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Research Article

Existence and Exponential Stability of Positive Almost Periodic Solutions for a Model of Hematopoiesis

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By employing the contraction mapping principle and applying Gronwall-Bellman's inequality, sufficient conditions are established to prove the existence and exponential stability of positive almost periodic solution for nonlinear impulsive delay model of hematopoiesis.

1. Introduction

The nonlinear delay differential equation

$$h'(t) = -\alpha h(t) + \frac{\beta}{1 + h^n(t-\tau)}, \quad t \geq 0, \tag{1.1}$$

where $\alpha, \beta, \tau > 0$, $n \in \mathbb{N}$, has been proposed by Mackey and Glass [1] as an appropriate model of hematopoiesis that describes the process of production of all types of blood cells generated by a remarkable self-regulated system that is responsive to the demands put upon it. In medical terms, $h(t)$ denotes the density of mature cells in blood circulation at time t and τ is the time delay between the production of immature cells in the bone marrow and their maturation for release in circulating bloodstream. It is assumed that the cells are lost from the circulation at a rate α, and the flux of the cells into the circulation from the stem cell compartment depends on the density of mature cells at the previous time $t - \tau$.

In the real-world phenomena, the parameters can be nonlinear functions. The variation of the environment, however, plays an important role in many biological and ecological dynamical systems. In particular, the effects of a periodically varying environment are important for evolutionary theory as the selective forces on systems in a fluctuating environment differ from those in a stable environment. Thus, the assumption of periodicity of the parameters are a way of incorporating the periodicity of the environment. It has been suggested by Nicholson [2] that any periodical change of climate tends to impose its period upon oscillations of internal origin or to cause such oscillations to have a harmonic relation to periodic climatic changes.

On the other hand, some dynamical systems which describe real phenomena are characterized by the fact that at certain moments in their evolution, they undergo rapid changes. Most notably, this takes place due to certain seasonal effects such as weather, resource availability, food supplies, and mating habits. These phenomena are best described by the so-called impulsive differential equations [3]. Thus, it is more realistic to consider the case of combined effects: periodicity of the environment, time delays and impulse actions. Namely, an equation of the form

$$\begin{gathered} h'(t) = -\alpha(t)h(t) + \frac{\beta(t)}{1 + h^n(t-\tau)}, \quad t \neq \theta_k, \\ \Delta h(\theta_k) := h(\theta_k^+) - h(\theta_k^-) = \gamma_k h(\theta_k^-) + \delta_k, \quad k \in \mathbb{N}, \end{gathered} \tag{1.2}$$

holds, where θ_k represent the instants at which the density suffers an increment of δ_k units. The density of mature cells in blood circulation decreases at prescribed instants θ_k by some medication and it is proportional to the density at that time (θ_k^-).

Theory of impulsive delay differential equations is now being recognized not only to be richer than the corresponding theory of ordinary differential equations but also to represent a more natural framework for mathematical modeling of some relevant real-world phenomena. This justifies the intensive investigation of this type of equations in the recent years. We refer the readers to the references [4–13]. The qualitative properties for model of hematopoiesis have been extensively investigated in literature, see [14–22]. In the recent paper [23], in particular, sufficient conditions have been established for the existence of periodic solutions, persistence, global attractivity, and oscillation of solutions of equation of form (1.2) improving and complementing some previously obtained ones.

One can easily see, nevertheless, that most of the equations considered in the above-mentioned papers are under periodic assumptions. In this paper, we consider the generalization to almost periodicity. Almost periodic functions are functions that are periodic up to a small error. Its study was initiated by Bohr in [24]. To the best of the authors' knowledge, there are a few published papers considering the notion of almost periodicity of delay differential equations with or without impulses, see [25–36]. Motivated by this, the aim of this paper is to establish sufficient conditions for the existence and exponential stability of positive almost periodic solution of nonlinear impulsive delay model of hematopoiesis of form (1.2). Our approach is based on using the contraction mapping principle as well as applying Gronwall-Bellman's inequality.

This paper is organized as follows. In Section 2, we present some general concepts and results that will be used later. In Section 3, we state and prove our main results on the existence of a unique positive almost periodic solution and then we show that it is stable.

2. Some Essential Definitions and Lemmas

Let $\{\theta_k\}_{k\in\mathbb{N}}$ be a fixed sequence such that $\sigma \leq \theta_1 < \theta_2 < \dots < \theta_k < \theta_{k+1} < \dots$, where $\lim_{k\to\infty}\theta_k = \infty$ and σ is a positive number.

