Oscillation and global attractivity in hematopoiesis model with periodic coefficients

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Abstract

In this paper we shall consider the nonlinear delay differential equation

\[ p'(t) = \frac{\beta(t)p^n(t - k\omega)}{1 + p^n(t - k\omega)} - \gamma(t)p(t), \]  

where \( k \) is a positive integer, \( \beta(t) \) and \( \gamma(t) \) are positive periodic functions of period \( \omega \). In the nondelay case we shall show that (*) has a unique positive periodic solution \( \bar{p}(t) \), and we will study the global attractivity of \( \bar{p}(t) \). In the delay case we shall establish some sufficient conditions for oscillation of all positive solutions of (*) about \( \bar{p}(t) \), and establish some sufficient conditions for the global attractivity of \( \bar{p}(t) \). Our results in this paper extend as well as improve the results in the autonomous case.

Keywords: Oscillation; Global attractivity; Hematopoiesis model

1. Introduction

In order to describe some physiological control systems, Mackey and Glass [20] proposed the following autonomous nonlinear delay differential equations as their appropriate models:

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\[ p'(t) = \frac{\beta p^m(t - \tau)}{1 + p^n(t - \tau)} - \gamma p(t) \]  \hspace{1cm} (1.1) \\
and \\
\[ x'(t) + \alpha V_m x(t)x^n(t - \tau) - \frac{k}{\theta^2 + x^n(t - \tau)} = \lambda, \quad t \geq 0, \]  \hspace{1cm} (1.2)

where \( \alpha, V_m, \beta, \tau, \lambda, \gamma \in (0, \infty), \quad n, m \in \mathbb{N} \).

Eq. (1.1) is proposed as a model of hematopoiesis (cell production), where \( p(t) \) denotes the density of mature cells in blood circulation, the cells are lost from the circulation at a rate \( \gamma \), the flux \( f(p(t - \tau)) = \frac{\beta p^m(t - \tau)}{1 + p^n(t - \tau)} \) of the cells into the circulation from the stem cell compartment depends on \( p(t - \tau) \) at time \( t - \tau \), and \( \tau \) is the time delay between the production of immature cells in the bone marrow and their maturation for release in circulating bloodstreams.

Eq. (1.2) is proposed as a model of “Dynamic Disease” involving respiratory disorders, where \( x(t) \) denotes the arterial CO\(_2\) concentration of a mammal, \( \lambda \) is the CO\(_2\) production rate, \( V_m \) denotes the maximum ventilation rate, and \( \tau \) is the time between oxygenation of blood in lungs and stimulation of chemoreceptors in the brainstem. For more details of the derivation and numerical study of the model, we refer to the articles by Mackey and Der Heiden [21] and Glass and Mackey [5].

In Eq. (1.1) when \( 0 = m < n \) this corresponds to a situation with negative feedback, with \( 0 < m < n \), we have mixed feedback and when \( 0 < m = n \) we have positive feedback. For more details we refer to the article of Mackey and Nechaeva [22].

For the qualitative behavior of all solutions of particular cases of Eq. (1.1) we refer to the following results:

In Eq. (1.1) when \( m = 0 \), El-Sheikh et al. [3] established some necessary and sufficient conditions for the oscillation of all positive solutions about the unique positive steady state \( \bar{p} \) and when \( m = 0, 1 \) Gopalsamy et al. [9] established some necessary and sufficient conditions for the oscillation of all positive solutions about the unique positive steady state \( \bar{p} \) and given some sufficient conditions for global attractivity. Also Karakostas et al. [15] investigated some sufficient conditions for uniformly asymptotically stable for Eq. (1.1) when \( m = 0, 1 \), and when \( m = 1 \) Hale and Sternberg [13] given interesting and nice results for the numerical and chaotic problems.

Recently, Saker [24] considered Eq. (1.1) and established some sufficient conditions for oscillation of all positive solutions about \( \bar{p} \), and also given some sufficient conditions for the global attractivity of \( \bar{p} \), and extended the results given by El-Sheikh et al. [3], Gopalsamy et al. [9].
Also, Kubiaczyk and Saker [17] considered Eq. (1.2) and established some necessary and sufficient conditions for oscillation of all positive solutions about its unique positive steady state $x^*$, some sufficient conditions for asymptotically stable of $x^*$ are obtained and proved that every nonoscillatory solution tends to $x^*$ when $t$ tends to infinity.

The variation of the environment 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 (e.g., seasonal effects of weather, resource availability, reproduce, food supplies, mating habits, etc.). It has been suggested by Nicholson [23] that any periodic 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. In view of this it is realistic to assume that the parameters in the models are periodic functions of period $\omega$. For convenience we will introduce the notation for a function $f$ of period $\omega$

$$f^* = \max_{0 \leq t \leq T} f(t) \quad \text{and} \quad f_0 = \min_{0 \leq t \leq T} f(t).$$

In this paper we consider the modification of (1.1) according to the environmental variation which given by the nonautonomous nonlinear delay differential equation

$$p'(t) = \frac{\beta(t)p^n(t - k\omega)}{1 + p^n(t - k\omega)} - \gamma(t)p(t), \quad (1.3)$$

where $k$ is positive integer and

$$\beta(t) \quad \text{and} \quad \gamma(t) \quad \text{are positive periodic functions of period } \omega \quad \text{and} \quad \beta_s > 2\gamma^*.$$  

For the oscillation and global attractivity of Eq. (1.2) with periodic coefficients we refer to the recent results of Saker and Agarwal [25].

