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# Existence, uniqueness and stability results of an iterative survival model of red blood cells with a delayed nonlinear harvesting term

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**Abstract.** In this article, a first-order iterative Lasota–Wazewska model with a nonlinear delayed harvesting term is discussed. Some sufficient conditions are derived for proving the existence, uniqueness and continuous dependence on parameters of positive periodic solutions with the help of Krasnoselskii's and Banach fixed point theorems along with the Green's functions method. Besides, at the end of this work, three examples are provided to show the accuracy of the conditions of our theoretical findings which are completely innovative and complementary to some earlier publications in the literature.

*Keywords*: Fixed point theorem, Green's function, iterative differential equation, Lasota–Wazewska model.
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## 1 Introduction

Throughout more than 60 years of the mathematical modeling of problems arising in hematology, a quite large amount of hematopoiesis models have been investigated by many authors. To our knowledge, the sixties of the past century can be regarded as a watershed in the history of the modeling of blood cell kinetics but the first timid attempts were focused on dealing with quite complex models (see [8, 16, 17]). The end of the following decade witnessed two turning points, the first work carried out by Wazewska and Lasota [19] in 1976 and the other done by Mackey and Glass [14] in the following year.

Let us cite for instance what we consider as remarkable contributions to this field that have been interested in studying the survival of red blood cells in the bone marrow of an animal.

In the end of the seventies of the past century and in one of the earliest papers in this topic which was and still is one of the most important milestones in the history of mathematical modeling of erythropoiesis, Wazewska-Czyzewska and Lasota [19] introduced, the following delayed differential equation

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with one constant delay:

$$x'(t) = -ax(t) + be^{-\gamma x(t-\tau)},$$

where they were interested in the problem of the existence of periodic solutions to this erythropoiesis model which was aimed at modelling and getting better understanding of the survival of red blood cells in an animal. In medical terms $x(t)$ stands for the density of mature red blood cells in the blood circulation at time $t$, $a > 0$ is the death rate of red blood cells, the positive constants $\gamma$ and $b$ are related to the production of red-blood cells per unit time and the time delay required to produce a mature red blood cell for release in circulating bloodstreams is denoted by the positive constant $\tau$.

Thirteen years later, in 1989, Kulenovic et al. [9] investigated the positive equilibrium of the following generalization of the Wazewska-Lasota model:

$$x'(t) = -ax(t) + \sum_{i=1}^{m} b_i e^{-\gamma x(t-\tau_i)}, \ t \geq 0, \ m \geq 1.$$

In [10], the authors applied the continuation theorem of Gaines and Mawhin to establish the existence and global attractivity of positive periodic solutions of the below Lasota-Wazewska model with time-varying parameters and delay.

$$x'(t) = -a(t)x(t) + b(t)e^{-\gamma(t)x(t-\tau(t))}.$$

While the authors in [11] used the fixed point theory for establishing the existence and global attractivity of the unique positive periodic solution of the Lasota-Wazewska model with time-varying parameters and multiple variable delays:

$$x'(t) = -a(t)x(t) + \sum_{i=1}^{m} b_i(t)e^{-\gamma_i(t)x(t-\tau_i(t))}.$$

The harvesting of blood cells plays a crucial role in the blood cell population dynamics since it is more than merely a reduction of blood cells by cupping therapy, blood sampling or a blood donation, to name a few but it is of prime interest to gain insight into the dynamical properties of the problem. For more details of the impact of the harvesting strategy in the population dynamics and the management of biological renewable see [3, 18] and references therein. Concerning, the Lasota-Wazewska models with harvesting term, the interested reader can consult the paper [5] where the authors studied the following delay Lasota-Wazewska model with a discontinuous harvesting term:

$$x'(t) = -a(t)x(t) + \sum_{i=1}^{m} b_i(t)e^{-\gamma_i(t)x(t-\tau_i(t))} - p(t)H(t),$$

where $H$ is a discontinuous function.

Motivated by the above works and taking into account the effect of the harvesting strategy which can exhibit many delayed reactions and retarded responses to stimuli, we set up a revisited Lasota-Wazewska model with an iterative production term and a nonlinear harvesting one that involves a constant delay as follows:

$$x'(t) = -a(t)x(t) + b(t)e^{-\gamma x^{[2]}(t)} - h(t, x(t-\tau)), \tag{1}$$

where $t \in [0, w]$, $x(0) = x(w)$, $a, b \in C([0, w], (0, +\infty))$, $h \in C([0, w] \times \mathbb{R}, (0, +\infty))$ are $w$-periodic functions with respect to the time variable, $\gamma$ is a positive constant, $x^{[2]}(t)$ is the second iterate of $x(t)$, $h$ is the harvesting term and $\tau > 0$ is the harvest delay.

