On almost periodic solutions for a model of hematopoiesis with an oscillatory circulation loss rate.

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Abstract

We establish and prove a fixed point theorem from which some sufficient conditions on the existence of positive almost periodic solutions for a model of hematopoiesis with oscillatory circulation loss rate are deduced. Some particular assumption under the nonlinearity of the equation has been previously considered by authors as fundamental for the study of almost periodic solutions of the model. The aim of this paper is to establish results without such assumption. Some examples are given to illustrate our results.

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1 Introduction

The following nonlinear model was proposed by Mackey and Glass [10] to describe the regulation of hematopoiesis:

\[
x'(t) = \sum_{k=1}^{M} r_k(t) \frac{x^m(t - \tau_k(t))}{1 + x^n(t - \tau_k(t))} - b(t)x(t). \tag{1}
\]

where \(x(t)\) is the concentration of cells in the circulating blood, \(f(x(t - \tau_k(t))) = r_k(t) \frac{x(t - \tau_k(t))^m}{1 + x(t - \tau_k(t))^n}\) is the flux function of cells into the blood stream and the delay \(\tau_k(t)\) is the time between the start of cellular production in the bone marrow and the release of mature cells into the blood stream at time \(t\).

The existence of almost periodic solutions for (1) has been extensively studied by a number of authors, for example, see [1, 5, 6, 8, 9] and references therein. In these works, we find that authors assume the following condition:

\[(H_0) \quad 0 \leq m \leq 1,\]

as fundamental for the study of (1). In addition, in [3, 6, 9], authors proposed the open problem of extending the existence results for (1) to the case \(m > 1\).

As pointed out in [3, 8], during some seasons the death rate becomes greater than the birth rate, so equations with oscillating coefficients have more realistic significance. In this work, with respect to equation (1) we will
assume that \( \lambda_k, n, m \) are positive constants, \( m > 1, r_k(t), b(t) \) and \( \tau_k(t) \in AP(\mathbb{R}), r_k(t) \) are positive, \( \tau_k(t) \) is nonnegative and \( b(t) \) is oscillating. To the best of our knowledge it is the first time to focus on the dynamic behavior of (1) without condition \((H_0)\).

Throughout the paper, for a bounded continuous function \( f \) we employ the notation

\[
 f^+ = \sup_{t \in \mathbb{R}} f(t) \quad \text{and} \quad f^- = \inf_{t \in \mathbb{R}} f(t).
\]

Moreover, it will be assumed that

\[
 M[b] = \lim_{t \to +\infty} \frac{1}{T} \int_t^{t+T} b(s) \, ds > 0, \quad v := \max_{1 \leq k \leq M} \{ \tau_k^+ \} > 0 \quad \text{and} \quad r_j^- > 0 \quad \text{for some} \ j \quad \text{(2)}
\]

and there exist a positive constant \( F^s \), such that

\[
 e^{-\int_s^t b(u) \, du} \leq F^s e^{-\int_t^s b^*(u) \, du}, \quad \text{for all} \ t, s \in \mathbb{R} \quad \text{such that} \ t \geq s, \quad \text{(3)}
\]

where \( b^* : \mathbb{R} \to (0, +\infty) \) is a bounded continuous function with positive infimum.

**Remark 1.1** It is worth noticing that when \( b^- > 0 \), inequation (3) is fulfilled with \( F^s = 1 \) and \( b^*(t) \equiv b(t) \). Thus, our techniques are applicable when \( b(t) \) is not oscillating.

## 2 Preliminaries

**Definition 2.1** (Corduneanu [4]) Let \( X \) be a Banach space. A function \( f : \mathbb{R} \to X \) is called **almost periodic** if for any \( \epsilon > 0 \) there exists a number \( l(\epsilon) > 0 \) such that any interval on \( \mathbb{R} \) of length \( l(\epsilon) \) contains at least one point \( \xi \) with the property that

\[
 ||f(t + \xi) - f(t)|| < \epsilon \quad \text{for all} \ t \in \mathbb{R}.
\]

**Definition 2.2** Let \( X \) be a real Banach space. A nonempty closed set \( C \subset X \) is called a **cone** if the following conditions are fulfilled:

\[
 (a) \ C + C \subset C \quad \quad (b) \ C \cap -C = \{0\} \quad \quad (c) \ C \text{ is convex},
\]

where \( 0 \) denotes the zero element of \( X \).

