Journal of Innovative Applied Mathematics and Computational Sciences

J. Innov. Appl. Math. Comput. Sci. **2**(2) (2022), 23–30. n2t.net/ark:/49935/jiamcs.v2i2.21

http://jiamcs.centre-univ-mila.dz/

Existence, uniqueness and stability of solutions to a delay hematopoiesis model

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Received 25 January 2022, Accepted 15 February 2022, Published 29 August 2022

Abstract. This work aims to investigate a delay hematopoiesis model where the delay depends on both the time and the current density of mature blood cells. Based on the Banach contraction principle, the Schauder's fixed point theorem and some properties of a Green's function, we establish several interesting existence and uniqueness results of positive periodic solutions for the proposed model. The derived results are new and generalize some previous studies.

Keywords: Fixed point theorem, Green's function, Mackey–Glass equation, Periodic solution, Positive solution.

2020 Mathematics Subject Classification: 47H10, 34K13.

1 Introduction

In the end of the seventies of the last century, Michael Mackey and Leon Glass [13] put forward the following hematopoiesis model with constant delay:

$$x'(t) = -a\, x(t) + p\, \frac{x(t-\tau)}{1+x(t-\tau)},$$

which describes the white blood cells production. Biologically, $x(t)$ is the current density of mature white blood cells in the blood circulation at time t, $a > 0$ is the destruction rate, $p\dfrac{x(t-\tau)}{1+x(t-\tau)}$ stands for the blood cell reproduction, $p > 0$ is the maximal production rate and the time delay $\tau > 0$ describes the duration of the maturational phase.

It is well known that the harvesting of mature blood cells such as hijama cupping, blood donation and sampling blood play an important role in the blood cell population dynamics. For this, by assuming that the coefficient are time varying and taking into account the harvesting strategy, the classical Mackey-Glass model can be modified into the following one:

$$x'(t) = -a(t)\, x(t) + p(t)\, \frac{x(t-\tau)}{1+x(t-\tau)} - H(t, x(t), x(t-\tau)), \tag{1.1}$$

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ISSN (electronic): 2773-4196

where H is the harvesting function.

Meanwhile, a lot of investigations have revealed that the time and state dependent delays are more realistic than other types of lags to describe real phenomena, especially in life sciences. Actually, in the production of blood cells, some growth factors and hormones that control the division of the hematopoietic stem cells, depend on time and the density of mature cells. So, we need to revisit the Mackey-Glass model (1.1) as follows:

$$x'(t) = -a(t)x(t) + p(t)\frac{x(t-\tau(t,x(t)))}{1+x(t-\tau(t,x(t)))} - H(t,x(t),x(t-\tau(t,x(t)))), \tag{1.2}$$

where $a, p \in C(\mathbb{R}, (0,\infty))$ are $\omega-$periodic and $H \in C\left([0,\omega] \times \mathbb{R}^2, (0,\infty)\right)$.

Throughout this paper we shall assume that the delay in equation (1.2) takes the form $\tau(t, x(t)) = t - x(t)$. Under this assumption, equation (1.2) becomes the following first order iterative differential equation:

$$x'(t) = -a(t)x(t) + p(t)\frac{x^{[2]}(t)}{1+x^{[2]}(t)} - H\left(t, x(t), x^{[2]}(t)\right), \tag{1.3}$$

where $x^{[2]}(t) = x(x(t))$.

For detailed information about such equations and their emerging theory we refer the reader to [1–12], [14–17].

The key focus of this work is on the existence, uniqueness and stability of positive periodic solutions for equation (1.3) by the use of an efficient technique based on converting the proposed equation into an integral one before applying two suitable fixed point theorems as well as the Green's functions method.

The present manuscript is organized as follows. The next section presents some necessary notations, definitions, and preliminary results that will be used throughout this work. In the third section, we apply Banach and Schauder's fixed point theorems combined with the use of some properties of an obtained Green's function to establish sufficient conditions for the existence, uniqueness, and continuous dependence on parameters of positive periodic and bounded solutions for equation (1.3).

2 Preliminaries

We assume the following hypotheses on the harvesting function:

$$H(t+\omega, x, y) = H(t, x, y), \text{ for all } t, x, y \in \mathbb{R}, \tag{2.1}$$

and there exist $k_1, k_2 > 0$, such that

$$|H(t, x_1, y_1) - H(t, x_2, y_2)| \leq k_1 |x_1 - x_2| + k_2 |y_1 - y_2|. \tag{2.2}$$

To proving the existence of at least one positive periodic solution of (1.3), we will convert it into an integral equation before employing the Schauder's fixed point theorem.