It is interesting to point here that $x^{[2]}(t)$ results from a delay $\tau_1(t, x(t)) = t - x(t)$ depending upon both the time and the density of mature red blood cells which describes the time duration between the division of hematopoietic stem cells (HSC) residing the bone marrow niche and their maturation for release in circulating bloodstream. This dependence on the density of mature red blood cells can be explained by the fact that some growth factors and hormones control the production and maturation of blood cells by playing an activator or inhibitor role as needed. Indeed, when the density of mature erythrocytes is low, the erythropoietin (EPO) produced by the kidneys with the aid of some other growth factors and some hormones such as thyroxine, sex steroids and pituitary hormones stimulate and accelerate the red blood cell division by increasing the synthesis of DNA, RNA, and hemoglobin in the cells and in the converse case, the division will be suppressed and slowed down.

So far, Eq. (1) which is a first order iterative differential equation that can be regarded as a special type of the class of time and state dependent delay differential equations, has not been investigated till now.

Unfortunately, although iterative differential equations appear widely in many applications such as models arising in epidemiology, biology and electrodynamics and although they have also fascinated many authors and hence gained much momentum recently, publications that handle such equations are still somewhat rare (see [1–4, 6, 7, 12, 13, 15, 20] and the references cited therein). Their unpopularity is partly due to the fact that their iterative terms that involve compositions of the unknown function with itself, may create some difficulties both when studying them and when applying the well-known methods. This is what motivates us, in turn, to investigate this topic and contribute to make up for this deficiency. Our idea here aims to diminish some of these difficulties by choosing an appropriate Banach space and its subset on the one hand, and utilizing an attractive technique based on the fixed point theory, some functional analysis tools as well as the Green's functions method, on the other hand.

More precisely, the current work principally probes into the existence, uniqueness and continuous dependence on parameters of positive periodic solutions for Eq. (1). To this end, we pursue the following key steps:

Firstly, we construct a Banach space and a closed convex and bounded subset of it with a twofold purpose: For biological realism, they should ensure the periodicity, positivity and boundedness of the sought solution if there exists, and also they should help us to control the iterative terms.

Secondly, we convert our periodic boundary value problem into an equivalent integral equation for transforming this problem into a fixed point one. So, fixed points of the obtained integral operator are solutions to Eq. (1) and vice versa.

Finally, we focus on two main issues:

($i$) the establishment of a set of sufficient criteria that guarantee the existence of at least one positive periodic solution of Eq. (1) with the periodic boundary conditions by the aid of the Krasnoselskii's fixed point theorem and some properties of the obtained Green's kernel in the second step. For this, the integral operator needs to satisfy the requirements of the used fixed-point theorem and we need especially to express it as a sum of two operators, one of them is completely continuous while the other is a contraction.

($ii$) the addition of some suitable conditions under which the contraction mapping principle can be applied and hence the positive periodic solution of the given problem becomes unique as well as the

reveal of the impact of the harvesting strategy on the solution and also we prove that small changes in the harvesting term *h* or the production rate *b* lead to small variations of the obtained findings.

The basic frame of this manuscript is planned in four sections. In the next section, before proceeding with the main part of this work, we introduce some assumptions and lemmas that play an important role in establishing our main outcomes while the third section is devoted to presenting our main results on the existence, uniqueness and continuous dependence of positive periodic solutions. In the fourth section, three examples are exhibited to support the obtained results. Finally, we conclude the paper by a brief conclusion.

## 2  Preliminaries

For $r_0, r_1, L > 0$, we consider the following closed, convex and bounded subset:

$$P_w(r_0, r_1, L) = \{x \in P_w, \ r_0 \le x(t) \le r_1, \ |x(t_2) - x(t_1)| \le L|t_2 - t_1|, \ \forall t_1, t_2 \in \mathbb{R}\},$$

of the Banach space of all $w-$periodic continuous functions

$$P_w = \{x \in \mathscr{C}(\mathbb{R}, \mathbb{R}), \ x(t+w) = x(t), \ \forall t \in \mathbb{R}\},$$

endowed with the norm

$$\|x\| = \sup_{t \in \mathbb{R}} |x(t)| = \sup_{t \in [0,w]} |x(t)|.$$

It follows from conditions $r_0 \le x(t) \le r_1$ and $|x(t_2) - x(t_1)| \le L|t_2 - t_1|$ in the definition of $P_w(r_0, r_1, L)$ that this subset is uniformly bounded and equicontinuous. So, the Arzelà-Ascoli theorem guarantees the compactness of $P_w(r_0, r_1, L)$.