Every cone \( C \) induces a partial order \( \leq \) in \( X \) given by

\[
 x \leq y \text{ if and only if} \ y - x \in C.
\]

If \( x \leq y \) and \( x \neq y \), we write \( x < y \). A set \( \{ z \in X \mid x \leq z \leq y \} \) is called an **order interval** and shall be denoted as \( [x, y] \). The interior of \( C \) shall be denoted by \( C^0 \). A cone \( C \) is called **normal** if there exists a constant \( N > 0 \) such that

\[
 0 \leq x \leq y \text{ implies that} \ ||x|| \leq N||y||.
\]

The smaller constant \( N \) satisfying the inequality is called the **normal constant** of \( C \).

We denote by \( AP(\mathbb{R}) \) the Banach space of almost periodic real functions defined on \( \mathbb{R} \), equipped with the usual supremum norm. Also, we denote

\[
 P := \{ x \in AP(\mathbb{R}) : x(t) \geq 0, \forall t \in \mathbb{R} \},
\]

the normal cone of nonnegative functions. It is easy to verify that

\[
 P^\circ = \{ x \in P : \exists \epsilon > 0 \text{ such that} \ x(t) \geq \epsilon, \forall t \in \mathbb{R} \}.
\]
Definition 2.3 (Guo and Lakshmikantham [7]) Let \((X, \leq)\) be an ordered Banach space and let \(E \subset X\). An operator \(\Phi : E \times E \to X\) is called a \textit{mixed monotone operator} if \(\Phi(x, y)\) is nondecreasing in \(x\) and nonincreasing in \(y\). An element \(\bar{x} \in E\) is called a \textit{fixed point} of \(\Phi\) if \(\Phi(\bar{x}, \bar{x}) = \bar{x}\).

We first establish the following abstract fixed point Lemma which will play an important role in sequel.

Lemma 2.1 Let \(\Phi\) be an operator \(\Phi : P^0 \to P^0\). Assume that

(I) there exist \(u_0, v_0 \in P^0\), \(u_0 < v_0\) such that \(u_0 \leq \Phi(u_0, v_0)\) and \(v_0 \geq \Phi(v_0, u_0)\);

(II) \(\Phi\) is a mixed monotone operator on \([u_0, v_0] \times [u_0, v_0]\);

(III) there exists a function \(\phi : [\frac{u_0}{v_0}, 1) \to (0, +\infty)\) such that \(\phi(\gamma) > \gamma\), for any \(x, y \in [u_0, v_0]\)

\[
\Phi(\gamma x, \gamma^{-1} y) \geq \phi(\gamma) \Phi(x, y), \quad \text{for all} \quad \gamma \in \left[\frac{u_0}{v_0}, 1\right).
\]

Then \(\Phi\) has exactly one fixed point \(\bar{x}\) in \([u_0, v_0]\).

Proof: Let \(u_n := \Phi(u_{n-1}, v_{n-1})\) and \(v_n := \Phi(v_{n-1}, u_{n-1})\), \(n \in \mathbb{N}\). By (I) and the mixed monotonicity of \(\Phi\), we have \(u_0 \leq u_1 = \Phi(u_0, v_0) \leq \Phi(v_0, u_0) = v_1 \leq v_0\), and inductively we obtain

\[
u_0 \leq u_1 \leq \ldots \leq u_n \leq \ldots \leq v_n \leq \ldots \leq v_1 \leq v_0.
\]

(4)

Since \(u_n\) is in the open set \(P^0\), there exists a constant \(\delta > 0\) such that for any \(\lambda \in (0, \delta)\), \(u_n - \lambda v_n \in P^0\).

Thus, the constant \(\lambda_n := \sup\{\lambda : u_n \geq \lambda v_n\}\) is well defined for each \(n \in \mathbb{N}_0\) and

\[u_n \geq \lambda_n v_n.\]

(5)

Moreover, from \(u_{n+1} \geq u_n \geq \lambda_n v_n \geq \lambda_n v_{n+1}\), it is easy to verify that \(\lambda_{n+1} \geq \lambda_n\). Thus, inductively we obtain

\[\lambda_0 \leq \lambda_1 \leq \ldots \leq \lambda_n \leq \ldots \leq 1.\]

In addition, since \(\frac{u_n}{v_n} \in \{\lambda : u_0 \geq \lambda v_0\}\), we have \(\frac{u_n}{v_n} \leq \lambda_n \leq 1\) for all \(n \in \mathbb{N}_0\).