For $L, M > 0$, let

$$\mathbb{K} = \{x \in \mathbb{X},\ 0 \leq x(t) \leq M,\ |x(t_2) - x(t_1)| \leq L|t_2 - t_1|,\ \forall t_1, t_2 \in [0,]\},$$

a convex bounded and closed subset of the Banach space $(\mathbb{X}, \|.\|)$ where

$$\mathbb{X} = \{x \in \mathcal{C}(\mathbb{R}, \mathbb{R}),\ x(t+\omega) = x(t)\},$$

and

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

Furthermore, we assume that

$$\omega\beta\left(H_0 + \|p\| + \left(k_1 + k_2\left(1+L\right)\right)M\right) \leq M, \tag{2.3}$$

and

$$\beta\left(H_0 + \|p\| + \left(k_1 + k_2\left(1+L\right)\right)M\right)\left(2+\omega\|a\|\right) \leq L, \tag{2.4}$$

where

$$\alpha = \frac{e^{-\int_0^\omega a(v)dv}}{e^{\int_0^\omega a(v)dv}-1},\ \beta = \frac{e^{\int_0^\omega a(v)dv}}{e^{\int_0^\omega a(v)dv}-1},$$

and

$$H_0 = \sup_{t\in[0,\omega]} H\left(t,0,0\right).$$

Remark 2.1. Thanks to Arzelà-Ascoli theorem, $\mathbb{K}$ is a compact subset of $\mathbb{X}$.

Let's begin our study with the following result, which ensures the conversion of our problem into an equivalent integral equation:

Lemma 2.2. *If the condition (2.1) holds, then $x \in \mathbb{K} \cap \mathcal{C}^1\left(\mathbb{R},\mathbb{R}\right)$ is a solution of (1.3) if and only if $x \in \mathbb{K}$ is a solution of the following integral equation:*

$$x\left(t\right) = \int_t^{t+\omega} \left[p\left(s\right)\frac{x^{[2]}(s)}{1+x^{[2]}(s)} - H\left(s,x(s),x^{[2]}(s)\right)\right] G\left(t,s\right) ds, \tag{2.5}$$

where

$$G\left(t,s\right) = \frac{e^{\displaystyle\int_t^s a(v)dv}}{e^{\displaystyle\int_0^\omega a(v)dv}-1}. \tag{2.6}$$

Remark 2.3. The function G satisfies

$$G(t+\omega, s+\omega) = G(t,s), \tag{2.7}$$

$$0 < \alpha \leq G\left(t,s\right) \leq \beta, \tag{2.8}$$

and

$$\int_{t_1}^{t_1+w} \left|G\left(t_2,s\right) - G\left(t_1,s\right)\right| ds \leq \beta w \|a\| \left|t_2 - t_1\right|. \tag{2.9}$$

Theorem 2.4. *(Schauder). Let Ω be a closed convex compact subset of a Banach space. Suppose that $\mathcal{A} : \Omega \to \Omega$ is continuous. Then there exists $z \in \Omega$ such that $z = \mathcal{A}z$.*

3 Main results

3.1 Existence

Now, to apply Schauder's fixed point theorem, we need to construct an operator $\mathcal{A} : K \to X$ as follows:

$$(\mathcal{A}\varphi)(t) = \int_t^{t+\omega} \left[p(s) \frac{\varphi^{[2]}(s)}{1+\varphi^{[2]}(s)} - H\left(s, \varphi(s), \varphi^{[2]}(s)\right) \right] G(t,s)\, ds. \tag{3.1}$$

From Lemma 2.2, fixed points of operator $\mathcal{A}$ are solutions of equation (1.3) and vice versa.

Remark 3.1. For all $t \in [0, \omega]$ and $\varphi \in K$ we have

$$(\mathcal{A}\varphi)(t+\omega) = (\mathcal{A}\varphi)(t),$$

so A is well defined.

