Asymptotic Properties and Oscillation of the Solutions in a Periodic Impulsive Hematopoiesis Model

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ABSTRACT

Background: The impulsive hematopoiesis model is an extension of the traditional hematopoiesis model that incorporates the concept of rapid bursts or "impulses" of blood cell production in response to certain stimuli or conditions. Finding suitable conditions for the oscillation and global attractiveness of a positive periodic solution in impulsive Hematopoiesis model is an a priori goal for periodic versions. Despite some recent additions, there is still a dearth of literature on this topic.

Materials and Methods: By employing the continuation theorem of coincidence degree since the continuous implies the survival of a mature cells for a long time. And by using the same technique of the proof that was used in model without impulsive is establish some new asymptotic properties for oscillation and sufficient conditions for the global attractiveness of the solutions of periodic impulsive hematopoiesis model with submitted a new suitable impulsive condition.

Results: In this work asymptotic Properties for oscillating solutions in a periodic impulsive hematopoiesis model is discuss. New sufficient conditions for oscillation of every positive solution around equilibrium and global attractiveness of all non-oscillating solutions around the equilibrium is given.

Conclusion: Some published results in the model without impulsive are improved and extended to the periodic impulsive hematopoiesis model. A numerical example is set up to show the accuracy and efficacy of the results that are provided.

Key words: Oscillation, Delay differential equation, Hematopoiesis models, Impulsive, Global attractivity.
INTRODUCTION

Differential equation describes a natural occurrence as a mathematical model. Numerous scholars investigate how nonlinear delay mathematical models behave qualitatively in single species as well as species that interact. There has been a great deal of research done on the qualitative analysis of delay models with constant coefficients (autonomous models). We are aware that a variety of biological and ecological dynamical systems heavily depend on the environment. For instance, the physical environment's elements, like as temperature and humidity, as well as the accessibility of resources like food, water, and other essentials, typically change with time on a seasonal or daily basis. Therefore, nonautonomous systems would be more accurate representations [1,2,3,4,5,6,7,8,9]. Studying oscillation and global stability of a certain kind of nonautonomous delay model in biology is one of the goals of our work. Many authors looked for sufficient conditions to ensure oscillatory property for delay differential equations (DDE). As a result, they established a lot of papers for oscillatory theory [10, 11,12,13,14,15,16].

The impulsive hematopoiesis model is an extension of the traditional hematopoiesis model that incorporates the concept of rapid bursts or "impulses" of blood cell production in response to certain stimuli or conditions. This model suggests that under specific circumstances such as infection, injury, or stress, there can be a rapid expansion of certain blood cell lineages to meet increased demand or replenish depleted populations. The hematopoiesis model and the impulsive hematopoiesis model are both theoretical frameworks used to understand the process of blood cell formation, also known as hematopoiesis.

The study of hematopoiesis, the process of blood cell production, is crucial in understanding various diseases and disorders related to blood cells. Mathematical modelling has emerged as a powerful tool to investigate the dynamics and behavior of hematopoiesis. One such model that has gained significant attention is the oscillation solution of impulsive hematopoiesis model. This model incorporates impulsive perturbations, which represent sudden changes or interventions in the system, such as drug treatments or bone marrow transplantation. Impulsive perturbations play a crucial role in hematopoietic processes, as they can significantly impact the dynamics and stability of blood cell populations [6,7,8,9].

The oscillation of solution for a periodic impulsive hematopoiesis model refers to the study of how blood cell production fluctuates over time in response to periodic impulses. This model is used to understand the dynamics of hematopoietic stem cells and their differentiation into various blood cell types. Research in this area has shown that the impulsive nature of hematopoiesis can lead to complex oscillatory behavior, with different cell types exhibiting different patterns of oscillation. Understanding these patterns is important for developing treatments for blood disorders and diseases. Overall, the study of oscillation in impulsive hematopoiesis models is an important area of research with potential implications for clinical practice [7,8,9,10].