We will consider solutions of (1.3) with initial conditions

$$p(t) = \phi(t), \quad \text{for} \quad -k\omega \leq t \leq 0, \quad \phi(0) > 0, \quad \phi \in C[-k\omega, 0, R^+] \quad (1.5)$$

If Eqs. (1.3) and (1.5) has to model the dynamics of the blood cell production, then it is important that $p$ remains positive for all $t > 0$, and this is not obvious from (1.3). We shall first examine this aspect briefly, note that if $p$ is defined for all $t > 0$, then $p$ cannot become unbounded for any finite value of $t$. We shall now show that solution of (1.3) and (1.5) remains positive and bounded. we note that $p(0) > 0$ and hence by continuity, $p(t) > 0$ for $t \in [0, \epsilon)$ for some $\epsilon > 0$. Suppose now $p(t)$ does not remain positive for all $t > 0$. Then from
\( p(0) = \phi(0) > 0 \), there exists \( t_1 > 0 \) such that \( p(t) > 0 \) for all \( t \in [0, t_1) \), \( p(t_1) = 0 \) and \( p'(t_1) < 0 \). But from (1.3) and (1.5) we obtain that
\[
p'(t_1) = \frac{\beta(t)\phi^m(t_1 - k\omega)}{1 + \phi^n(t_1 - k\omega)} > 0.
\]
This contradiction proves that \( p(t) > 0 \) for all \( t \in [0, t_1) \).

Now define
\[
f(x) = \frac{x^m}{1 + x^n}.
\]
We note that \( f(0) = 0 \), \( f(x) > 0 \) for \( x > 0 \), \( f \) decreasing in \( x \), \( f(x) \to 0 \) when \( x \to \infty \) and continuous on \([0, \infty)\). Then one can see that for all \( x \geq 0 \)
\[
f(x) \leq \tilde{f} = \begin{cases} 1 & \text{if } n = m, \\ \frac{\omega_1^n}{1 + \omega_1^n} & \text{if } n > m,
\end{cases}
\]
where \( \omega_1 = (m/(n - m))^{1/n} \). Now, since \( p(t) > 0 \) for all \( t \geq 0 \), then from (1.3), (1.5) and (1.6) we have
\[
p'(t) + \gamma(t)p(t) \leq \beta^* \tilde{f}.
\]
Then
\[
p(t) \leq \left( p(0) - \frac{\beta^* \tilde{f}}{\gamma_*} \right)e^{-\gamma_* t} + \frac{\beta^* \tilde{f}}{\gamma_*} \leq \max \left\{ p(0), \frac{\beta^* \tilde{f}}{\gamma_*} \right\}.
\]
Thus it follows that \( \bar{p}(t) \) is defined for all \( t \) and bounded.

Our aim in this paper in Section 2 is to prove that there exists a unique positive periodic solution \( \bar{p}(t) \) of Eq. (1.3) in the nondelay case, i.e., when \( \omega = 0 \), and study the global attractivity of \( p(t) \). In the delay case we prove that every nonoscillatory solution tends to \( \bar{p}(t) \) when \( t \) tends to infinity and give some sufficient conditions for oscillation of all positive solutions of Eq. (1.3) about \( \bar{p}(t) \) and estimate the lower and upper bounds of the oscillatory solutions and finally we establish some sufficient condition for global attractivity of \( \bar{p}(t) \). Our results in this paper extend as well as improve the results in [3,9,15,24].

**Definition 1.** Suppose that \( p(t) \) and \( \bar{p}(t) \) are two positive solutions of Eq. (1.3) on \([t - k\omega, \infty)\). By saying that \( p(t) \) is asymptotically attractive to \( \bar{p}(t) \) we mean \( \lim_{t \to \infty} [p(t) - \bar{p}(t)] = 0 \). We say that \( \bar{p}(t) \) is globally attractive if \( \bar{p}(t) \) is asymptotically attractive to all other positive solutions.

**Definition 2.** A function \( p(t) \) is said to oscillate about \( \bar{p}(t) \) if the function \( (p(t) - \bar{p}(t)) \) has arbitrarily large zeros. Otherwise \( p(t) \) is called nonoscillatory. When \( \bar{p}(t) = 0 \), we say \( p(t) \) oscillates about zero or that it simply oscillates.
For some contributions of qualitative behavior of some periodic population dynamics we refer the reader to the articles [6–8,10,11,14,25–28,30].

In the sequel, when we write a functional inequality we will assume that it holds for all sufficiently large values of $t$.

2. Main results

First, we shall consider the nondelay periodic equation

$$p'(t) = \frac{\beta(t)p^m(t)}{1 + p^n(t)} - \gamma(t)p(t)$$

with $p(0) > 0$, where $\beta(t)$ and $\gamma(t)$ are periodic functions of period $\omega$. We will show that (2.1) has a unique positive periodic solution $\bar{p}(t)$ and proved that $\bar{p}(t)$ is a global attractor of all other positive solutions.

Throughout this paper we will assume that $m = 0, 1$ and $n > m$.

**Theorem 2.1.** Assume that (1.4) holds.

(a) Then, there exists a unique $\omega$-periodic positive solution $\bar{p}(t)$ of Eq. (2.1).