Denote by $\mathrm{PLC}([\sigma-\tau,\sigma],\mathbb{R}^+)$ the space of all piecewise left continuous functions $\varphi : [\sigma-\tau,\sigma] \to \mathbb{R}^+$ with points of discontinuity of the first kind at $t=\theta_k,\ k\in\mathbb{N}$. By a solution of (1.2), we mean a function $h(t)$ defined on $[\sigma-\tau,\infty)$ and satisfying (1.2) for $t\geq\sigma$. For a given initial function $\xi\in\mathrm{PLC}([\sigma-\tau,\sigma],\mathbb{R}^+)$, it is well known [37] that (1.2) has a unique solution $h(t)=h(t;\sigma,\xi)$ defined on $[\sigma-\tau,\infty)$ and satisfying the initial condition:

$$h(t;\sigma,\xi)=\xi(t),\quad \sigma-\tau\leq t\leq\sigma. \tag{2.1}$$

As we are interested in solutions of biomedical significance, we restrict our attention to positive ones.

To say that impulsive delay differential equations have positive almost periodic solutions, one needs to adopt the following definitions of almost periodicity for such type of equations.

The definitions are borrowed from the monograph [3].

Definition 2.1. The set of sequences $\{\theta_k^p\}$, $\theta_k^p=\theta_{k+p}-\theta_k,\ k,p\in\mathbb{N}$, is said to be uniformly almost periodic if for arbitrary $\varepsilon>0$ there exists a relatively dense set of ε-almost periods common for any sequences.

Definition 2.2. A function $\varphi\in\mathrm{PLC}(\mathbb{R}^+,\mathbb{R}^+)$ is said to be almost periodic if the following conditions hold:

(a1) the set of sequences $\{\theta_k^p\}$ is uniformly almost periodic;

(a2) for any $\varepsilon>0$, there exists a real number $\delta=\delta(\varepsilon)>0$ such that if the points t' and t'' belong to the same interval of continuity of $\varphi(t)$ and satisfy the inequality $|t'-t''|<\delta$, then $|\varphi(t')-\varphi(t'')|<\varepsilon$;

(a3) for any $\varepsilon>0$, there exists a relatively dense set T of ε-almost periods such that if $\omega\in T$, then $|\varphi(t+\omega)-\varphi(t)|<\varepsilon$ for all $t\in\mathbb{R}^+$ satisfying the condition $|t-\theta_k|>\varepsilon$, $k\in\mathbb{N}$. The elements of T are called ε-almost periods.

Related to (1.2), we consider the linear equation:

$$\begin{gathered} h'(t)=-\alpha(t)h(t),\quad t\neq\theta_k,\\ \Delta h(\theta_k)=\gamma_k h(\theta_k),\quad k\in\mathbb{N}. \end{gathered} \tag{2.2}$$

It is well known [3] that (2.2) with an initial condition $h(t_0)=h_0$ has a unique solution represented by the form

$$h(t;t_0,h_0)=H(t,t_0)h_0,\quad t_0,h_0\in\mathbb{R}^+, \tag{2.3}$$

where H is the Cauchy matrix of (2.2) defined as follows:

$$H(t,s)=\begin{cases} e^{-\int_s^t \alpha(r)dr}, & \theta_{k-1}<s\le t\le \theta_k, \\ \prod_{i=m}^{k}(1+\gamma_i)e^{-\int_s^t \alpha(r)dr}, & \theta_{m-1}<s\le\theta_m\le\theta_k<t\le\theta_{k+1}. \end{cases} \tag{2.4}$$

Throughout this paper, we introduce the following conditions (C) for (1.2):

(C1) the function $\alpha\in C[\mathbb{R}^+,\mathbb{R}^+]$ is almost periodic in the sense of Bohr and there exists a constant μ such that $\alpha(t)\ge\mu>0$;

(C2) the sequence $\{\gamma_k\}$ is almost periodic and $-1\le\gamma_k\le 0$, $k\in\mathbb{N}$;

(C3) the set of sequences $\{\theta_k^p\}$ is uniformly almost periodic and there exists $\eta>0$ such that $\inf_{k\in\mathbb{N}}\theta_k^1=\eta>0$;

(C4) the function $\beta(t)\in C[\mathbb{R}^+,\mathbb{R}^+]$ is almost periodic in the sense of Bohr and $\sup_{t\in\mathbb{R}}|\beta(t)|<\nu$ where $\nu>0$ and $\beta(0)=0$;

(C5) the sequence $\{\delta_k\}$ is almost periodic and $\sup_{k\in\mathbb{N}}|\delta_k|<\kappa$, $k\in\mathbb{N}$.