The study of oscillation and global attractivity of solutions for periodic impulsive hematopoiesis models is an important area of research in mathematical biology. In recent years, several researchers have investigated the dynamics of such models and have provided valuable insights into the behavior of these systems. One such study was conducted by Zhang et al. (2018) [8], they analyzed a periodic impulsive hematopoiesis model with feedback control. The authors used Lyapunov functionals to establish the global attractivity of the positive periodic solution and showed that the system exhibits oscillatory behavior under certain conditions. Another notable contribution to this field was made by Liu et al. (2019) [9], who studied a periodic impulsive hematopoiesis model with time delays. The authors used a combination of analytical and numerical
techniques to investigate the stability and bifurcation properties of the system. They found that the model exhibits rich dynamical behavior, including stable periodic oscillations, unstable periodic orbits, and chaotic attractors. Hadeed and Mohamad 2022[7], discussed the oscillation solutions of a Hematopoiesis model in both cases delay and non-delay were parameters are continuous positive \( \omega \)-periodic functions. They presented sufficient conditions for the oscillation of all positive solutions of it about equilibrium and established sufficient conditions for the global attractivity. Also, Hadeed and Mohamad 2023[17], studied the problem of oscillating solutions for an impulsive hematopoiesis model with positive and negative coefficients is investigated. They construct several oscillation criteria. Overall, these studies demonstrate the importance of understanding the dynamics of periodic impulsive hematopoiesis models in order to gain insights into the behavior of biological systems.

The most of parameters in the actual world events are not fixed constants; instead, they are estimated using specific statistical techniques, and the estimates get better with time. Additionally, the environment's variability has a significant impact on a number of ecological and biological dynamical systems. Since the selection pressures acting on systems in an oscillating environment are different from those acting on systems in a stable environment, the impacts of a periodically fluctuating environment are particularly crucial for evolutionary theory. However, some dynamical systems exhibit rapid changes at specific points in their evolution, which serves to distinguish them from others. The weather, the availability of resources, the use of drugs or radiation in the treatment of hematological illnesses, food supplies, pharmacological factors, mating behavior, and other seasonal influences are the main causes of this. Take into consideration in our study the case of mixed effects: impulsive actions, time delays, and periodicity of the environment in the equation of the hematopoiesis model of the form

\[
\mathcal{H}'(t) + \delta(t)\mathcal{H}(t) - \beta(t) \frac{1}{1 + \mathcal{H}^n(t-m\omega)} = 0, \, t \neq t_k \quad k = 1, 2, \ldots
\]

\[
\mathcal{H}(t_k^+) + b_k\mathcal{H}(t_k) = a_k\mathcal{H}(t_k^+), \quad t = t_k \quad k = 1, 2, \ldots
\]

where \( \delta(t), \beta(t) \) are periodic positive functions of period \( \omega \) and \( n, m \in N \). Let

\[
\mathcal{C} = \mathcal{C}[\{[-m\omega, 0], R}\] be the space of continuous functions \( \varphi \) equipped with the supremum norm \( \| \varphi \|_C = \max_{-m\omega \leq \theta \leq 0} | \varphi | \) by certain interpretations of the model, we consider the solution of (1) together with the initial condition: \( \mathcal{H}(0) = \varphi, \varphi \in C_0 \), when \( C_0 = \{ \varphi \in C : \varphi(\theta) \geq 0 \text{ for } \theta \in [-m\omega, 0], \varphi(0) > 0 \} \).

Throughout this paper the following assumptions are used:

- \( (M_1) \) \( 0 < t_1 < t_2 < \ldots \) are fixed impulsive points such that \( \lim_{k \to \infty} t_k = \infty \);
- \( (M_2) \beta(t), \delta(t) \in (0, \infty) \) are integrable functions, \( n, m \in N \);
- \( (M_3) \{a_k\}, \{b_k\} \) are real sequence such that \( b_k > -a_k, k \in N \);
- \( (M_4) \beta(t), \delta(t) \) and \( \prod_{0 < t_k < t}(a_k + b_k) \) are positive periodic functions of period \( \omega > 0 \).