For the sake of simplicity, we will adopt the following notations:

$$a_1 = \sup_{t \in [0,w]} a(t), \quad b_0 = \inf_{t \in [0,w]} b(t),$$

$$b_1 = \sup_{t \in [0,w]} b(t), \quad h_1 = \sup_{\theta \in [0.w]} h(\theta, 0),$$

$$A_0 = \frac{\exp\left(-\int_0^w a(v)dv\right)}{\exp\left(\int_0^w a(v)dv\right) - 1}, \quad A_1 = \frac{\exp\left(\int_0^w a(v)dv\right)}{\exp\left(\int_0^w a(v)dv\right) - 1}.$$

It's not hard to prove the following lemma through which we can transform our problem into an equivalent integral equation.

**Lemma 1.** $x \in P_w(r_0, r_1, L) \cap \mathscr{C}^1(\mathbb{R}, \mathbb{R})$ *is a solution of Eq.* (1) *if and only if* $x \in P_w(r_0, r_1, L)$ *is a solution of the following integral equation:*

$$x(t) = \int_t^{t+w} G(t, \theta) b(\theta) e^{-ax^{[2]}(\theta)} d\theta - \int_t^{t+w} h(\theta, x(\theta - \tau)) G(t, \theta) d\theta, \tag{2}$$

*where*

$$G(t, \theta) = \frac{\exp\left(\int_t^\theta a(v)dv\right)}{(\exp\left(\int_0^w a(v)dv\right)) - 1}.$$

*Proof.* Suppose that $x \in P_w(r_0, r_1, L) \cap \mathscr{C}^1(\mathbb{R}, \mathbb{R})$ is a solution of Eq. (1) then

$$\left[x'(t) + a(t)x(t)\right] e^{\int_0^t a(v)dv} = \left[b(t)e^{-\gamma x^{[2]}(t)} - h(t, x(t-\tau))\right] e^{\int_0^t a(v)dv}.$$

Hence

$$\int_t^{t+w} \left[x'(\theta) + a(\theta)x(\theta)\right] e^{\int_0^\theta a(v)dv} d\theta = \int_t^{t+w} e^{\int_0^\theta a(v)dv} \left[b(\theta)e^{-\gamma x^{[2]}(\theta)} - h(\theta, x(\theta-\tau))\right] d\theta.$$

Thanks to the periodic properties, we get

$$x(t) \left(\exp\left(\int_t^{t+w} a(v)dv\right) - \exp\left(\int_0^t a(v)dv\right)\right)$$
$$= \exp\left(\int_0^t a(v)dv\right) \left[\exp\left(\int_t^{t+w} a(v)dv\right) - 1\right] x(t)$$
$$= \int_t^{t+w} \left[b(\theta)e^{-\gamma x^{[2]}(\theta)} - h(\theta, x(\theta-\tau))\right] \exp\left(\int_0^\theta a(v)dv\right) d\theta.$$

That is,

$$x(t) = \int_t^{t+w} \left[b(\theta)e^{-\gamma x^{[2]}(\theta)} - h(\theta, x(\theta-\tau))\right] \frac{\exp\left(\int_0^\theta a(v)dv\right)\exp\left(-\int_0^t a(v)dv\right)}{\exp\left(\int_0^w a(v)dv\right) - 1} d\theta$$
$$= \int_t^{t+w} \left[b(\theta)e^{-\gamma x^{[2]}(\theta)} - h(\theta, x(\theta-\tau))\right] \frac{\exp\left(\int_t^\theta a(v)dv\right)}{\exp\left(\int_0^w a(v)dv\right) - 1} d\theta$$
$$= \int_t^{t+w} \left[b(\theta)e^{-\gamma x^{[2]}(\theta)} - h(\theta, x(\theta-\tau))\right] G(t, \theta) d\theta.$$

Conversely, if we assume that $x$ is a solution of the integral equation (2) in $P_w(r_0, r_1, L)$, then the differentiation of Eq. (2) leads to the desired result. $\square$

**Remark 1.** *The Green's kernel $G(t, \theta)$ is bounded as follows:*

$$0 < A_0 \leq G(t, \theta) \leq A_1, \tag{3}$$

*and for all $t_2, t_1 \in [0, w]$ with $t_1 < t_2$ we have*

$$\int_{t_1}^{t_1+w} |G(t_2, \theta) - G(t_1, \theta)| d\theta \leq A_1 w a_1 |t_2 - t_1|. \tag{4}$$

Throughout this paper, we impose the following hypotheses which will be used in the sequel:

The function $h(t, x)$ is globally Lipschitz with respect to the second variable $x$, i.e., there exists a positive constant $\mu$ such that

$$|h(t, x(t)) - h(t, y(t))| \leq \mu |x(t) - y(t)|. \tag{5}$$

We suppose further that the following estimates are satisfied:

$$wA_1b_1 \leq r_1, \tag{6}$$

$$w\left(A_0b_0e^{-\gamma r_1} - (\mu r_1 + h_1)A_1\right) \geq r_0, \tag{7}$$

$$A_1\left(2 + wa_1\right)\left(b_1 + h_1 + \mu r_1\right) \leq L, \tag{8}$$

and

$$wA_1\mu < 1. \tag{9}$$

**Lemma 2.** *[20] For all $x, y \in P_w(r_0, r_1, L)$, we have $\left\|x^{[2]} - y^{[2]}\right\| \leq (1 + L)\|x - y\|$.*

