpha(\phi(0) - \psi(0)) \geq (\alpha - \delta)(\phi(0) - \psi(0)).$$

Therefore, if choosing $\alpha \geq \delta$, we have

$$f_c(\phi) - f_c(\psi) + \alpha(\phi(0) - \psi(0)) \geq 0.$$

This completes the proof.

Remark 1 If $n = 1$, the function $h(y) = \frac{y}{1+y}$ is increasing for all $y > 0$. When $\beta > \delta$ the condition (A2)

is hold.

Define the profile set

$$\Gamma^* = \left\{ \phi \in C(\mathbb{R}, \mathbb{R}) : \begin{array}{l} (i) \ \phi \text{ is nondecreasing in } \mathbb{R}, \\ (ii) \ \lim_{t \rightarrow -\infty} \phi(t) = k_1, \ \lim_{t \rightarrow \infty} \phi(t) = k_2, \end{array} \right\}.$$

Next we will discuss the existence problem by using the method of upper and lower solutions that are defined as follows:

Definition 2 The piecewise smooth functions $\bar{\phi}$ and $\underline{\phi}$ in $C(\mathbb{R}, \mathbb{R})$ are called upper and lower solution of (3.1) if $\bar{\phi} \geq \underline{\phi}$ and if

$$c\bar{\phi}'(t) - \bar{\phi}''(t) \geq -\delta\bar{\phi}(t) + \frac{\beta\bar{\phi}(t-c\tau)}{1+\bar{\phi}''(t-c\tau)} \text{ in } \mathbb{R}$$

and $\bar{\phi}$ satisfies the above differential inequalities in reversed order.
Define

$$\Delta_c(\lambda) = \lambda^2 - c\lambda - \delta + \beta e^{-c\lambda\tau},$$

then we have the following lemmas.

Lemma 3 *There exists $c^* > 0$ such that for $c > c^*$, $\Delta_c(\lambda) = 0$ has two positive real roots, $0 < \lambda_1 < \lambda_2$ and*

$$\Delta_c(\lambda) = \begin{cases} > 0, & \text{for } \lambda > \lambda_2, \\ < 0, & \text{for } \lambda \in (\lambda_1, \lambda_2), \\ > 0, & \text{for } \lambda < \lambda_1. \end{cases}$$

Since the proof of this lemma is similar to that of Claim 2.3 of [19], we omit it. Next we first construct the upper solution of (3.1).

Lemma 4 *Assume $c > c^*$, then $\bar{\phi}(t) = \min\{k_2, e^{\lambda_1 t}\}$ is an upper solution of (3.1) and $\bar{\phi} \in \Gamma^*$.*

Proof 2 *It is easy to verify that $\bar{\phi} \in \Gamma^*$. We show that $\bar{\phi}$ is an upper solution of (3.1).*

Let t_0 be such that $e^{\lambda_1 t_0} = k_2$.

i) For $t \geq t_0$, $\bar{\phi}'(t) = 0$, $\bar{\phi}''(t) = 0$, $\bar{\phi}(t) = k_2$, $\bar{\phi}(t-c\tau) \leq k_2$. thus

$$\bar{\phi}''(t) - c\bar{\phi}'(t) - \delta\bar{\phi}(t) + \frac{\beta\bar{\phi}(t-c\tau)}{1+\bar{\phi}''(t-c\tau)} \leq \delta k_2 + \frac{\beta\bar{\phi}(t-c\tau)}{1+\bar{\phi}''(t-c\tau)} \leq 0.$$

ii) For $t < t_0$, $\bar{\phi}(t) = e^{\lambda_1 t}$ and $\bar{\phi}(t-c\tau) = e^{\lambda_1(t-c\tau)}$, thus

$$\begin{aligned} \bar{\phi}''(t) - c\bar{\phi}'(t) - \delta\bar{\phi}(t) + \frac{\beta\bar{\phi}(t-c\tau)}{1+\bar{\phi}''(t-c\tau)} &\leq \bar{\phi}''(t) - c\bar{\phi}'(t) - \delta\bar{\phi}(t) + \beta\bar{\phi}(t-c\tau) \\ &\leq e^{\lambda_1 t} (\lambda_1^2 - c\lambda_1 - \delta + \beta e^{-c\lambda_1\tau}) = e^{\lambda_1 t} \Delta_c(\lambda_1) = 0. \end{aligned}$$

According to the discussion above, we know that $\bar{\phi}$ is an upper solution of (1.5). This completes the proof.

We now give the lower solution to (1.5). Let $c > c^*$ and $0 < \lambda_1 < \lambda_2$ be the same as those given in Lemma 3.2. Take $\varepsilon > 0$ such that $\varepsilon < \lambda_1 < \lambda_1 + \varepsilon < \lambda_2$. Define $\underline{\phi} = \max\{0, (1 - Me^{\varepsilon t})e^{\lambda_1 t}\}$, where the constant $M > 1$ is to be determined.