We take into account the nonimpulsive delay hematopoiesis model under the aforementioned conditions:

\[
h'(t) = \frac{v(t)}{\mu(t) + h^n(t-m\omega)} - \delta(t)h(t),
\]

where \( \delta(t), \beta(t), \mu(t) \) and \( v(t) \) are positive periodic functions of period \( \omega \). From Theorum 1 in [11] the asymptotic properties of the system (1) are equivalent to the equation (2).
Note that, since $\prod_{0<t_k<\ell}(a_k + b_k) > 0$, the transformation
\[ \mathcal{H}(t) = \prod_{0<t_k<\ell}(a_k + b_k)h(t), \]
preserves the asymptotic properties of the equation (1) and (2). According to Theoram1 [11], it is sufficient to demonstrate this for (2) with initial condition $h(0) = \varphi, \varphi \in C_1$ in order to demonstrate the continuous solution of (1) where
\[ C_1 = \{ \varphi \in C: \varphi(\theta) \geq 0 \text{ for } \theta \in [−m\omega, 0], \varphi(0) > 0 \}. \]


2. BASIC CONCEPTS

We introduce some fundamental ideas related to the global attractivity and oscillation of all hematopoiesis model solutions.

**Definition 1.** [13] A solution $\mathcal{H}(t)$ of equation (1) is classified as oscillatory on the interval $[t_0, \infty)$ if it has infinitely many zeros for $t \geq t_1 \geq t_0$. This means that there exists a sequence $\{t_n\}$ such that $\mathcal{H}(t_n) = 0$ and $\lim_{n \to \infty} t_n = \infty$. If $\mathcal{H}(t)$ does not have infinitely many zeros on this interval, it is considered nonoscillatory and either eventually positive or negative.

**Definition 2.** [13] Assuming that (1) is satisfied on the interval $[t_0, \infty)$, let $\mathcal{H}(t)$ and $\overline{\mathcal{H}}(t)$ be positive solutions. The condition for $\mathcal{H}(t)$ to be asymptotically attractive to $\overline{\mathcal{H}}(t)$ is that the limit of $\mathcal{H}(t) - \overline{\mathcal{H}}(t)$ as $t$ approaches infinity is equal to zero. If $\mathcal{H}(t)$ is asymptotically attractive to all positive solutions of (1), it is referred to as globally attractive.

**Definition 3.** [10] If $(\mathcal{H}(t) - \overline{\mathcal{H}}(t))$ has infinitely large zeros, then function $\mathcal{H}(t)$ is considered to oscillate around $\overline{\mathcal{H}}(t)$. If there are a finite number of zeros, then $\mathcal{H}(t)$ is non-oscillatory.

When $\overline{\mathcal{H}}(t)$ equal to zero, we refer to $\mathcal{H}(t)$ as simply oscillating or oscillating around zero.

The following Theorem (1) is very helpful

**Theoram1.** [11] Let $(\mathcal{M}_1)$-($\mathcal{M}_4$) holds. Then

i) If $h(t)$ is a solution of (2) on $[-m\omega, \infty)$, then $\mathcal{H}(t) = \prod_{0<t_k<\ell}(a_k + b_k)h(t)$ is a solution of (1) on $[-m\omega, \infty)$.

ii) If $\mathcal{H}(t)$ is a solution of (1) on $[-m\omega, \infty)$, then $h(t) = \prod_{0<t_k<\ell}(a_k + b_k)^{-1} \mathcal{H}(t)$ is a solution of (2) on $[-m\omega, \infty)$.

3. MAIN RESULTS AND DISCUSSION

In this section, we demonstrate that, in the absence of a delay, the periodic solution, $\mathcal{H}(t)$ of the equation (1), is a global attractor. Therefore, it will be demonstrated that all of the positive solutions to equation (1) $\mathcal{H}(t)$ that do not fluctuate around $\overline{\mathcal{H}}(t)$ converge to $\overline{\mathcal{H}}(t)$. Finally, will establish sufficient conditions for global attractivity of $\overline{\mathcal{H}}(t)$. 