**Remark 2.** *From condition (5), we get*

$$|h(\theta, x(t))| \leq \mu r_1 + h_1. \tag{10}$$

*In addition, by applying the mean value theorem to the function $f(z) = \exp(-\gamma z)$ over the interval $\left[x^{[2]}(\theta), y^{[2]}(\theta)\right]$, we obtain*

$$e^{-\gamma x^{[2]}(\theta)} - e^{-\gamma y^{[2]}(\theta)} = -\gamma e^{-\gamma \zeta(\theta)}\left(x^{[2]}(\theta) - y^{[2]}(\theta)\right),$$

*where $\zeta(\theta)$ is between $x^{[2]}(\theta)$ and $y^{[2]}(\theta)$.*

*Since $\gamma > 0$ and $0 < r_0 \leq \zeta(\theta) \leq r_1$, then $\left|e^{-\gamma \zeta(\theta)}\right| = e^{-\gamma \zeta_2(\theta)} < 1$ and*

$$\left|e^{-\gamma x^{[2]}(\theta)} - e^{-\gamma y^{[2]}(\theta)}\right| = \left|-\gamma e^{-\gamma \zeta(\theta)}\left(x^{[2]}(\theta) - y^{[2]}(\theta)\right)\right|$$

$$= |-\gamma|\left|e^{-\gamma \zeta(\theta)}\right|\left|x^{[2]}(\theta) - y^{[2]}(\theta)\right|$$

$$\leq \gamma\left|x^{[2]}(\theta) - y^{[2]}(\theta)\right|.$$

*According to Lemma 2, we get*

$$\left|e^{-\gamma x^{[2]}(\theta)} - e^{-\gamma y^{[2]}(\theta)}\right| \leq \gamma(1 + L)\|x - y\|, \tag{11}$$

*for all $x, y \in P_w(r_0, r_1, L)$.*

## 3    Main results

The main goal of this section is to prove the existence, uniqueness and structural stability of positive periodic solutions to Eq. (1) by using an efficient technique based on Krasnoselskii's and Banach fixed point theorems as well as the Green's functions method.

For achieving our target, we define an operator $T$ that can be expressed as a sum of two operators $T_1$ and $T_2$ as follows: $T = T_1 + T_2 : P_w(r_0, r_1, L) \longrightarrow P_w$ where $T_1, T_2 : P_w(r_0, r_1, L) \longrightarrow P_w$,

$$(T_1x)(t) = \int_t^{t+w} G(t, \theta)b(\theta)e^{-\gamma x^{[2]}(\theta)}d\theta, \tag{12}$$

and

$$(T_2 x)(t) = -\int_t^{t+w} h(\theta, x(\theta - \tau)) G(t, \theta) d\theta. \tag{13}$$

By virtue of the periodic properties, we conclude that operators $T_1$ and $T_2$ are well defined.

**Lemma 3.** *Assume that conditions* (6)-(8) *hold, then*

$$(T_1 x) + (T_2 y) \in P_w(r_0, r_1, L),$$

*for all $x, y \in P_w(r_0, r_1, L)$.*

*Proof.* Let $x, y \in P_w(r_0, r_1, L)$, then

$$\begin{aligned}
(T_1 x)(t) + (T_2 y)(t) &= \int_t^{t+w} G(t, \theta) b(\theta) e^{-\gamma x^{[2]}(\theta)} d\theta - \int_t^{t+w} h(\theta, y(\theta - \tau)) G(t, \theta) d\theta \\
&\leq \int_t^{t+w} G(t, \theta) b(\theta) e^{-\gamma x^{[2]}(\theta)} d\theta.
\end{aligned}$$

From (3) and (6), we get

$$(T_1 x)(t) + (T_2 y)(t) \leq w A_1 b_1 \leq r_1.$$

According to (3), (7) and (10), we deduce that

$$(T_1 x)(t) + (T_2 y)(t) \geq w A_0 b_0 e^{-\gamma r_1} - (\mu r_1 + h_1) w A_1 \geq w\left[A_0 b_0 e^{-\gamma r_1} - (\mu r_1 + h_1) A_1\right] \geq r_0.$$

Consequently,

$$r_0 \leq (T_1 x)(t) + (T_2 y)(t) \leq r_1, \tag{14}$$

for all $x, y \in P_w(r_0, r_1, L)$.