We claim that \(\lambda := \lim_{n \to +\infty} \lambda_n = 1\). Otherwise, suppose that \(\lambda < 1\) and consider the following two cases:

Case 1. Suppose that there exists \(\pi\) such that \(\lambda \pi = \bar{x}\). Then \(u_n \geq \bar{x} v_n\) for all \(n > \pi\) which, together with (II), (III) and (4), yield

\[u_{n+1} = \Phi(u_n, v_n) \geq \Phi(\lambda v_n, \lambda^{-1} u_n) \geq \phi(\lambda) \Phi(v_n, u_n) = \phi(\lambda) v_{n+1}.
\]

Thus, \(\lambda_{n+1} \geq \phi(\lambda) > \bar{x}\), which contradicts the fact that \(\lambda_{n+1} = \bar{x}\).

Case 2. Suppose that \(\lambda_n < \bar{x}\), for all \(n\). In view of (II), (III) and (4), we have

\[
u_{n+1} \geq \Phi(\lambda_n v_n, \lambda_n^{-1} u_n) = \Phi\left(\frac{\lambda_n}{\bar{x}} \lambda^{-1} v_n, \frac{1}{\lambda_n} \lambda^{-1} u_n\right) \\
\geq \phi\left(\frac{\lambda_n}{\bar{x}}\right) \Phi\left(\bar{x} v_n, \bar{x}^{-1} u_n\right) > \frac{\lambda_n}{\bar{x}} \phi\left(\bar{x}\right) \phi(v_n, u_n) > \frac{\lambda_n}{\bar{x}} \phi\left(\bar{x}\right) v_{n+1}.
\]

Thus, \(\lambda_{n+1} \geq \frac{\lambda_n}{\bar{x}} \phi\left(\bar{x}\right)\). Letting \(n \to \infty\), we obtain \(\bar{x} \geq \phi\left(\bar{x}\right) > \bar{x}\), a contradiction.
In view of (4)-(5), it follows that
\[ 0 \leq u_{n+k} - u_n \leq v_n - u_n \leq v_n - \lambda_n v_n = (1 - \lambda_n) v_n \leq (1 - \lambda_n) v_0, \quad \text{for any } n, k \in \mathbb{N}. \quad (6) \]
It is followed by the normality of \( P \) and (6),
\[ ||u_{n+k} - u_n|| \leq N(1 - \lambda_n)||v_0|| \to 0 \quad \text{as } n \to \infty. \]
Thus, \( \{u_n\}_{n \in \mathbb{N}} \) is a Cauchy sequence. This implies that there exists \( \overline{\pi} \in [u_0, v_0] \) such that \( u_n \to \overline{\pi} \). Similarly,
\[ 0 \leq v_n - u_n \leq v_n - \lambda_n v_n = (1 - \lambda_n) v_n \leq (1 - \lambda_n) v_0 \]
and
\[ ||v_n - u_n|| \leq N(1 - \lambda_n)||v_0|| \to 0 \quad \text{as } n \to \infty, \]
which implies that \( v_n \to \overline{\pi} \). From the mixed monotonicity of \( \Phi \) on \([u_0, v_0]\), we have
\[ u_{n+1} = \Phi(u_n, v_n) \leq \Phi(\overline{\pi}, \overline{\pi}) = \overline{v}, \quad v_{n+1} = \Phi(v_n, u_n) = v_{n+1}. \]
We conclude that \( \overline{\pi} = \Phi(\overline{\pi}, \overline{\pi}) \).

Suppose now that \( \overline{\pi} \in [u_0, v_0] \) is a fixed point of \( \Phi \). Let \( \alpha := \sup\{\tilde{\alpha} \in (0, 1) : \tilde{\alpha}\overline{\pi} \leq \overline{\pi} \leq \tilde{\alpha}^{-1} \overline{\pi}\} \). Since \( \overline{\pi}, \overline{\pi} \) have positive infimum, \( \alpha \) is well defined. In addition, \( \alpha \overline{\pi} \leq \overline{\pi} \leq \alpha^{-1} \overline{\pi} \) and \( \alpha \in \left[\frac{u_0}{v_0}, 1\right] \). Suppose that \( \alpha \in \left[\frac{u_0}{v_0}, 1\right] \), then
\[ \overline{\pi} = \Phi(\overline{\pi}, \overline{\pi}) \leq \Phi(\frac{1}{\alpha} \overline{\pi}, \alpha \overline{\pi}) \leq \phi(\alpha)^{-1} \Phi(\overline{\pi}, \overline{\pi}) = \phi(\alpha)^{-1} \overline{\pi}, \]
and
\[ \overline{\pi} = \Phi(\overline{\pi}, \overline{\pi}) \geq \Phi(\alpha \overline{\pi}, \frac{1}{\alpha} \overline{\pi}) \geq \phi(\alpha) \Phi(\overline{\pi}, \overline{\pi}) = \phi(\alpha) \overline{\pi}. \]
Thus, by the definition of \( \alpha \) we have \( \phi(\alpha) \leq \alpha \), a contradiction. Therefore \( \overline{\pi} = \overline{\pi} \), and the proof is complete.