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Theorem 2. Suppose that \( h(t) \) be a positive solution of (2), and assume that 
\( \delta(t), \beta(t), \mu(t), v(t) \) are periodic positive functions of period \( \omega \). Then 
\[
\lim_{t \to \infty} (h(t) - \bar{h}(t)) = 0. \tag{3}
\]

Proof: Let \( h(t) > \bar{h}(t) \) for sufficiently large \( t \) (where \( h(t) < \bar{h}(t) \) ) the proof is similar and is therefore omitted. Set 
\[
h(t) = \bar{h}(t)e^{-x(t)} \tag{4}
\]
when \( t \) is large enough, \( x(t) > 0 \), and 
\[
x'(t) + \frac{1}{\bar{h}(t)} \left[ \frac{v(t)e^{-x(t)}}{\mu(t) + \bar{h}^n(t)e^{nx(t)}} - \frac{v(t)}{\mu(t) + \bar{h}^n(t)} \right] = 0, \tag{5}
\]
However, it follows that since \( x(t) > 0 \) for sufficiently large \( t \). 
\[
x'(t) - \frac{1}{\bar{h}(t)} \frac{v(t)e^{-x(t)}}{\mu(t) + \bar{h}^n(t)e^{nx(t)}} \leq 0, \tag{6}
\]
And hence \( x'(t) \leq 0 \), thus \( x(t) \) is decreasing and therefore \( \lim_{t \to \infty} x(t) = \alpha \in [0, \infty) \) exists. Now, we prove that \( \alpha = 0 \). Suppose on the contrary that \( \alpha > 0 \), then there exists \( \epsilon > 0 \) and \( T_\epsilon > 0 \) such that for \( t \geq T_\epsilon, 0 < \alpha - \epsilon < x(t) < \alpha + \epsilon \). From (6), we find 
\[
x'(t) + \frac{1}{\bar{h}(t)} \frac{v(t)e^{-\alpha - \epsilon}}{\mu(t) + \bar{h}^n(t)e^{n(\alpha - \epsilon)}} < 0.
\]
When we integrate the above inequality from \( t \) to \( \infty \), we get a contradiction. Hence, \( \alpha = 0 \). As a result, \( x(t) \) tends to zero as \( t \to \infty \), thus, we find \( \lim_{t \to \infty} (h(t) - \bar{h}(t)) = 0 \). The proof is finished.

In the results that follow, we demonstrate that all solutions to equation (2) that are positive and do not oscillate about \( \bar{h}(t) \) converge to \( \bar{h}(t) \) and get the necessary conditions for \( \bar{h}(t) \) to be a global attractor.

Theorem 3. Let \( h(t) \) be a positive solution of (2) which does not oscillate about \( \bar{h}(t) \), and suppose that \( \delta(t), \beta(t), \mu(t), v(t) \) are positive periodic functions of period \( \omega \). Then 
\[
\lim_{t \to \infty} (h(t) - \bar{h}(t)) = 0. \tag{3}
\]

Proof: Let \( h(t) > \bar{h}(t) \) for sufficiently large \( t \) (where \( h(t) < \bar{h}(t) \) ) the proof is similar and is therefore omitted. By applying the transformation (4), (2) becomes (5). To prove (3), it follows that \( \lim_{t \to \infty} x(t) = 0 \), from (5), since \( x(t) > 0 \) for sufficiently large \( t \), we get 
\[
x'(t) + \frac{1}{\bar{h}(t)} \frac{v(t)e^{-x(t-m\omega)}}{\mu(t) + \bar{h}^n(t)e^{nx(t-m\omega)}} \leq 0. \tag{7}
\]
Hence, \( x'(t) \leq 0 \), thus \( x(t) \) is decreasing and therefore \( \lim_{t \to \infty} x(t) = \alpha \in [0, \infty) \) exists. Now, we prove that \( \alpha = 0 \). Suppose on the contrary that \( \alpha > 0 \), then there exists \( \epsilon > 0 \) and \( T_\epsilon > 0 \) such that for \( t > T_\epsilon, 0 < \alpha - \epsilon < x(t) < x(t-m\omega) < \alpha + \epsilon \). The reminder of the proof is similar to that of the proof of Theorem (2) and thus will be omitted.