Now, let $t_1, t_2 \in [0, w]$, then

$$|(T_1 x + T_2 y)(t_2) - (T_1 x + T_2 y)(t_1)| \leq |(T_1 x)(t_2) - (T_1 x)(t_1)| + |(T_2 y)(t_2) - (T_2 y)(t_1)|.$$

We have

$$\begin{aligned}
|(T_1 x)(t_2) - (T_1 x)(t_1)| &= \left| \int_{t_2}^{t_2+w} G(t_2, \theta) b(\theta) e^{-\gamma x^{[2]}(\theta)} d\theta - \int_{t_1}^{t_1+w} G(t_1, \theta) b(\theta) e^{-\gamma x^{[2]}(\theta)} d\theta \right| \\
&= \left| \int_{t_2}^{t_1} G(t_2, \theta) b(\theta) e^{-\gamma x^{[2]}(\theta)} d\theta + \int_{t_1}^{t_1+w} G(t_2, \theta) b(\theta) e^{-\gamma x^{[2]}(\theta)} d\theta \right. \\
&\quad \left. + \int_{t_1+w}^{t_2+w} G(t_2, \theta) b(\theta) e^{-\gamma x^{[2]}(\theta)} d\theta - \int_{t_1}^{t_1+w} G(t_1, \theta) b(\theta) e^{-\gamma x^{[2]}(\theta)} d\theta \right|.
\end{aligned}$$

So

$$\begin{aligned}
|(T_1 x)(t_2) - (T_1 x)(t_1)| &\leq \int_{t_2}^{t_1} G(t_2, \theta) b(\theta) e^{-\gamma x^{[2]}(\theta)} d\theta + \int_{t_1+w}^{t_2+w} G(t_2, \theta) b(\theta) e^{-\gamma x^{[2]}(\theta)} d\theta \\
&\quad + \int_{t_1}^{t_1+w} |G(t_2, \theta) - G(t_1, \theta)| b(\theta) e^{-\gamma x^{[2]}(\theta)} d\theta.
\end{aligned}$$

By virtue of $(3)$ and $(4)$, we obtain

$$|(T_1x)(t_2) - (T_1x)(t_1)| \leq 2A_1b_1|t_2 - t_1| + b_1A_1wa_1|t_2 - t_1|$$
$$= A_1b_1(2 + wa_1)|t_2 - t_1|. \tag{15}$$

On the other hand, we have

$$|(T_2y)(t_2) - (T_2y)(t_1)| = \left| \int_{t_2}^{t_2+w} h(\theta, y(\theta - \tau))G(t_2, \theta)d\theta - \int_{t_1}^{t_1+w} h(\theta, y(\theta - \tau))G(t_1, \theta)d\theta \right|$$
$$= \left| \int_{t_2}^{t_1} h(\theta, y(\theta - \tau))G(t_2, \theta)d\theta + \int_{t_1}^{t_1+w} h(\theta, y(\theta - \tau))G(t_2, \theta)d\theta \right.$$
$$\left. + \int_{t_1+w}^{t_2+w} h(\theta, y(\theta - \tau))G(t_2, \theta)d\theta - \int_{t_1}^{t_1+w} h(\theta, y(\theta - \tau))G(t_1, \theta)d\theta \right|.$$

So

$$|(T_2y)(t_2) - (T_2y)(t_1)| \leq \int_{t_2}^{t_1} h(\theta, y(\theta - \tau))G(t_2, \theta)d\theta + \int_{t_1+w}^{t_2+w} h(\theta, y(\theta - \tau))G(t_2, \theta)d\theta$$
$$+ \int_{t_1}^{t_1+w} |G(t_2, \theta) - G(t_1, \theta)|h(\theta, y(\theta - \tau))d\theta.$$

Thanks to $(3)$, $(4)$ and $(10)$, we arrive at

$$|(T_2y)(t_2) - (T_2y)(t_1)| \leq 2A_1(\mu r_1 + h_1)|t_2 - t_1| + (\mu r_1 + h_1)A_1wa_1|t_2 - t_1|$$
$$= A_1(\mu r_1 + h_1)[2 + wa_1]|t_2 - t_1|. \tag{16}$$

According to $(8)$, $(15)$ and $(16)$, we obtain

$$|(T_1x + T_2y)(t_2) - (T_1x + T_2y)(t_1)| \leq L|t_2 - t_1|, \tag{17}$$

for all $x, y \in P_w(r_0, r_1, L)$ and $t_1, t_2 \in [0, w]$.