**Lemma 2.2** Let \( x(t) \) be a solution of
\[ x'(t) = f(t, x(t - \tau_1(t)), \ldots, x(t - \tau_M(t))) - b(t)x(t). \quad (7) \]
If \( x(t) \) is defined in the whole real line, then
\[ x(t) = \int_{-\infty}^{t} e^{-\int_{s}^{t} b(u)du} f(t, x(t - \tau_1(t)), \ldots, x(t - \tau_M(t)))ds, \quad \text{for all } t \in \mathbb{R}. \quad (8) \]
**Proof:** Let \( t_1, \in \mathbb{R} \). Integrating (7) from \( t_1 \) to \( t \), we have
\[ x(t) = x(t_1)e^{-\int_{t_1}^{t} b(u)du} + \int_{t_1}^{t} e^{-\int_{s}^{t} b(u)du} f(t, x(t - \tau_1(t)), \ldots, x(t - \tau_M(t)))ds. \]
In addition, as \( x(t) \) is defined on the whole real line, by taking the limit on the right-hand side of the equality
we obtain (8). The proof is complete.

**Remark 2.1** Let \( A, m, n \) be positive constants, with \( m > 1 \). Define the constant \( B \) as
\[ B := A \left[ \frac{n A^n}{(m - 1)(1 + A^n)} \right]^{\frac{1}{n - m + 1}}. \quad (9) \]
Thus,
\[ B > A \text{ if and only if } A > \left( \frac{m - 1}{n - m + 1} \right)^{\frac{1}{n}}. \quad (10) \]
3 Existence of almost periodic solutions.

**Theorem 3.1** Let \( n > m - 1 > 0 \) and \( n \leq m \). Let \( A \) be a constant such that \( A > \left( \frac{m-1}{n-m+1} \right)^{\frac{1}{n}} \) and \( B \) defined in [3]. Furthermore, assume that

\[
\frac{1 + A^n}{A^{m-1}} \leq \sum_{k=1}^{M} \frac{\lambda_k r_k^-}{b^+} \leq F^s \sum_{k=1}^{M} \frac{\lambda_k r_k^+}{(b^s)^-} \leq \frac{1 + B^n}{B^{m-1}}. \tag{11}
\]

Then (1) has a unique almost periodic solution \( x(t) \) such that \( A \leq x(t) \leq B \).

**Proof:** Consider the positive constant functions \( u_0 = A \) and \( v_0 = B \). Set the operator

\[
\Phi(t) := \int_{-\infty}^{t} e^{-\int_s^t b(u)du} \sum_{k=1}^{M} \lambda_k r_k(s) \frac{x^m(s-\tau_k(s))}{1 + x^n(s-\tau_k(s))} ds \quad \text{for all } t \in \mathbb{R}. \tag{12}
\]

Clearly the function \( f(u) = \frac{u^m}{1 + u^n} \) is nondecreasing on \([A, B]\). Thus, we deduce that \( \Phi \) is a nondecreasing operator on \([u_0, v_0]\). It follows from properties of almost periodic functions that \( \Phi(P_0) \subset \text{AP}(\mathbb{R}) \). Moreover, \( \Phi \) satisfies \( \Phi(P_0) \subset P_0 \). Indeed, let \( x \in P_0 \), there exists \( \epsilon > 0 \) such that \( x(t) \geq \epsilon \) for all \( t \in \mathbb{R} \). Then,

\[
\Phi(x)(t) \geq \int_{-\infty}^{t} e^{-b^+(t-s)} \sum_{k=1}^{M} \lambda_k r_k(s) \frac{\epsilon^m}{1 + \epsilon^n} ds \geq \sum_{k=1}^{M} \frac{\lambda_k r_k^-}{b^+} \frac{\epsilon^m}{1 + \epsilon^n} := \tilde{\epsilon} > 0.
\]