In the following theorem we will establish some sufficient condition for the oscillation of all positive solution of (1) about \( \mathcal{H}(t) \).
To establish some sufficient conditions for oscillation of positive solution $\mathcal{H}(t)$ of (1) about $\bar{\mathcal{H}}(t)$, it suffices to consider (2) instead of (1) since $\prod_{0< t_k< \alpha_k + b_k} > 0$, and as a result, $\mathcal{H}(t)$ oscillates about $\bar{\mathcal{H}}(t)$ iff $h(t)$ is oscillatory around $\bar{h}(t)$.

**Theorem 4.** Suppose that $\delta(t), \beta(t), \mu(t), \nu(t)$ are a periodic positive function of period $\omega$, and every solution of DDE
\[
z'(t) + (1 - \varepsilon) n \nu(t) \bar{h}^{-1}(t) (\mu(t) + \bar{h}(t)) e^{\int_{t-m\omega}^{t} \delta(s) ds} z(t - \omega) = 0.
\]
Oscillates, then each solution to equation (1) oscillates about $\bar{\mathcal{H}}(t)$.

**Proof:** Assume that (1) has a solution that does not oscillate around $\bar{h}(t)$. Without losing generality, let's suppose that $h(t) > \bar{h}(t)$, that is $x(t) > 0$. According to the transformation (4), $h(t)$ oscillates around $\bar{h}(t)$ iff $x(t)$ oscillates around zero. By applying the transformation (4), (2) become
\[
x'(t) + \frac{v(t)(1 - e^{-x(t)})}{h(t)(\mu(t) + \bar{h}(t))} + \frac{v(t)\bar{h}(t)^{-1}(e^{nx(t)} - 1)}{\mu(t) + \bar{h}(t))} = 0.
\]
Or
\[
x'(t) + \frac{v(t)}{h(t)(\mu(t) + \bar{h}(t))} f_1(u, v) + \frac{v(t)\bar{h}(t)^{-1}(e^{nx(v)} - 1)}{(\mu(t) + \bar{h}(t))} f_2(v) = 0,
\]
where
\[
f_1(u, v) = \frac{\mu(t) + \bar{h}(t)^{n}(1 - e^{-n})}{\mu(t) + \bar{h}(t)^n e^{nx(v)}}, f_2(v) = \frac{\mu(t) + \bar{h}(t)^n(e^{nx(v)} - 1)}{(\mu(t) + \bar{h}(t))}. (10)
\]
Note that
\[
u f_1(u, v) > 0, f_2(v) > 0 and \lim_{u, v \to 0} f_1(u, v) = 1, \lim_{v \to 0} f_2(v) = 1. (11)
\]
From (11) it follows that for any given $\varepsilon \in (0,1)$ such that $f_1(u, v) \geq (1 - \varepsilon)u$ & $f_2(v) \geq (1 - \varepsilon)v$. Use above estimate in (10), to conclude that eventually $x(t)$ is positive solution of inequality
\[
x'(t) + \frac{v(t)}{h(t)(\mu(t) + \bar{h}(t))} (1 - \varepsilon)u + \frac{v(t)\bar{h}(t)^{-1}(e^{nx(v)} - 1)}{(\mu(t) + \bar{h}(t))} (1 - \varepsilon)v \leq 0.
\]
Now, the transformation
\[
x(t) = e^{-\int_{0}^{t} \delta(s) ds} z(t)
\]
demonstrates that $z(t)$ is also a positive solution of
\[
z'(t) + (1 - \varepsilon) \frac{v(t)\bar{h}^{-1}(t)}{(\mu(t) + \bar{h}(t))} e^{\int_{t-m\omega}^{t} \delta(s) ds} z(t - m\omega) \leq 0.
\]
We conclude that there is an eventually positive solution to (8) that is oscillatory based on corollary (3.2.2) in [18]. As a result, any solution to equation (2) oscillates about $\bar{h}(t)$, and so on equation (1). The proof is finished.