(b) For every other positive solution $p(t)$ of (2.1) the limit

$$\lim_{t \to \infty} |p(t) - \bar{p}(t)| = 0.$$  

**Proof.** To prove (a), we define the function

$$f(p) = \frac{\beta p^m}{1 + p^n} - \gamma p,$$

where $\beta$ and $\gamma$ are positive constants and $\beta > 2\gamma$. Clearly, $f(1) = (\beta/2) - \gamma > 0$ and $f(\infty) = -\infty$. Thus, $f(p) = 0$ has a positive root $p_0 \in (1, \infty)$. Now, we define two more functions

$$f_1(p) = \frac{\beta p^m}{1 + p^n} - \gamma^* p, \quad f_2(p) = \frac{\beta^* p^m}{1 + p^n} - \gamma^* p.$$  

It is clear that $f_1(p)$ and $f_2(p)$ have positive zeros $p_1$ and $p_2$, respectively, i.e., $f_1(p_1) = 0$ and $f_2(p_2) = 0$. Further, $p_2 > p_1$. Now, suppose that $p(t) = p(t, 0, p_0)$ where $p_0 > 1$ is the unique solution of (2.1) through $(0, p_0)$.

We claim that if $p_0 \in [p_1, p_2]$ then $p(t) \in [p_1, p_2]$ for all $t \geq 0$. Otherwise, let $t^* = \inf \{t > 0 | p(t) > p_2\}$. Then it is easy to see that there exists $\bar{t} \geq t^*$ such that $p(\bar{t}) > p_2$ and $p'(\bar{t}) \geq 0$. However, then from (2.1) and the fact that $p(\bar{t}) > p_2$, we have

$$p'(\bar{t}) = \frac{\beta(\bar{t})p^m(\bar{t})}{1 + p^n(\bar{t})} - \gamma(\bar{t})p(\bar{t}) < \left[ \frac{\beta^* p_2^n}{1 + p_2^n} - \gamma^* p_2 \right] = 0.$$
Then \( p'(t) < 0 \) which is a contradiction. By similar arguments, we can show that \( p(t) \geq p_1 \) for all \( t \geq 0 \). Hence in particular, \( p_\infty = p(\infty, 0, p_0) \in [p_1, p_2] \).

Now, we define a mapping \( F : [p_1, p_2] \to [p_1, p_2] \) as follows: for each \( p_0 \in [p_1, p_2] \), \( F(p_0) = p_\infty \). Since the solution \( p(t, 0, p_0) \) depends continuously on the initial value \( p_0 \), it follows that \( F \) is continuous and maps the interval \([p_1, p_2]\) into itself. Therefore, \( F \) has a fixed point \( p_\infty \). In view of the periodicity of \( \beta \) and \( \gamma \), it follows that the unique solution \( p(t) = p(t, 0, p_\infty) \) of Eq. (2.1) through the initial point \((0, p_0)\) is a positive periodic with period \( \omega \). The proof of (a) is complete.

Now, we shall prove (b). Assume that \( p(t) > \bar{p}(t) \) for sufficiently large (the proof when \( p(t) < \bar{p}(t) \) is similar and hence omitted). Set

\[
p(t) = \bar{p}(t) + x(t).
\] (2.4)

Then \( x(t) > 0 \) for \( t \) sufficiently large, and

\[
x'(t) + \gamma(t)x(t) + \frac{\beta(t)(\bar{p}(t))^m}{(1 + (\bar{p}(t))^n)} - \frac{\beta(t)(x(t) + \bar{p}(t))^m}{1 + (\bar{p}(t) + x(t))^n} = 0.
\]

However, since \( x(t) > 0 \) for \( t \) sufficiently large, it follows that

\[
x'(t) + \frac{\beta(t)(\bar{p}(t))^m}{(1 + (\bar{p}(t))^n)} - \frac{\beta(t)(x(t) + (\bar{p}(t))^m)}{1 + (\bar{p}(t) + x(t))^n} \leq 0
\]

and hence

\[
x'(t) \leq - \left( \frac{\beta(t)(\bar{p}(t))^m}{(1 + (\bar{p}(t))^n)} - \frac{\beta(t)(x(t) + (\bar{p}(t))^m)}{1 + (\bar{p}(t) + x(t))^n} \right) < 0. \] (2.5)

Thus, \( x(t) \) is decreasing, therefore

\[
\lim_{t \to \infty} x(t) = \alpha \in [0, \infty) \text{ exists.}
\]

Now, we shall prove that \( \alpha = 0 \). If \( \alpha > 0 \), then there exist \( \epsilon > 0 \) and \( T_\epsilon > 0 \) such that for \( t \geq T_\epsilon \), \( \alpha - \epsilon < x(t) < \alpha + \epsilon \). But, then from (2.5), we find

\[
x'(t) + \frac{\beta(t)(\bar{p}(t))^m}{1 + (\bar{p}(t))^n} - \frac{\beta(t)(\alpha - \epsilon + (\bar{p}(t))^m)}{1 + (\bar{p}(t) + \alpha - \epsilon)^n} \leq 0, \quad t \geq T_\epsilon.
\]

Now, an integration of the last inequality from \( T_\epsilon \) to \( \infty \), immediately gives a contradiction. Hence \( \alpha = 0 \), and therefore \( x(t) \) tends to zero as \( t \to \infty \). Thus, we have \( \lim_{t \to \infty} [p(t) - \bar{p}(t)] = 0 \). This completes the proof. \( \Box \)

**Remark 1.** It is clear that in the proof of Theorem 2.1 (b) instead of (2.5) the inequality \( x'(t) + \gamma(t)x(t) \leq 0 \) can be used to get the same conclusion that \( x(t) \to 0 \) as \( t \to \infty \).
Remark 2. From the proof of Theorem 2.1 it follows that the unique \( \omega \)-periodic positive solution \( \tilde{p}(t) \) of (2.1) satisfies \( p_1 \leq \tilde{p}(t) \leq p_2 \). Thus, an interval for the location of \( \tilde{p}(t) \) is readily available.