Now, by virtue of (3) and (11) we find

\[
\Phi(u_0) = \int_{-\infty}^{t} e^{-\int_s^t b(u)du} \sum_{k=1}^{M} \lambda_k r_k(s) \frac{u_0^m}{1 + u_0^n} ds \geq \sum_{k=1}^{M} \frac{\lambda_k r_k^-}{b^+} \frac{u_0^m}{1 + u_0^n} \geq u_0, \quad \text{and}
\]

\[
\Phi(v_0)(t) \leq F^s \sum_{k=1}^{M} \frac{\lambda_k r_k^+}{(b^s)^-} \frac{v_0^m}{1 + v_0^n} \leq v_0.
\]

Finally, it only remains to show that condition (IV) of Lemma 2.1 is satisfied. Moreover, for each \( \gamma \in \left[ \frac{A}{B}, 1 \right] \), \( x \in [u_0, v_0] \) and \( t \in \mathbb{R} \), from the monotonicity of \( f(u) = \frac{1 + u^n}{1 + \gamma u^n} \), we have

\[
\Phi(\gamma x)(t) = \int_{-\infty}^{t} e^{-\int_s^t b(u)du} \sum_{k=1}^{M} \lambda_k r_k(s) \frac{x^m(s-\tau_k(s))}{1 + x^n(s-\tau_k(s))} \gamma^m \frac{1 + x^n(s-\tau_k(s))}{1 + \gamma x^n(s-\tau_k(s))} ds \\
\geq \Phi(x)(t) \gamma^m \frac{1 + u_0^n}{1 + \gamma u_0^n} := \Phi(x)(t) \phi(\gamma),
\]

where \( \phi : \left[ \frac{A}{B}, 1 \right] \to (0, +\infty) \) is the mapping defined by

\[
\phi(\gamma) = \gamma^m \frac{1 + A^n}{1 + \gamma A^n} \tag{13}.
\]
Thus, 
\[ \Phi(\gamma x) \geq \phi(\gamma)\Phi(x), \text{ for each } \gamma \in \left[ \frac{A}{B}, 1 \right] \text{ and } x \in [u_0, v_0]. \]

In order to prove that \( \phi(\gamma) > \gamma \), for convenience, we define the function \( M(\gamma) := \gamma^m - (1 + A^n) - (1 + \gamma^n A^n). \)

It is easy to verify that \( M(\gamma) \) achieves the maximum in \( \gamma_{\text{max}} = \left[ (m-1)(1+A^n) \right]^{\frac{1}{n-1}} = \frac{A}{B}. \) \( M(1) = 0 \) and \( M(\gamma) \) is strictly decreasing in \( \left( \frac{A}{B}, 1 \right) \), which implies that \( M(\gamma) > 0 \) for all \( \gamma \in \left( \frac{A}{B}, 1 \right) \). Thus, \( \Phi(\gamma) > \gamma \) for \( \gamma \in \left[ \frac{A}{B}, 1 \right) \). 

Thus, \( \Phi \) satisfies all the assumptions of Lemma 2.1 and \( \Phi \) has a unique fixed point \( x \in [u_0, v_0] \subset P^0 \). By Lemma 2.2, \( x(t) \) is the unique almost periodic solution of (1) which satisfies \( A \leq x(t) \leq B \). \[ \blacksquare \]

**Theorem 3.2** Let \( n > m > 1 \). Let \( A \) be a constant such that \( \left( \frac{m-1}{n-m+1} \right)^{\frac{1}{n}} < A \leq \left( \frac{m}{n-m} \right)^{\frac{1}{n}} \leq B \), with \( B \) defined in (3). Assume that

\[
\frac{1 + A^n}{A^{m-1}} \leq \sum_{k=1}^{M} \frac{\lambda_k r_k^-}{b^+} \leq F^s \sum_{k=1}^{M} \frac{\lambda_k r_k^+}{(b^+)^n} \leq \left( \frac{m}{n-m} \right)^{\frac{1}{n}}. \tag{14}
\]

Then (1) has a unique almost periodic solution \( x(t) \) such that \( x(t) \geq A \).