Lemma 5 *For $M > \frac{\beta e^{-2\lambda_1 c\tau} (1 + e^{-\varepsilon c\tau})^2}{-\Delta_c(\lambda_1 + \varepsilon)}$, $\underline{\phi}(t) = \max\{0, (1 - Me^{\varepsilon t})e^{\lambda_1 t}\}$ is a lower solution for Equation (3.1).*

Proof 3 *Let $t_1 = \frac{1}{\varepsilon} \ln\left(\frac{1}{M}\right)$, then $t_1 < 0$ for $M > 1$ and*

$$\underline{\phi}(t) = \begin{cases} 0, & \text{for } t > t_1, \\ (1 - Me^{\varepsilon t})e^{\lambda_1 t}, & \text{for } t < t_1. \end{cases}$$

i) For $t > t_1$, $\underline{\phi}(t) = 0$, $\underline{\phi}(t-c\tau) = 0$, $\underline{\phi}'(t) = 0$, and $\underline{\phi}''(t) = 0$. Hence

$$c\underline{\phi}'(t) - \underline{\phi}''(t) + \delta\underline{\phi}(t) - \frac{\beta\underline{\phi}(t-c\tau)}{1+\underline{\phi}''(t-c\tau)} = 0$$

ii) For $t < t_1$, we have

$$\begin{aligned}\underline{\phi}'(t) &= [\lambda_1 - M(\varepsilon + \lambda_1)e^{\varepsilon t}]e^{\lambda_1 t}, \\ \underline{\phi}''(t) &= [\lambda_1^2 - M(\varepsilon + \lambda_1)^2 e^{\varepsilon t}]e^{\lambda_1 t}, \\ \underline{\phi}(t - c\tau) &= [1 - Me^{\varepsilon(t-c\tau)}]e^{\lambda_1(t-c\tau)}.\end{aligned}$$

It is easy to check that $0 \leq (1 - Me^{\varepsilon(t-c\tau)})e^{\lambda_1(t-c\tau)} < 1$. It follows that $1 + \underline{\phi}'' < \frac{1}{1 - \underline{\phi}}$. Therefore

$$\begin{aligned}\underline{\phi}''(t) - c\underline{\phi}'(t) - \delta\underline{\phi}(t) + \frac{\beta\underline{\phi}(t - c\tau)}{1 + \underline{\phi}''(t - c\tau)} \\ \geq \underline{\phi}''(t) - c\underline{\phi}'(t) - \delta\underline{\phi}(t) + \beta\underline{\phi}(t - c\tau)[1 - \underline{\phi}''(t - c\tau)] \\ = [\lambda_1^2 - M(\varepsilon + \lambda_1)^2 e^{\varepsilon t}]e^{\lambda_1 t} - c[\lambda_1 - M(\varepsilon + \lambda_1)e^{\varepsilon t}]e^{\lambda_1 t} - \delta(1 - Me^{\varepsilon t})e^{\lambda_1 t} \\ + \beta[1 - Me^{\varepsilon(t-c\tau)}]e^{\lambda_1(t-c\tau)}[1 - (1 - Me^{\varepsilon(t-c\tau)})e^{\lambda_1(t-c\tau)}] \\ = e^{\lambda_1 t} [\Delta_c(\lambda_1) - Me^{\varepsilon t} \Delta_c(\lambda_1 + \varepsilon) - \beta e^{-2\lambda_1 c\tau} e^{\lambda_1 \tau} (1 - Me^{\varepsilon(t-c\tau)})] \\ \geq e^{\lambda_1 t} [-Me^{\varepsilon t} \Delta_c(\lambda_1 + \varepsilon) - \beta e^{-2\lambda_1 c\tau} e^{\varepsilon t} (1 - Me^{\varepsilon(t-c\tau)})] \\ = e^{(\lambda_1 + \varepsilon)t} [-M \Delta_c(\lambda_1 + \varepsilon) - \beta e^{-2\lambda_1 c\tau} (1 - Me^{\varepsilon(t-c\tau)})].\end{aligned}$$

Note that

$$\begin{aligned}1 - Me^{\varepsilon(t-c\tau)} &> 1 - Me^{\varepsilon t_1} e^{-\varepsilon c\tau} = 1 - e^{-\varepsilon c\tau}, \\ 1 - Me^{\varepsilon(t-c\tau)} &< 1 + Me^{\varepsilon t_1} e^{-\varepsilon c\tau} < 1 + e^{-\varepsilon c\tau}.\end{aligned}$$

Since $t < t_1 < 0$, $\varepsilon < \lambda_1$, we have $[1 - Me^{\varepsilon(t-c\tau)}]^2 < (1 - e^{\varepsilon c\tau})^2$. Thus

$$\begin{aligned}\underline{\phi}''(t) - c\underline{\phi}'(t) - \delta\underline{\phi}(t) + \frac{\beta\underline{\phi}(t - c\tau)}{1 + \underline{\phi}''(t - c\tau)} &= e^{(\lambda_1 + \varepsilon)t} [-M \Delta_c(\lambda_1 + \varepsilon) - \beta e^{-2\lambda_1 c\tau} (1 - Me^{\varepsilon(t-c\tau)})] \\ &\geq e^{(\lambda_1 + \varepsilon)t} [-M \Delta_c(\lambda_1 + \varepsilon)] \left[M - \frac{\beta e^{-2\lambda_1 c\tau} (1 + e^{-\varepsilon c\tau})^2}{-\Delta_c(\lambda_1 + \varepsilon)} \right].\end{aligned}$$

If we choose

$$M > \frac{\beta e^{-2\lambda_1 c\tau} (1 + e^{-\varepsilon c\tau})^2}{-\Delta_c(\lambda_1 + \varepsilon)},$$

then $\underline{\phi}''(t) - c\underline{\phi}'(t) - \delta\underline{\phi}(t) + \frac{\beta\underline{\phi}(t - c\tau)}{1 + \underline{\phi}''(t - c\tau)} \geq 0$. Thus $\underline{\phi}$ is a lower solution of (3.1).

It is clear that $k_1 \leq \underline{\phi} \leq \bar{\phi} \leq k_2$. Summarizing the above conclusions, we give our main result of this paper below.

Theorem 2 *If $\frac{n}{n-1} > \frac{\beta}{\delta} > 1$, $n \in (1, \infty)$, or $n = 1$, $\beta > \delta$, then for every $c > c^*$, the problem (1.2) has a*

traveling wave front which connects the equilibria $k_1 = 0$ and $k_2 = \left[\frac{\beta}{\delta} - 1\right]^{\frac{1}{n}}$.

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