It is clear that the unique \( \omega \)-periodic positive solution \( \tilde{p}(t) \) of (2.1) is also an \( \omega \)-periodic positive solution of (1.3). Conversely, if (1.3), (1.5) has a \( \omega \)-periodic positive solution \( \tilde{p}(t) \), then \( \tilde{p}(t) \) is a \( \omega \)-periodic solution of (2.1). Hence, Eq. (1.3) has a unique \( \omega \)-periodic positive solution \( \tilde{p}(t) \). In the non-delay case, we saw that in Theorem 2.1 that every positive solution of Eq. (1.3) converges to the unique positive periodic solution \( \tilde{p}(t) \). Naturally, we expect the same behavior for small delays. In the following results first we prove that every positive solution of Eq. (1.3) which does not oscillate about \( \tilde{p}(t) \) converges to \( \tilde{p}(t) \), obtain sufficient conditions for oscillation of all positive solutions of (1.3) about \( \tilde{p}(t) \), and finally, obtain condition for \( \tilde{p}(t) \) to be a global attractor.

Theorem 2.2. Assume that (1.4) holds. Let \( p(t) \) be a positive solution of (1.3) which does not oscillate about \( \tilde{p}(t) \). Then (2.2) holds.

**Proof.** Assume that \( p(t) > \tilde{p}(t) \) for \( t \) sufficiently large (the proof when \( p(t) < \tilde{p}(t) \) is similar and will be omitted). The transformation (2.3) implies that \( x(t) > 0 \) and satisfies

\[
x'(t) + \gamma(t)x(t) + \frac{\beta(t)(\tilde{p}(t))^m}{(1 + (\tilde{p}(t))^n)} - \frac{\beta(t)(x(t) - k\omega + \tilde{p}(t))^m}{1 + (\tilde{p}(t) + x(t) - k\omega))^n} = 0. \tag{2.6}
\]

To prove (2.2) we may to prove that \( \lim_{t \to \infty} x(t) = 0 \). From (2.6), since \( x(t) > 0 \) for \( t \) sufficiently large, we get

\[
x'(t) + \frac{\beta(t)(\tilde{p}(t))^m}{(1 + (\tilde{p}(t))^n)} - \frac{\beta(t)(x(t) - k\omega + \tilde{p}(t))^m}{1 + (\tilde{p}(t) + x(t) - k\omega))^n} \leq 0. \tag{2.7}
\]

Thus \( x(t) \) is decreasing, and therefore

\[
\lim_{t \to \infty} x(t) = \alpha \in [0, \infty) \text{ exists.}
\]

Now we shall prove that \( \alpha = 0 \). If \( \alpha > 0 \), then there exist \( \varepsilon > 0 \) and \( T_\varepsilon > 0 \) such that for \( t \geq T_\varepsilon \),

\[
0 < \alpha - \varepsilon < x(t) < x(t - k\omega) < \alpha + \varepsilon.
\]

Then from (2.7) we find

\[
x'(t) + \frac{\beta(t)(\tilde{p}(t))^m}{(1 + (\tilde{p}(t))^n)} - \frac{\beta(t)(x(t) - \alpha + \varepsilon + \tilde{p}(t))^m}{1 + (\tilde{p}(t) + x(t) - \alpha + \varepsilon))^n} \leq 0, \quad t \geq T_\varepsilon. \tag{2.8}
\]

But, now an integration of (2.8) from \( T_\varepsilon \) to \( \infty \) leads to a contradiction. Thus \( \alpha = 0 \), and hence \( x(t) \) tends to zero as \( t \to \infty \), then
\[ \lim_{t \to \infty} (p(t) - \bar{p}(t)) = 0. \]

This completes the proof. \( \square \)

Now, we shall prove the following oscillation result for the Eq. (1.3).

**Theorem 2.3.** Assume that (1.4) holds, and every solution of the delay differential equation

\[ Z'(t) + (1 - \varepsilon)Q(t) \exp \left( \int_{t-k\omega}^{t} \delta(s) \, ds \right) Z(t - k\omega) = 0 \]  
oscillates, where

\[ Q(t) = \frac{\beta(t)(n-m)(\bar{p}(t))^{n+m-1} - \beta(t)m(\bar{p}(t))^{m-1}}{(1 + (\bar{p}(t))^n)^2}, \quad \varepsilon \in (0,1). \]

Then, every solution of (1.3) oscillates about \( \bar{p}(t) \).

**Proof.** Assume for the sake of contradiction that (1.3) has a solution which does not oscillate about \( \bar{p}(t) \). Without loss of generality we assume that \( p(t) > \bar{p}(t) \), so that \( x(t) > 0 \). (The case \( p(t) < \bar{p}(t) \) implies that \( x(t) < 0 \) for which the proof is similar. In fact, we will see below that if \( x(t) \) is negative solution of (2.10) then \( U(t) = -x(t) \) is positive solution of (2.10)). From the transformation (2.4) it is clear that \( p(t) \) oscillates about \( \bar{p}(t) \) if and only if \( x(t) \) oscillates about zero. The transformation (2.4) transforms (1.3) to

\[ x'(t) + \gamma(t)x(t) + \frac{\beta(t)(\bar{p}(t))^m}{(1 + (\bar{p}(t))^n)} - \frac{\beta(t)(x(t - k\omega) + \bar{p}(t))_\alpha}{1 + (\bar{p}(t) + x(t - k\omega))_\alpha} = 0 \]

or

\[ x'(t) + \gamma(t)x(t) + \frac{\beta(t)(n-m)(\bar{p}(t))^{n+m-1} - \beta(t)m(\bar{p}(t))^{m-1}}{(1 + (\bar{p}(t))^n)^2} f(x(t - k\omega)) = 0, \]

where

\[ f(u) = \frac{(1 + (\bar{p}(t))^n)^2}{\beta(t)(n-m)(\bar{p}(t))^{n+m-1} - \beta(t)m(\bar{p}(t))^{m-1}} \times \left\{ \frac{(\bar{p}(t))^m}{1 + (\bar{p}(t))^n} - \frac{(\bar{p}(t) + u)^m}{1 + (\bar{p}(t) + u)^n} \right\}. \]  