**Proof:** The proof is divided into 2 steps.

**Step 1.** Let \( x(t) \) an almost periodic solution of (1). According to Lemma 2.2, (3), (14) and the fact that

\[
\sup_{u \geq 0} \left\{ \frac{u^m}{1 + u^n} \right\} \leq 1, \text{ for } n \geq m \geq 0, \tag{15}
\]

we have

\[
x(t) \leq \int_{-\infty}^{t} e^{-\int_{u}^{t} b(u) du} \sum_{k=1}^{M} \lambda_k r_k(s) ds \leq F^s \sum_{k=1}^{M} \frac{\lambda_k r_k^+}{(b^+)^n} \leq \left( \frac{m}{n-m} \right)^{\frac{1}{n}} := V, \quad \text{for all } t \in \mathbb{R}. \tag{17}
\]

**Step 2.** Let us define the following truncated function \( h \) for \( x > 0 \), namely

\[
h(x) := \begin{cases} 
\frac{x^m}{1+x^n} & \text{if } x \leq V \\
\frac{V^m}{1+V^n} & \text{if } x > V 
\end{cases}, \tag{16}
\]

with \( V \) defined in Step 1. Let us consider the following associated equation:

\[
x'(t) = \sum_{k=1}^{M} \lambda_k r_k(t) h(x(t - \tau_k(t))) - b(t)x(t). \tag{17}
\]

We define the nonlinear operator \( \Theta \) on \( P^0 \) by,

\[
\Theta(x)(t) := \int_{-\infty}^{t} e^{-\int_{s}^{t} b(u) du} \sum_{k=1}^{M} \lambda_k r_k(s) h(x(s - \tau_k(s))) ds, \quad t \in \mathbb{R}. \]

Let \( u_0 := A \) and \( v_0 := B \). It is not difficult to prove that \( \Theta \) is a non-decreasing operator and \( \Theta(P^0 \times P^0) \subset P^0 \). For each \( x \in [A, B] \) and \( \gamma \in \left[ \frac{A}{B}, 1 \right) \), we have
where \( \phi \) is the same as in (13). Letting \( \theta(\gamma) = \min\{\phi(\gamma), 1\} \), it is readily verified that for each \( \gamma \in \left[\frac{A}{B}, 1\right] \) and \( x \in [u_0, v_0] \),

\[
\Theta(\gamma x) \geq \theta(\gamma) \Theta(x),
\]

where \( \theta(\gamma) : = \min\{\phi(\gamma), 1\} \). Analogously to the proof in Theorem 3.1 we can show that \( \theta(\gamma) > \gamma \) for all \( \gamma \in \left[\frac{A}{B}, 1\right] \), and that the remaining assumptions of Lemma 2.1 are satisfied. Thus, \( \Theta \) has a unique fixed point \( \tilde{x} \in [u_0, v_0] \). In addition, from Lemma 2.2 and (14), we get

\[
\tilde{x}(t) = \int_{-\infty}^{t} e^{-\int_{t}^{s} b(u) du} \sum_{k=1}^{M} \lambda_k r_k(s) h(\tilde{x}(s - \tau_k(s))) ds \leq F^8 \sum_{k=1}^{M} \frac{\lambda_k r_k^+}{(b^*)^-} \leq V
\]

which yields that \( h(\tilde{x}(s - \tau_k(s))) = \frac{\tilde{x}_m(s - \tau_k(s))}{1 + \tilde{x}_m(s - \tau_k(s))} \). Thus, again by Lemma 2.2, \( \tilde{x} \) is a solution for (1), with \( \tilde{x}(t) \geq A \) for all \( t \in \mathbb{R} \).

Let \( \tilde{z} \) be an almost periodic solution for (1) such that \( \tilde{z}(t) \geq A \) for all \( t \in \mathbb{R} \). Thus, by Step 1 we conclude that \( \tilde{z} \) is an almost periodic solution for (17) such that \( A \leq \tilde{z} \leq V \leq B \), which means that \( \tilde{x} = \tilde{z} \). The proof is complete.