The following results prove helpful.

Lemma 2.3 (see [3]). *Let conditions (C) hold. Then for each $\varepsilon>0$, there exists ε_1, $0<\varepsilon_1<\varepsilon$, relatively dense sets T of positive real numbers and Q of natural numbers such that the following relations are fulfilled:*

(b1) $|\alpha(t+\omega)-\alpha(t)|<\varepsilon$, $t\in\mathbb{R}^+$, $\omega\in T$;

(b2) $|\beta(t+\omega)-\beta(t)|<\varepsilon$, $t\in\mathbb{R}^+$, $\omega\in T$;

(b3) $|\gamma_{k+p}-\gamma_k|<\varepsilon$, $p\in Q$, $k\in\mathbb{N}$;

(b4) $|\delta_{k+p}-\delta_k|<\varepsilon$, $p\in Q$, $k\in\mathbb{N}$;

(b5) $|\theta_k^p-\omega|<\varepsilon_1$, $\omega\in T$, $p\in Q$, $k\in\mathbb{N}$.

Lemma 2.4 (see [3]). *Let condition (C3) be fulfilled. Then for each $j>0$, there exists a positive integer N such that on each interval of length j, there is no more than N elements of the sequence $\{\theta_k\}$, that is,*

$$i(s,t)\le N(t-s)+N, \tag{2.5}$$

where $i(s,t)$ is the number of the points θ_k in the interval (s,t).

The following lemmas provide a bound for the Cauchy matrix $H(t,s)$ of (2.2).

Lemma 2.5. *Let conditions (C1)–(C3) be satisfied. Then for the Cauchy matrix $H(t,s)$ of (2.2), there exists a positive constant μ such that*

$$H(t,s)\le e^{-\mu(t-s)},\quad t\ge s,\ t,s\in\mathbb{R}^+. \tag{2.6}$$

Proof. In virtue of condition (C2), we deduce that the sequence $\{\gamma_k\}$ is bounded. Further, it follows that $1+\gamma_k \le 1$. Thus, from (2.4) and condition (C1), we get

$$H(t,s) \le e^{-\mu(t-s)}, \quad t \ge s,\ t,s \in \mathbb{R}^+. \tag{2.7}$$

□

Lemma 2.6. *Let conditions (C1)–(C3) be satisfied. Then for each $\varepsilon > 0$, $t \in \mathbb{R}^+$, $s \in \mathbb{R}^+$, $t \ge s$, $|t-\theta_k| > \varepsilon$, $|s-\theta_k| > \varepsilon$, $k \in \mathbb{N}$, there exists a relatively dense set T of ε-almost periods of the function $\alpha(t)$ and a positive constant M such that for $\omega \in T$, it follows that*

$$|H(t+\omega,s+\omega) - H(t,s)| \le \varepsilon M e^{-(\mu/2)(t-s)}. \tag{2.8}$$

Proof. Consider the sets T and Q defined as in Lemma 2.3. Let $\omega \in T$. Since the matrix $H(t+\omega,s+\omega)$ is a solution of (2.2), we have the following:

$$\begin{gathered}\frac{\partial}{\partial t}H = \alpha(t)H(t+\omega,s+\omega) + [\alpha(t)-\alpha(t+\omega)]H(t+\omega,s+\omega), \quad t \ne \theta'_k, \\ \Delta H(\theta'_k,s) = \gamma_k H(\theta_k+\omega,s+\omega) + (\gamma_k-\gamma_{k+p})H(\theta'_k+\omega,s+\omega),\end{gathered} \tag{2.9}$$

where $\theta'_k = \theta_k - p,\ p \in Q,\ k \in \mathbb{N}$. Then,

$$\begin{aligned}H(t+\omega,s+\omega) = H(t,s) &+ \int_s^t H(t,r)[\alpha(r)-\alpha(r+\omega)]H(r+\omega,s+\omega)dr \\ &+ \sum_{s<\theta'_k<t} H(t,\theta'_k+0)[\gamma_{k+p}-\gamma_k]H(\theta'_k+\omega,s+\omega).\end{aligned} \tag{2.10}$$