Finally, it follows from $(14)$ and $(17)$ that $(T_1x) + (T_2y) \in P_w(r_0, r_1, L)$. $\qquad\square$

**Lemma 4.** *Assume that the condition* $(9)$ *holds. Then, $T_2$ is a contraction.*

*Proof.* For all $x, y \in P_w(r_0, r_1, L)$, we have

$$|(T_2x)(t) - (T_2y)(t)| \leq \int_t^{t+w} G(t, \theta)|h(\theta, x(\theta - \tau)) - h(\theta, y(\theta - \tau))|d\theta.$$

Taking into account $(3)$ and the Lipschitz condition $(5)$ we get

$$\|T_2x - T_2y\| \leq wA_1\mu\|x - y\|. \tag{18}$$

From $(9)$ we infer that $T_2$ is a contraction. $\qquad\square$

**Lemma 5.** *The mapping $T_1$ is completely continuous on $P_w(r_0, r_1, L)$.*

*Proof.* Since $P_w(r_0, r_1, L)$ is a compact subset of $P_w$ and since any continuous operator maps every compact set into compact one, then to show that $T_1$ is a compact operator it's suffices to show that it is continuous. For all $x, y \in P_w(r_0, r_1, L)$, we have

$$|(T_1 x)(t) - (T_1 y)(t)| = \int_t^{t+w} G(t, \theta) b(\theta) \left| e^{-\gamma x^{[2]}(\theta)} - e^{-\gamma y^{[2]}(\theta)} \right| d\theta.$$

By virtue of the Green's function property (3) and the estimate (11), we obtain

$$\|T_1 x - T_1 y\| \le w A_1 b_1 \gamma (1 + L) \|x - y\|, \tag{19}$$

and accordingly operator $T_1$ is Lipschitz continuous and hence continuous. Therefore, $T_1$ is continuous and compact which means that it is a completely continuous operator. □

Now, we state and prove our first existence theorem.

**Theorem 1.** *If the conditions* (5)-(9) *hold, then Eq.* (1) *has at least one positive periodic solution in* $P_w(r_0, r_1, L)$.

*Proof.* In view of Lemmas 3-5 all requirements of the Krasnoselskii's fixed point theorem are fulfilled, so $T = T_1 + T_2$ has at least one fixed point $x \in P_w(r_0, r_1, L)$ such that $T(x) = x$, which means that $x$ is a positive periodic solution to equation (1). □

Next, we establish the existence and uniqueness of the positive periodic solution.

**Theorem 2.** *If the conditions* (5)-(9) *and the following estimate:*

$$w A_1 (b_1 \gamma (1 + L) + \mu) < 1, \tag{20}$$

*hold, then Eq.* (1) *has one and only one positive periodic solution.*

*Proof.* First, we notice that under the same conditions of Lemma 3 and by using the same technique as that in its proof, we can prove that $T$ maps $P_w(r_0, r_1, L)$ into itself.

Next, from (18) and (19) we get

$$\|Tx - Ty\| \le w A_1 (b_1 \gamma (1 + L) + \mu) \|x - y\|,$$

for all $x, y \in P_w(r_0, r_1, L)$. It follows from (20) that $T$ is a contraction mapping and thereby by virtue of the contraction mapping principle, $T$ has one and only one fixed point in $P_w(r_0, r_1, L)$, which is the unique positive periodic solution of Eq. (1). □

Now, we prove that the unique solution depends continuously upon the harvesting term $h$ and the production rate $b$.

**Theorem 3.** *Suppose that the conditions of Theorem 2 hold. Then, the unique solution of* (1) *depends continuously on parameters b and h.*

*Proof.* Let $x$ be the unique solution of Eq. (1), so $x$ satisfies the integral equation (2), i.e.,

$$x(t) = \int_t^{t+w} G(t,\theta) b(\theta) e^{-\gamma x^{[2]}(\theta)} d\theta - \int_t^{t+w} h(\theta, x(\theta - \tau)) G(t,\theta) d\theta,$$

and let $\widetilde{x}$ be a solution of the perturbed equation with small perturbations in the harvesting term and the production rate which satisfy the requirements of Theorem 2. So, $\widetilde{x}$ satisfies the following integral equation:

$$\widetilde{x}(t) = \int_t^{t+w} G(t,\theta) \widetilde{b}(\theta) e^{-\gamma \widetilde{x}^{[2]}(\theta)} d\theta - \int_t^{t+w} \widetilde{h}(\theta, \widetilde{x}(\theta - \tau)) G(t,\theta) d\theta.$$

where $\widetilde{b}$ and $\widetilde{h}$ are the perturbed parameters.