## 4 Examples

Consider the following model of hematopoiesis with multiple time-varying delays:

\[
x'(t) = \frac{1}{2} \left( 5 + \cos \left( \sqrt{2}t \right) \right) \frac{x^m(t - 2 \cos t)}{1 + x^n(t - 2 \cos t)} + \frac{1}{4} \left( 13 + \frac{3}{5} \sin \left( \sqrt{3}t \right) \right) \frac{x^m(t - 2 \sin t)}{1 + x^n(t - 2 \sin t)} - (1 + 1.2 \cos (400t)) x(t).
\]

(19)

It is seen that, \( b(t) = 1 + 1.2 \cos (400t), \ M[1] = 1, \ b^+ = 2.2, \ b^*(t) = 1, \ (b^*)^- = 1 \) and \( F^8 = e^{\frac{4}{\sqrt{3}}} \approx 81.14408 \) and

\[
2.6116 \approx \frac{1 + A^n}{A^m - 1} < \frac{5.75}{2.2} = \frac{\sum_{k=1}^{M} \lambda_k r_k^-}{b^+} \leq F^8 \sum_{k=1}^{M} \frac{\lambda_k r_k^+}{(b^*)^-} = e^{\frac{1.2}{2.2}} 6.4 < \frac{1 + B^n}{B^m - 1} \approx 6.4479.
\]

Thus, all assumptions of Theorem 3.1 are satisfied. Therefore, equation (14) has a unique almost periodic solution \( x(t) \), which satisfies \( 4 \leq x(t) \leq 4 \left( \frac{10}{9} \right)^{- \frac{1}{2}} \).

**Example 4.1** Consider \( m = \frac{11}{10} \) and \( n = \frac{1}{2} \) in (17). Let \( A := 4 > \left( \frac{m-1}{n-m+1} \right)^{\frac{1}{n}} = 0.0625 \), so \( B = 4 \left( \frac{10}{9} \right)^{\frac{1}{2}} \approx 81.14408 \) and

\[
2.6116 \approx \frac{1 + A^n}{A^m - 1} < \frac{5.75}{2.2} = \frac{\sum_{k=1}^{M} \lambda_k r_k^-}{b^+} \leq F^8 \sum_{k=1}^{M} \frac{\lambda_k r_k^+}{(b^*)^-} = e^{\frac{1.2}{2.2}} 6.4 < \frac{1 + B^n}{B^m - 1} \approx 6.4479.
\]

Thus, all assumptions of Theorem 3.1 are satisfied. Therefore, equation (14) has a unique almost periodic solution \( x(t) \) such that \( 4 \leq x(t) \leq 4 \left( \frac{10}{9} \right)^{- \frac{1}{2}} \).

**Example 4.2** Consider \( m = \frac{11}{10} \) and \( n = \frac{12}{10} \) in (19). Let \( A := 1.3 > \left( \frac{m-1}{n-m+1} \right)^{\frac{1}{n}} \approx 0.13557 \), so \( B \approx 7.56193 \) and

\[
\frac{1 + A^n}{A^m - 1} \approx 2.30866 \leq 5.75 = \frac{\sum_{k=1}^{M} \lambda_k r_k^-}{b^+} \leq F^8 \sum_{k=1}^{M} \frac{\lambda_k r_k^+}{(b^*)^-} = F^8 6.4 \approx 6.4385 \leq \left( \frac{m}{n-m} \right)^{\frac{1}{n}} \leq B.
\]

Thus, all assumptions of Theorem 3.2 are satisfied. Therefore, equation (14) has a unique almost periodic solution \( x(t) \) such that \( x(t) \geq 1.3 \).
5 Concluding remarks and open problem

The fixed point theorems, employed in previous works to establish existence results for the hematopoiesis model, involve functions such as \( \phi : (0,1) \to (0, +\infty) \) or \( \phi : (0,1) \times P^o \times P^o \to (0, +\infty) \) satisfying \( \phi(\gamma) > \gamma \) or \( \phi(\gamma, x, y) > 0 \) for all \( x, y \in P^o \) and \( \gamma \in (0,1) \) (see for example [2, 5, 6, 11]). Unfortunately, these theorems fail when \( m > 1 \) since the aforementioned assumptions about \( \phi \) are not fulfilled when \( \gamma \approx 0 \). Moreover, to the best of our knowledge, the authors only study the model of hematopoiesis with \( m \leq 1 \). This implies that our results are new and they complement previously known results.

It is worth to notice that the approach used in this paper cannot be applied to equation (1) with \( 0 < n \leq m - 1 \). In fact, for \( u_0, v_0 \in P^o \), such that \( u_0 < v_0 \) conditions \( \Phi(u_0) \geq u_0 \), \( \Phi(v_0) \leq v_0 \) cannot be satisfied simultaneously, as it is required in Lemma 2.1. It is an open and interesting problem.

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