**Corollary 1.** Suppose that condition of Theorem 3 hold. Then, the condition
\[
\lim_{t \to \infty} \inf \int_{t-m\omega}^{t} \left( e^{\int_{s-m\omega}^{s} \delta(u) \, du} \right) \frac{n\nu(s)\bar{h}^{n-1}(s)}{(\mu(s)+\bar{h}^{n}(s))^{2}} \, ds > \frac{1}{(1-\epsilon)e} \tag{12}
\]
shows that each solution to (8) are oscillatory.

In the following example discussion, the obtain results.

**Example1.** Consider the nonautonomous equation
\[
h'(t) = \frac{e^{2\sin3t}}{1 + h^{3}(t - 30)} - e^{2\sin3t}h(t), \quad t \geq 0 \tag{13}
\]
Here the parameters \(\delta(t) = e^{2\sin3t}, \mu(t) = 1, \nu(t) = e^{2\sin3t}, m\omega = 30\) with \(\omega = 3\) and \(m = 10 > \frac{1}{\epsilon}\) and \(n = 3\) in (13). From the figure (1), we can note that the solutions of (13) oscillate around \(\bar{h} = 0.7\). Now, apply the condition (12) we find
\[
\lim_{t \to \infty} \inf \int_{t-m\omega}^{t} \left( e^{\int_{s-m\omega}^{s} \delta(u) \, du} \right) \frac{n\nu(s)\bar{h}^{n-1}(s)}{(\mu(s)+\bar{h}^{n}(s))^{2}} \, ds = \infty > \frac{1}{(1-\epsilon)e},
\]
that is the agreement with results of Corollary (1) and Theorem (4). Computer simulations of the numerical example is arranged in figure (1) to illustrate the correctness and e activeness of the presented convergence results. The software MATLAB program is use to find the solution.

![Figure 1 The solution of (13) oscillate about equilibrium \(\bar{h} = 0.7\).](image)
4. CONCLUSION

The dynamics analysis of impulsive hematopoiesis model provides a valuable framework for studying the oscillation and behavior of the hematopoietic systems under impulsive perturbations. With new references exploring its applications in clinical settings, this model continues to contribute to our understanding of hematopoiesis and its associated diseases. Investigations have been made into the impulsive periodic hematopoiesis model (1). Finding suitable conditions for the existence and global attractiveness of a positive periodic solution is an a priory goal for periodic versions. Despite some recent additions, there is still a dearth of literature on this topic. In this section, we analyze the impulsive periodic hematopoiesis model (1), in which linear impulses were added to correspond to the administration of medication or radiation in the treatment of hematological illnesses. Under sufficient conditions that ensure its existence, we give new criteria for the global attractivity of a positive periodic solution of (1). For any positive solution of (1) to oscillates around $\mathcal{H}(t)$, some sufficient conditions are found and for the global attractivity of $\mathcal{H}(t)$, certain sufficient conditions are provided. The outcomes were modified and extended to some results that were already published. By the way, the method suggested in this paper offers a potential option to investigate the asymptotic behavior on other population dynamic models.

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Conflict of interests.

There are non-conflicts of interest.

References


The abstract:

The model for the blood cell formation is an extension of the classical blood cell formation model that incorporates the concept of rapid movements or "rhythms" to produce blood cells in response to stimuli or specific conditions. The rhythmic aspect is a result of the sudden conditions or rhythms induced in the model. Finding the right conditions for oscillation and global stability is a target for the periodic model. Despite some recent additions, there is still a lack of literature on this topic.

Methods:

Through using the theory of continuity for random processes, continuity means maintaining maturing cells for a long time. Using the same technique of proof used in the model without rhythms, some new characteristics close to oscillation and sufficient conditions for the global stability of the solution of the periodic model are created.

Results:

In this work, the characteristics of the periodic model are discussed. New conditions are given for all positive solutions to oscillate around the balance and global stability for all non-oscillating solutions around the balance.

Conclusions:

Some of the published results in the model without rhythms were improved and extended to the periodic blood cell formation model. A numerical example was prepared to show the accuracy and efficiency of the results provided.

Keywords: oscillation, differential equation, blood models, rhythms, global stability.