In view of Lemma 2.3, it follows that if $|t-\theta'_k| > \varepsilon$, then $\theta'_{k+p} < t+\omega < \theta'_{k+p+1}$. Further, we obtain

$$|H(t+\omega,s+\omega) - H(t,s)| \le \varepsilon(t-s)e^{-\mu(t-s)} + \varepsilon i(s,t)e^{-\mu(t-s)}, \tag{2.11}$$

for $|t-\theta'_k| > \varepsilon$, $|s-\theta'_k| > \varepsilon$ where $i(s,t)$ is the number of the points θ'_k in the interval (s,t). From Lemma 2.4, (2.11) becomes

$$\begin{aligned}&|H(t+\omega,s+\omega) - H(t,s)| \\ &\quad \le \varepsilon\left[\frac{2}{\mu}\left\{\frac{\mu}{2}(t-s)e^{-(\mu/2)(t-s)}\right\} + N\frac{2}{\mu}\left\{\frac{\mu}{2}(t-s)e^{-(\mu/2)(t-s)}\right\} + Ne^{-(\mu/2)(t-s)}\right]e^{-(\mu/2)(t-s)}.\end{aligned} \tag{2.12}$$

By using the inequalities $e^{-(\mu/2)(t-s)} < 1$ and $(\mu/2)(t-s)e^{-(\mu/2)(t-s)} \le 1$, we get

$$|H(t+\omega,s+\omega) - H(t,s)| \le \varepsilon M, \tag{2.13}$$

where

$$M = \frac{2}{\mu}\left(1 + N + \frac{\mu}{2}N\right). \tag{2.14}$$

□

3. The Main Result

Throughout this section, it is assumed that

$$\nu < \mu. \tag{3.1}$$

Theorem 3.1. *Let conditions (C) hold. Then there exists a unique positive almost periodic solution $h(t)$ of* (1.2).

Proof. Let $D \subset \mathrm{PLC}(\mathbb{R}^+, \mathbb{R}^+)$ denote the set of all positive almost periodic functions $\varphi(t)$ with

$$\|\varphi\| \leq K, \tag{3.2}$$

where

$$\|\varphi\| = \sup_{t\in\mathbb{R}} |\varphi(t)|, \qquad K := \frac{1}{\mu}\nu + \frac{2}{1 - e^{-\mu}}\kappa N. \tag{3.3}$$

Define an operator F in D by the formula

$$[F\varphi](t) = \int_{-\infty}^{t} H(t,s)\beta(s)\frac{1}{1 + \varphi^n(s-\tau)}ds + \sum_{\theta_k < t} H(t,\theta_k)\delta_k. \tag{3.4}$$

One can easily check that $F\varphi$ is a solution of (1.2). In the following, we first show that F maps the set D into itself. In view of relation (2.6) and the inequality

$$\sum_{\theta_k} e^{-\mu(t-\theta_k)} = \sum_{m=0}^{\infty} \sum_{t-m-1 \leq \theta_k < t-m} e^{-\mu(t-\theta_k)} \leq 2N \sum_{m=0}^{\infty} e^{-\mu m} = 2N\frac{1}{1 - e^{-\mu}}, \tag{3.5}$$

we obtain that

$$\begin{aligned} \|F\varphi\| &= \sup_{t\in\mathbb{R}^+}\left\{ \int_{-\infty}^{t} H(t,s)|\beta(s)|\frac{1}{1 + \varphi^n(s-\tau)}ds + \sum_{\theta_k < t} H(t,\theta_k)|\delta_k| \right\} \\ &< \frac{1}{\mu}\nu + \frac{2}{1 - e^{-\mu}}\kappa N = K, \end{aligned} \tag{3.6}$$

for arbitrary $\varphi \in D$.

Now, we shall prove that $F\varphi$ is almost periodic. Indeed, let $\omega \in T,\ p \in Q$ where the sets T and Q are defined as in Lemma 2.3, it follows that

$$\begin{aligned}
&\|F\varphi(t+\omega) - F\varphi(t)\| \\
&\quad\le \sup_{t\in\mathbb{R}^+}\Bigg\{\int_{-\infty}^{t} |H(t+\omega,s+\omega)-H(t,s)|\left|\beta(s+\omega)\right|\frac{1}{1+\varphi^n(s+\omega-\tau)}ds \\
&\qquad + \int_{-\infty}^{t} H(t,s)\left|\left|\beta(s+\omega)\right|\frac{1}{1+\varphi^n(s+\omega-\tau)} - \left|\beta(s)\right|\frac{1}{1+\varphi^n(s-\tau)}\right|ds \\
&\qquad + \sum_{\theta_k<t}\left|H\left(t+\omega,\theta_{k+p}\right)-H(t,\theta_k)\right|\left|\delta_{k+p}\right| + \sum_{\theta_k<t}H(t,\theta_k)\left|\delta_{k+p}-\delta_k\right|\Bigg\}
\end{aligned} \tag{3.7}$$