We have

$$|x(t) - \widetilde{x}(t)| \leq \int_t^{t+w} G(t,\theta) \left| b(\theta) e^{-\gamma x^{[2]}(\theta)} - \widetilde{b}(\theta) e^{-\gamma \widetilde{x}^{[2]}(\theta)} \right| d\theta$$

$$+ \int_t^{t+w} G(t,\theta) \left| h(\theta, x(\theta - \tau)) - \widetilde{h}(\theta, \widetilde{x}(\theta - \tau)) \right| d\theta$$

$$\leq \int_t^{t+w} G(t,\theta) \left| b(\theta) e^{-\gamma x^{[2]}(\theta)} - b(\theta) e^{-\gamma \widetilde{x}^{[2]}(\theta)} \right.$$

$$\left. + b(\theta) e^{-\gamma \widetilde{x}^{[2]}(\theta)} - \widetilde{b}(\theta) e^{-\gamma \widetilde{x}^{[2]}(\theta)} \right| d\theta$$

$$+ \int_t^{t+w} G(t,\theta) \left| h(\theta, x(\theta - \tau)) - \widetilde{h}(\theta, x(\theta - \tau)) \right.$$

$$\left. + \widetilde{h}(\theta, x(\theta - \tau)) - \widetilde{h}(\theta, \widetilde{x}(\theta - \tau)) \right| d\theta.$$

So

$$|x(t) - \widetilde{x}(t)| \leq \int_t^{t+w} b(\theta) \left| e^{-\gamma x^{[2]}(\theta)} - e^{-\gamma \widetilde{x}^{[2]}(\theta)} \right| G(t,\theta) d\theta$$

$$+ \int_t^{t+w} e^{-\gamma \widetilde{x}^{[2]}(\theta)} \left| b(\theta) - \widetilde{b}(\theta) \right| G(t,\theta) d\theta$$

$$+ \int_t^{t+w} \left| h(\theta, x(\theta - \tau)) - \widetilde{h}(\theta, x(\theta - \tau)) \right| G(t,\theta) d\theta$$

$$+ \int_t^{t+w} \left| \widetilde{h}(\theta, x(\theta - \tau)) - \widetilde{h}(\theta, \widetilde{x}(\theta - \tau)) \right| G(t,\theta) d\theta.$$

Using (3), (5) and (11) we get

$$|x(t) - \widetilde{x}(t)| \leq wA_1 \|b\| \gamma (1+L) \|x - \widetilde{x}\| + wA_1 \left\| b - \widetilde{b} \right\| + wA_1 \left\| h - \widetilde{h} \right\| + wA_1 \mu \|x - \widetilde{x}\|$$

$$= wA_1 (\|b\| \gamma (1+L) + \mu) \|x - \widetilde{x}\| + wA_1 \left\| b - \widetilde{b} \right\| + wA_1 \left\| h - \widetilde{h} \right\|.$$

Thus

$$\|x - \widetilde{x}\| (1 - wA_1 (\|b\| \gamma (1+L) + \mu)) \leq wA_1 \left( \left\| b - \widetilde{b} \right\| + \left\| h - \widetilde{h} \right\| \right).$$

By virtue of the condition (20), we arrive at

$$\|x - \widetilde{x}\| \leq \frac{wA_1}{(1 - wA_1 (\|b\| \gamma (1+L) + \mu))} \left( \left\| b - \widetilde{b} \right\| + \left\| h - \widetilde{h} \right\| \right).$$

This completes the proof.                                                                                                    □

## 4 Illustrative examples

To validate our main results on the existence, uniqueness and continuous dependence of positive periodic solutions, we provide the following examples:

**Example 1.** Let us consider the following iterative Lasota-Wazewska differential equation:

$$\frac{dx}{dt} = -c_1(t)x(t) + c_2(t)e^{-\frac{1}{20}x^{[2]}(t)} - c_3(t), \tag{21}$$

with

$$c_1(t) = 0.01 + 0.009\left(\cos^4\frac{2\pi}{19}t\right), \quad c_2(t) = 0.02 + 0.03\cos^2\frac{2\pi}{19}t, \quad c_3(t) = \frac{1}{\pi^9} + \frac{1}{3\pi^9}\frac{x(t-\tau)}{1+x(t-\tau)},$$

in the set $P_w(r_0, r_1, L) = P_{19}(0.8, 4.25, 0.6)$. Here $c_1(t)$ is the death rate of red blood cells, $c_2(t)$ is related to the production of red blood cells per unit time and $c_3(t)$ is the harvesting function $h$. We choose a period of 19 days since the period can vary from a few weeks up to few months.