(2.11)
Note that
\[ uf(u) > 0 \text{ for } u \neq 0 \quad \text{and} \quad \lim_{u \to 0} \frac{f(u)}{u} = 1. \] (2.12)

From (2.12) it follows that there exists \( \varepsilon \in (0, 1) \) such that \( f(u) \geq (1 - \varepsilon)u \).

Using this estimate in (2.10), we find that \( x(t) \) is a positive solution of the differential inequality
\[ x'(t) + \delta(t)x(t) + Q(t)(1 - \varepsilon)x(t - k\omega) \leq 0. \] (2.13)

Now, the transformation
\[ x(t) = \exp \left( - \int_0^t \delta(s) \, ds \right) z(t) \]
implies that \( z(t) \) is also a positive solution of the differential inequality
\[ z'(t) + \exp \left( \int_0^t \gamma(s) \, ds \right) Q(t)(1 - \varepsilon)z(t - k\omega) \leq 0. \] (2.14)

But, then by Corollary 3.2.2 [12] there exists an eventually positive solution of the delay differential equation (2.9). This contradicts our assumption that every solution of (2.9) is oscillatory. Thus, in conclusion every positive solution of (1.3) oscillates about \( \bar{p}(t) \). □

**Remark 3.** For the oscillation of the delay differential Eq. (2.9) several known criteria can be employed. For example, the results given in [12] and [18] when applied to (2.9) lead to the following corollary.

**Corollary 2.1.** Assume that (1.4) holds. Then,
\[ \Theta_\varepsilon = \liminf_{t \to \infty} \int_{t-k\omega}^t \exp \left( \int_{t-k\omega}^t \gamma(\eta) \, d\eta \right) Q(s)(1 - \varepsilon) \, ds > \frac{1}{e}, \]

or
\[ \Gamma_\varepsilon = \limsup_{t \to \infty} \int_{t-k\omega}^t \exp \left( \int_{t-k\omega}^t \gamma(\eta) \, d\eta \right) Q(s)(1 - \varepsilon) \, ds > 1 \]

implies that every solution of (2.9) is oscillatory.

**Remark 4.** Clearly, if the strict inequalities hold in Corollary 2.1 for \( \varepsilon = 0 \), then the same must be true for some sufficiently small \( \varepsilon > 0 \) also. Thus, we can restate Corollary 2.1 as follows:

**Corollary 2.2.** Assume that (1.4) holds. Then,
\[ \Theta_0 = \liminf_{t \to \infty} \int_{t-k\omega}^t \exp \left( \int_{t-k\omega}^t \gamma(\eta) \, d\eta \right) Q(s) \, ds > \frac{1}{e} \] (2.15)
or
\[
\Gamma_0 = \limsup_{t \to \infty} \int_{t-k_0}^t \exp \left( \int_{t-k_0}^t \gamma(\eta) \, d\eta \right) Q(s) \, ds > 1
\]  
(2.16)
implies that every solution of (2.9) is oscillatory.

From Theorem 2.3 and Corollary 2.2 the following oscillation criterion for (1.5) is immediate.

**Theorem 2.4.** Assume that (1.4) holds. Then, (2.15) or (2.16) implies that every solution of (1.3) oscillates about \( \bar{p}(t) \).

**Remark 5.** Note that if \( \beta(t) \equiv \beta > 0 \) and \( \gamma(t) \equiv \gamma > 0 \), then \( p_1 = \bar{p} = p_2 \) is the unique positive equilibrium point of the autonomous equation (1.1), and in this case condition (2.16) reduces to (2.11) in [24], and when \( m = 0 \) condition (2.16) reduces to condition (2.8) in [9] and when \( m = 1 \) condition (2.16) reduces to the condition (2.8) in [3] and condition (3.11) in [9]. Thus our theorems extend the results of [3,9,24].

For the oscillation of (1.3) it is clear that between the conditions (2.15) and (2.16) there is a gap when the limit

\[
\lim_{t \to \infty} \int_{t-k_0}^t \exp \left( \int_{t-k_0}^t \delta(\eta) \, d\eta \right) Q(s)(1 - \varepsilon) \, ds
\]
does not exist. To fill this gap partially we can employ some known results from the literature. For example, the criterion of Erbe and Zhang [4] when applied to first order delay differential equation (2.9) guarantees that every solution of (1.3) oscillates about \( \bar{p}(t) \) provided

\[
0 < \Theta_\varepsilon \leq \frac{1}{e}
\]

and

\[
\Gamma_0 > 1 - \frac{\Theta_0^2}{4}.
\]  
(2.17)

We also note that on the following work of Chao [2] condition (2.17) can be improved by

\[
\Gamma_0 > 1 - \frac{\Theta_0^2}{2(1 - \Theta_0)}
\]  
(2.18)

whereas a result of Yu et al. [31,32] gives an improvement over (2.18) to

\[
\Gamma_0 > 1 - \frac{(1 - \Theta_0) - \sqrt{1 - 2\Theta_0 - \Theta_0^2}}{2}.
\]  
(2.19)
Finally, we remark that condition (2.19) can be improved further by employing the recent results presented in [16].