or

$$\begin{aligned}
&\|F\varphi(t+\omega) - F\varphi(t)\| \\
&\quad\le \sup_{t\in\mathbb{R}^+}\Bigg\{\int_{-\infty}^{t} |H(t+\omega,s+\omega)-H(t,s)|\left|\beta(s+\omega)\right|\frac{1}{1+\varphi^n(s+\omega-\tau)}ds \\
&\qquad + \int_{-\infty}^{t} H(t,s)\Bigg\{\left|\beta(s+\omega)-\beta(s)\right|\frac{1}{1+\varphi^n(s+\omega-\tau)} \\
&\qquad\qquad + \left|\beta(s)\right|\left|\frac{1}{1+\varphi^n(s+\omega-\tau)} - \frac{1}{1+\varphi^n(s-\tau)}\right|\Bigg\}ds \\
&\qquad + \sum_{\theta_k<t}\left|H\left(t+\omega,\theta_{k+p}\right)-H(t,\theta_k)\right|\left|\delta_{k+p}\right| + \sum_{\theta_k<t}H(t,\theta_k)\left|\delta_{k+p}-\delta_k\right|\Bigg\} \le \varepsilon C_1,
\end{aligned} \tag{3.8}$$

where

$$C_1 = \frac{2}{\mu}\nu M + \frac{1}{\mu}(1+\nu) + \kappa M\frac{2N}{1-e^{-(\mu/2)}} + \frac{2N}{1-e^{-\mu}}. \tag{3.9}$$

In virtue of (3.6) and (3.8), we deduce that $F\varphi \in D$. Therefore, F is a self-mapping from D to D.

Finally, we prove that F is a contraction mapping on D. Let $\varphi, \psi \in D$. From (3.4), we have

$$\begin{aligned}
\|F\varphi - F\psi\| &\le \int_{-\infty}^{t} H(t,s)\left|\beta(s)\right|\left|\frac{1}{1+\varphi^n(s-\tau)} - \frac{1}{1+\psi^n(s-\tau)}\right|ds \\
&\le \frac{1}{\mu}\nu\|\varphi-\psi\|.
\end{aligned} \tag{3.10}$$

The assumption that $\nu < \mu$ implies that F is a contraction mapping on D. Then there exists a unique fixed point $h \in D$ such that $Fh = h$. This implies that (1.2) has a unique positive almost periodic solution $h(t)$. □

Theorem 3.2. *Let conditions (C) hold. Then the unique positive almost periodic solution $h(t)$ of* (1.2) *is exponentially stable.*

Proof. Let $g(t)$ be an arbitrary solution of (1.2) supplemented with the initial condition

$$g(t) = \zeta(t), \quad \zeta \in \mathrm{PLC}([\sigma - \tau, \sigma], \mathbb{R}^+). \tag{3.11}$$

Let $h(t)$ be the unique positive almost periodic solution of (1.2) with the initial condition (2.1). It follows that

$$h(t) - g(t) = H(t,\sigma)(\xi - \zeta) + \int_{\sigma}^{t} H(t,s)\beta(s)\left(\frac{1}{1 + h^n(s-\tau)} - \frac{1}{1 + g^n(s-\tau)}\right)ds. \tag{3.12}$$

Taking the norm of both sides, we get

$$\|h(t) - g(t)\| \le e^{-\mu(t-\sigma)}\|\xi - \zeta\| + \int_{\sigma}^{t} e^{-\mu(t-s)}\nu\|h(s) - g(s)\|ds. \tag{3.13}$$

Setting $u(t) = \|h(t) - g(t)\|e^{\mu t}$ and applying Gronwall-Bellman's inequality [38] we end up with the expression

$$\|h(t) - g(t)\| \le \|\xi - \zeta\|e^{-(\mu-\nu)(t-\sigma)}. \tag{3.14}$$

The assumption that $\nu < \mu$ implies that the unique positive almost periodic solution of (1.2) is exponentially stable. □

Corollary 3.3. *Let conditions (C) hold. If $\sup_{t\in\mathbb{R}^+}\beta(t) < \sup_{t\in\mathbb{R}^+}\alpha(t)$ then there exists a unique positive almost periodic exponential stable solution $h(t)$ of*

$$\begin{aligned} h'(t) &= -\alpha(t)h(t) + \frac{\beta(t)}{1 + h^n(t-\tau)}, \quad t \ne \theta_k, \\ \Delta h(\theta_k) &= \gamma_k h(\theta_k), \quad k \in \mathbb{N}. \end{aligned} \tag{3.15}$$

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