We have

$$a_1 = 0.019, \ \ b_0 = 0.02, \ \ b_1 = 0.05, \ \ A_0 \approx 2.6806, \ \ A_1 \approx 4.4562, \ \ \gamma = \frac{1}{20}, \ \ \mu = \frac{1}{3\pi^9} \ \ \text{and} \ \ h_1 = \frac{1}{\pi^9}.$$

So

$$wA_1b_1 \approx 4.2334 \leq r_1 = 4.25,$$
$$w\left(A_0b_0e^{-\gamma r_1} - (\mu r_1 + h_1)A_1\right) \approx 0.81676 \geq r_0 = 0.8,$$
$$A_1(2 + wa_1)(b_1 + \mu r_1 + h_1) \approx 0.52691 \leq L = 0.6,$$
$$wA_1\mu \approx 0.00094678 < 1.$$

The additional condition (20) in Theorem 2

$$wA_1(b_1\gamma(1+L) + \mu) \approx 0.33962 < 1,$$

is fulfilled. Furthermore, if $x$ is the unique solution of Eq. (21) and if $\widetilde{x}$ is a solution of the perturbed equation with the perturbed parameters $\widetilde{b}$ and $\widetilde{h}$, then we arrive at

$$\|x - \widetilde{x}\| \leq (128.21)\left(\left\|b - \widetilde{b}\right\| + \left\|h - \widetilde{h}\right\|\right).$$

Since all the conditions of Theorems 2 and 3 are satisfied, Eq. (21) has a unique positive periodic solution in $P_{19}(0.8, 4.25, 0.6)$ that depends continuously on the harvesting term $h$ and the production rate $b$.

The next example highlights the power of Theorem 1 to establish an existence result even when the Banach fixed point theorem cannot be applied.

**Example 2.** Let us consider the same iterative Lasota-Wazewska differential equation (21) with the same period in the subset $P_w(r_0, r_1, L) = P_{19}(0.8, 4.25, 3.8)$. We have

$$wA_1(b_1\gamma(1+L) + \mu) \approx 1.017 > 1.$$

So, the additional condition (20) in Theorem 2 is not fulfilled while all the conditions of Theorem 1 are satisfied which means that Eq. (21) in this case admits at least one positive periodic solution in $P_{19}(0.8, 4.25, 3.8)$ which is not necessarily unique.

**Example 3.** Let us consider the following iterative Lasota-Wazewska differential equation:

$$\frac{dx}{dt} = -\left(0.02 + 0.009\left(\sin^2\frac{2\pi}{11}t\right)\right)x(t) + \left(0.01 + 0.04\left(\sin^2\frac{2\pi}{11}t\right)\right)\exp\left(-\frac{1}{5}x^{[2]}(t)\right)$$
$$-\left(\frac{1}{17\pi^5} + \frac{1}{19\pi^5}\frac{x(t-\tau)}{1+x(t-\tau)}\right), \tag{22}$$

in the set $P_w(r_0, r_1, L) = P_{11}\left(0.13, 2.35, \frac{1}{2}\right)$. We have

$$a_1 = 0.029, \quad b_0 = 0.01, \quad b_1 = 0.05, \quad A_0 \approx 2.4692, \quad A_1 \approx 4.233, \quad \gamma = \frac{1}{5}, \quad \mu = \frac{1}{19\pi^5} \quad \text{and} \quad h_1 = \frac{1}{17\pi^5}.$$

Thus

$$wA_1b_1 \approx 2.3282 \le r_1 = 2.35,$$
$$w\left(A_0b_0e^{-\gamma r_1} - (\mu r_1 + h_1)A_1\right) \approx 0.14199 \ge r_0 = 0.13,$$
$$A_1(2 + wa_1)(b_1 + \mu r_1 + h_1) \approx 0.49667 \le L = \frac{1}{2},$$
$$wA_1\mu \approx 0.0080083 < 1.$$

The additional condition in Theorem 2

$$wA_1(b_1\gamma(1+L) + \mu) \approx 0.70645 < 1,$$

is fulfilled. We conclude by Theorem 2 that Eq. (22) possesses one only one periodic positive solution in $P_{11}\left(0.13, 2.35, \frac{1}{2}\right)$. Moreover, let $x$ be the unique solution of Eq. (22) and let $\widetilde{x}$ be a solution of the perturbed equation with the perturbed parameters $\widetilde{b}$ and $\widetilde{h}$. We get

$$\|x - \widetilde{x}\| \le (158.62)\left(\left\|b - \widetilde{b}\right\| + \left\|h - \widetilde{h}\right\|\right),$$

which proves that the unique positive periodic solution $x$ depends continuously upon the harvesting term $h$ and the production rate $b$.

## 5  Conclusion

The present paper was devoted to study a revisited survival red blood cells model with an iterative production term and a delayed harvesting one. By virtue of the Krasnoselskii's fixed point theorem together with Arzelà- Ascoli theorem and some useful properties of an obtained Green's function and by assuming also that the harvesting function and the coefficients in the model are positive, continuous and common periodic, we derived some sufficient conditions that enabled us to prove the existence of at least one positive periodic solution. Furthermore, under an additional condition and by means of the Banach fixed point theorem, the existence and dependence continuous of the unique positive periodic solution on the production rate $b$ and the harvesting function $h$ are established. Our theoretical results which extend some related works in the literature were justified by three examples.

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