In a different direction we can employ the results of Li [19] and Shen and Tang [29] to give another infinite set of sufficient conditions for oscillation of Eq. (1.3) which indicate that the condition (2.15) is no longer necessary.

**Theorem 2.5.** Assume that \((1.4)\) holds. If
\[
\frac{1}{e} \leq \int_{t-k\omega}^{t} P(s) \, ds
\]
and
\[
\int_{t_0+\omega}^{\infty} P(t) \left\{ \exp \left( \int_{t-k\omega}^{t} P(s) \, ds - \frac{1}{e} \right) ds - 1 \right\} dt = \infty,
\] (2.20)
where \(P(t) = \exp (\int_{t-k\omega}^{t} \delta(\eta) \, d\eta) Q(t)(1 - \varepsilon).\) Then every solution of Eq. (1.3) oscillates.

**Theorem 2.6.** Assume that \((1.4)\) holds. If
\[
\lim \inf_{t \to \infty} P_n(t) > \frac{1}{e^n} \quad \text{and} \quad \lim \inf_{t \to \infty} \overline{P}_n(t) > \frac{1}{e^n}. \quad (2.21)
\]
Then every solution of Eq. (1.3) oscillates, where
\[
P_1(t) = \int_{t-k\omega}^{t} P(s) \, ds, \quad t \geq t_0 + k\omega,
\]
\[
P_{K+1}(t) = \int_{t-k\omega}^{t} P(s) P_k(s) \, ds, \quad t \geq t_0 + (K-1)k\omega, \quad K = 1, 2, \ldots,
\]
\[
\overline{P}_1(t) = \int_{t}^{t+k\omega} P(s) \, ds, \quad t \geq t_0 \quad \text{and}
\]
\[
\overline{P}_{K+1}(t) = \int_{t}^{t+k\omega} P(s) \overline{P}_k(s) \, ds, \quad t \geq t_0, \quad K = 1, 2, \ldots
\]

As we saw in Theorem 2.2 every nonoscillatory solution of Eq. (1.3) tends to \(\bar{p}(t)\) as \(t \to \infty\), we establish now certain upper and lower estimates for solution of Eq. (1.3) which oscillate about \(\bar{p}(t)\).

**Theorem 2.7.** Assume that \((1.4)\) holds. Then their exists a \(T\) such that for all \(t \geq T\)
\[
p_1 \exp(-\gamma^*k\omega) < p(t) < p_2 + \int \beta^*k\omega.
\] (2.22)
Proof. First, we show the upper bound in (2.22). For this, let $k\omega \leq t_1 < t_2 < \cdots < t_l < \cdots$ be a sequence of zeros of $p(t) - \tilde{p}(t)$ with $\lim_{t \to \infty} t_l = \infty$. Our strategy is to show that the upper bound holds in each interval $(t_l, t_{l+1})$. For this, let $\xi_l \in (t_l, t_{l+1})$ be a point where $p(t)$ obtains its maximum in $(t_l, t_{l+1})$, then it suffices to show that

$$p(\xi_l) < p_2 + \tilde{f}\beta^*k\omega = P_2. \quad (2.23)$$

We can assume that there exists a $\xi_l$ where $p(\xi_l) > p_2$, otherwise there is nothing to prove, since $p'(\xi_l) = 0$, it follows that

$$0 = p'(\xi_l) < \frac{\beta^*p(t)(\xi_l - k\omega)}{1 + (p(\xi_l - k\omega))^\mu} - \gamma^*p(\xi_l)$$

and hence

$$0 < \frac{\beta^*p(t)(\xi_l - k\omega)}{1 + (p(\xi_l - k\omega))^\mu} - \gamma^*p(\xi_l).$$

Thus, if $p(t)$ attains its maximum at $\xi_l$, then it follows (cf. the proof of Theorem 2.1) that $p(\xi_l) > p_2$, $p(\xi_l - k\omega) < p_2$. Now, since $p(\xi_l) > p_2$ and $p(\xi_l - k\omega) < p_2$, we can let $\xi_l$ be the first zero of $p(t) - p_2$ in $(\xi_l - k\omega, \xi_l)$ that is $p(\xi_l) = p_2$. Integrating (1.3) from $\xi_l$ to $\xi_l$ we have

$$p(\xi_l) - p(\xi_l) = \int_\xi^{\xi_l} \left( \frac{\beta(t)p(t)(t-k\omega)}{1 + p^\mu(t-k\omega)} - \gamma(t)p(t) \right) dt < \int_\xi^{\xi_l} \beta(t)\tilde{f} dt$$

$$< \int_{\xi_l-k\omega}^{\xi_l} \beta^*\tilde{f} dt < \tilde{f}\beta^*k\omega,$$

where $\tilde{f}$ is defined by (1.6), which immediately gives (2.23). Hence there exists $T_1$ such that $p(t) < p_2$. 

Now we shall show the lower bound in (2.22) for all $t \geq T_1 + k\omega$. For this, following as above let $\mu_l \in (t_l, t_{l+1})$ be a point where $p(t)$ attains its minimum in $(t_l, t_{l+1})$. Then, it suffices to show that

$$p(\mu_l) > p_1 \exp(-\gamma^*k\omega) = P_1. \quad (2.24)$$

Now assume that there exists a $\mu_l$ where $p(\mu_l) < p_1$, otherwise there is nothing to prove. Since $p'(\mu_l) = 0$, we have

$$0 = p'(\mu_l) > \frac{\beta_1p(\mu_l - k\omega)}{1 + (p(\mu_l - k\omega))^\mu} - \gamma^*p(\mu_l). \quad (2.25)$$

Thus (cf. Theorem 2.1), it is necessary that $p(\mu_l - k\omega) > p_1$. Hence, there exists $\bar{\mu}_l \in (\mu_l - k\omega, \mu_l)$, where $p(\bar{\mu}_l) = p_1$. Integrating (1.3) from $\bar{\mu}_l$ to $\mu_l$, we have

$$\ln \frac{p(\mu_l)}{p(\bar{\mu}_l)} > \int_{\bar{\mu}_l}^{\mu_l} -\gamma(t) dt > \int_{\bar{\mu}_l}^{\mu_l} -\gamma^* dt > \int_{\mu_l-k\omega}^{\mu_l} -\gamma^* dt$$

(2.26)

which immediately leads to (2.24). The proof is complete. \qed
The following theorem provides sufficient condition for the global attractivity of $\bar{p}(t)$.

**Theorem 2.8.** Assume that (1.4) holds, and
\[
\lim_{s \to \infty} \int_{s - k\omega}^{s} \beta(s)(n - m)(\bar{p}(s) + P_2)^{n+m-1} - \beta(s)m(\bar{p}(s) + P_1)^{m-1} \left(1 + (\bar{p}(s) + P_1)^{\gamma(t)\omega}\right) ds \left(1 + (\bar{p}(s) + P_1)^{n}\right)^{-2} < \frac{\pi}{2}.
\]
(2.27)

Then every positive solution of Eq. (1.3) satisfies (2.2) where
\[
P_1 = p_1 \exp(-\gamma^* k\omega) \quad \text{and} \quad P_2 = p_2 + \bar{f} \beta^* k\omega.
\]
(2.28)

**Proof.** We have already established (2.2) when $\omega = 0$ (see Theorem 2.1), and for the positive solutions of (1.3) which are nonoscillatory about $\bar{p}(t)$ (see Theorem 2.2). So it remains to establish (2.2) for the positive solutions of (1.3) which oscillates about $\bar{p}(t)$. Let $p(t)$ be an arbitrary positive solution of Eq. (1.3), in view of Theorem 2.7 we found that
\[
P_1 < p(t) < P_2.
\]

Set
\[
p(t) = \bar{p}(t) + x(t).
\]
Then Eq. (1.3) reduces to
\[
x'(t) + \gamma(t)x(t) + \frac{\beta(t)(\bar{p}(t))^{m}}{1 + (\bar{p}(t))^{n}} - \frac{\beta(t)(\bar{p}(t) + x(t - k\omega))^{m}}{1 + (\bar{p}(t) + x(t - k\omega))^{n}} = 0.
\]
(2.29)

Then to prove (2.2) we may to prove that
\[
\lim_{t \to \infty} x(t) = 0.
\]

Put
\[
G(t, u) = \frac{\beta(t)(\bar{p}(t))^{m}}{1 + (\bar{p}(t))^{n}} - \frac{\beta(t)(\bar{p}(t) + u)^{m}}{1 + (\bar{p}(t) + u)^{n}}.
\]

Then
\[
\frac{\partial G(t, u)}{\partial u} = \frac{\beta(t)(n - m)(\bar{p}(t) + u)^{n+m-1} - \beta(t)m(\bar{p}(t) + u)^{m-1}}{(1 + (\bar{p}(t) + u)^{n})^{2}}
\]
and from (2.29) we have
\[
x'(t) + \gamma(t)x(t) + G(t, x(t - k\omega)) - G(t, 0) = 0.
\]
(2.30)

By the mean value theorem we can write (2.30) in the form
\[
x'(t) + \gamma(t)x(t) + F(t)x(t - k\omega) = 0,
\]
where

\[ F(t) = \frac{\partial G(t, u)}{\partial u} \bigg|_{u=\xi(t)} = \frac{\beta(t)(n - m)(p(t) + \xi(t))^{n+1} - \beta(t)m(p(t) + \xi(t))^{m-1}}{(1 + (p(t) + \xi(t))^{n+1}),} \]

where \( \xi(t) \) lies between \( p(t) \) and \( p(t - \tau) \). Then

\[
x'(t) + \gamma(t)x(t) = \frac{\beta(t)(n - m)(p(t) + \xi(t))^{n+1} - \beta(t)m(p(t) + \xi(t))^{m-1}}{(1 + (p(t) + \xi(t))^{n+1})} x(t - k\omega) = 0.
\]

Set

\[ x(t) = e^{-\int_{0}^{t} \gamma(s) \, ds} y(t) \]

which implies that

\[
y'(t) + \frac{\beta(n - m)(p(t) + \xi(t))^{n+1} - \beta m(p(t) + \xi(t))^{m-1}}{(1 + (p(t) + \xi(t))^{n+1})} e^{\int_{t-k\omega}^{t} \gamma(0) \, d\theta} \times y(t - k\omega) = 0. \tag{2.31}
\]

But

\[
\lim_{s \to \infty} \int_{s-k\omega}^{s} \frac{\beta(s)(n - m)(p(s) + \xi(s))^{n+1} - \beta(s)m(p(s) + \xi(s))^{m-1}}{(1 + (p(s) + \xi(s))^{n+1})} \times e^{\int_{s-k\omega}^{t} \gamma(0) \, d\theta} ds \times e^{\int_{s-k\omega}^{t} \gamma(0) \, d\theta} ds < \lim_{s \to \infty} \int_{s-k\omega}^{s} \frac{\beta(s)(n - m)(p(s) + P_2)^{n+1} - \beta(s)m(p(s) + P_1)^{m-1}}{(1 + (p(s) + P_1)^{n+1})} \times e^{\int_{s-k\omega}^{t} \gamma(0) \, d\theta} ds.
\]

Then by a known result (Theorem 2.1.5 [18]) and the condition (2.27) every solution of Eq. (2.31) satisfies \( \lim_{t \to \infty} y(t) = 0 \), which implies that \( \lim_{t \to \infty} x(t) = 0 \). Then \( \lim_{t \to \infty} [p(t) - \tilde{p}(t)] = 0 \). The proof is complete. \( \square \)

**Remark 6.** Note that if \( \beta(t) \equiv \beta > 0 \) and \( \gamma(t) \equiv \gamma > 0 \), then \( p_1 = \tilde{p} = p_2 \) is the unique positive equilibrium point of the autonomous equation (1.1), and in this case condition (2.27) reduces to (2.17) in [24].
Theorem 2.9. Assume that (1.4) holds, and
\[ \gamma_s > \frac{\beta (n - m) (P_2)^{n+m-1} - \beta' m (P_1)^{m-1}}{(1 + (P_1)^n)^2}. \] (2.32)

Then every positive solution of Eq. (3.1) satisfies (2.2).

Proof. Let \( p(t) \) be an arbitrary positive solution of Eq. (1.3), in view of Theorem 2.8 we found that \( x(t) \) satisfies Eq. (2.29). We shall compute the proof by showing that our assumption imply that

\[ \lim_{t \to \infty} x(t) = 0. \]

Consider a Lyapunov functional \( V(t) = V(x(t)) \) as follows

\[ V(t) = |x(t)| + \int_{t-\infty}^t \left[ \frac{\beta(s)(\bar{p}(s) + x(s))^m}{1 + (\bar{p}(s) + x(s))^n} - \frac{\beta(s)(\bar{p}(s))^m}{1 + (\bar{p}(s))^n} \right] ds. \] (2.33)

Since \( x(t) \) is bounded from below (due to the property of \( p(t) \)), one can verify that the integral in (2.33) converges uniformly for \( t > 0 \), and hence differentiable in \( t \). Calculating the upper derivative of \( V \) along the solution of (2.29) we obtain

\[ \frac{dV}{dt} = \text{sgn}[x(t)] \left\{ -\gamma(t)|x(t)| + \frac{\beta(s)(\bar{p}(s) + x(t))^m}{1 + (\bar{p}(s) + x(t))^n} - \frac{\beta(t)(\bar{p}(t))^m}{1 + (\bar{p}(t))^n} \right\} \]

\[ \leq -\gamma(t)|x(t)| + \frac{\beta(t)(n - m)(\zeta(t))^{n+m-1} - \beta(t)m(\zeta(t))^{m-1}}{(1 + (\zeta(t))^n)^2} |x(t)|, \]

where \( \zeta(t) \) lies between \( \bar{p}(t) \) and \( \bar{p}(t) + x(t) \) and

\[ \text{sgn}[x(t)] = \begin{cases} 1 & \text{if } x(t) > 0 \text{ or } x(t) = 0 \text{ and } \frac{dx}{dt} > 0, \\ 0 & \text{if } x(t) = 0 \text{ and } \frac{dx}{dt} > 0, \\ -1 & \text{if } x(t) < 0 \text{ or } x(t) = 0 \text{ and } \frac{dx}{dt} < 0. \end{cases} \]

Hence we have

\[ \frac{dV}{dt} + \left\{ \gamma(t) - \frac{\beta(t)(n - m)(\zeta(t))^{n+m-1} - \beta(t)m(\zeta(t))^{m-1}}{(1 + (\zeta(t))^n)^2} \right\} |x(t)| \leq 0. \]
As we proved that \( p(t) \) is bonded then we have for \( t \geq T \)

\[
\frac{dV}{dt} + \left\{ \gamma - \frac{\beta^*(n-m)(P_2)^{n+m-1} - \beta^*m(P_1)^{m-1}}{((1 + P_1)^n)^2} \right\} |x(t)| \leq 0.
\]

Integrating from \( T \) to \( t \) we have

\[
V(t) + \left\{ \gamma - \frac{\beta^*(n-m)(P_2)^{n+m-1} - \beta^*m(P_1)^{m-1}}{((1 + P_1)^n)^2} \right\} \int_T^t |x(s)| \, ds \leq V(T) < \infty
\]

which implies by our assumption that

\[ x(t) \in L_1[T, \infty). \]

Then By Barbalat’s Lemma [1] we conclude that

\[ \lim_{t \to \infty} x(t) = 0 \]

and hence (2.2) is satisfied. The proof is complete. \( \square \)

**Remark 7.** Note that if \( \beta(t) \equiv \beta > 0 \) and \( \gamma(t) \equiv \gamma > 0 \), then \( p_1 = \bar{p} = p_2 \) is the unique positive equilibrium point of the autonomous equation (1.1). In the case when \( m = 0 \) condition (2.32) reduces to

\[
\frac{\beta n \bar{p}^{n-1}}{(1 + \bar{p}^n)^2} < \gamma
\]

which is compatible with the condition for uniformly asymptotically stable in Theorem 3.3 in [15], and when \( m = 1 \) condition (2.32) reduces to the condition

\[
\frac{\beta(n - 1) \bar{p}^{n-1} - \beta}{(1 + \bar{p}^n)^2} < \gamma
\]

which compatible with the condition (4.30) in [15]. Thus our Theorem 2.9 extended and improved the results of [15] and we note that the results in [15] can not be applied in the nonautonomous case.

**References**