Lemma 3.2. *If condition (2.2) holds, then operator A is continuous.*

Proof. Let $\varphi, \theta \in \mathbb{K}$, we have

$$\begin{aligned} |(\mathcal{A}\varphi)(t) - (\mathcal{A}\theta)(t)| &\le \int_t^{t+\omega} G(t,s)\, p(s) \left| \frac{\varphi^{[2]}(s)}{1+\varphi^{[2]}(s)} - \frac{\theta^{[2]}(s)}{1+\theta^{[2]}(s)} \right| ds \\ &+ \int_t^{t+\omega} G(t,s) \left| H\left(s, \varphi(s), \varphi^{[2]}(s)\right) - H\left(s, \theta(s), \theta^{[2]}(s)\right) \right| ds. \end{aligned}$$

By using (2.2), (2.8) and Lemma 2.1, [17], we obtain

$$\|\mathcal{A}\varphi - \mathcal{A}\theta\| \le \beta\omega\left((\|p\| + k_2)(1+L) + k_1 \right) \|\varphi - \theta\|.$$

Consequently, $\mathcal{A}$ is Lipschitz continuous and hence continuous. □

Lemma 3.3. *Let conditions (2.2)-(2.4) hold and suppose that*

$$p(t) \frac{\varphi^{[2]}(t)}{1+\varphi^{[2]}(t)} - H\left(s, \varphi(t), \varphi^{[2]}(t)\right) \ge 0, \tag{3.2}$$

for all $t \in [0, \omega]$ and $\varphi \in \mathbb{K}$. Then

$$\mathcal{A}(\mathbb{K}) \subset \mathbb{K}.$$

Proof.
Step 1: If $\varphi \in K$, then

$$\begin{aligned} (\mathcal{A}\varphi)(t) &= \int_t^{t+\omega} \left[p(s) \frac{\varphi^{[2]}(s)}{1+\varphi^{[2]}(s)} - H\left(s, \varphi(s), \varphi^{[2]}(s)\right) \right] G(t,s)\, ds \\ &\le \int_t^{t+\omega} p(s) \frac{\varphi^{[2]}(s)}{1+\varphi^{[2]}(s)} G(t,s)\, ds \\ &+ \int_t^{t+\omega} H\left(s, \varphi(s), \varphi^{[2]}(s)\right) G(t,s)\, ds \\ &\le \omega\beta\left(H_0 + \|p\| + (k_1 + k_2(1+L)) M \right). \end{aligned}$$

From (2.3), we obtain

$$(\mathcal{A}\varphi)(t) \leq M,$$

and from (3.2) we get

$$0 \leq (\mathcal{A}\varphi)(t).$$

Then

$$0 \leq (\mathcal{A}\varphi)(t) \leq M, \ \forall t \in [0,\omega], \ \forall \varphi \in \mathbb{K}. \tag{3.3}$$

Step 2: Let $\varphi \in K$ and $t_1, t_2 \in [0,\omega]$. Taking into account the assumptions (2.2), (2.8), (2.9) and Lemma 2.1, [17], it yields

$$\begin{aligned}
|(\mathcal{A}\varphi)(t_2) - (\mathcal{A}\varphi)(t_1)| &\leq 2\beta \left(H_0 + \|p\| + (k_1 + k_2(1+L))M\right)|t_2 - t_1| \\
&\quad + \beta\omega \|a\| \left(H_0 + \|p\| + (k_1 + k_2(1+L))M\right)|t_2 - t_1| \\
&= \beta \left(H_0 + \|p\| + (k_1 + k_2(1+L))M\right)(2 + \omega \|a\|)|t_2 - t_1|.
\end{aligned}$$

By virtue of (2.4), we get

$$|(\mathcal{A}\varphi)(t_2) - (\mathcal{A}\varphi)(t_1)| \leq L|t_2 - t_1|. \tag{3.4}$$

Thanks to (3.3) and (3.4), we find

$$\mathcal{A}(\mathbb{K}) \subset \mathbb{K},$$

which completes the proof. □

Now, we can state and prove our first existence result as follows:

Theorem 3.4. *If the assumptions (2.1)-(2.4) and (3.2) are fulfilled, then equation (1.3) has at least one positive periodic solution in* $\mathbb{K}$.

Proof. As a consequence of the compactness of $\mathbb{K}$, Lemmas 3.2 and 3.3, all conditions of Schauder's fixed point theorem are fulfilled. So, we conclude that $\mathcal{A}$ has at least one fixed point in $\mathbb{K}$ which is a solution of equation (1.3). □

3.2 Existence and Uniqueness

Theorem 3.5. *Besides the assumptions (2.1)-(2.4), we suppose that*

$$\beta\omega\left((\|p\| + k_2)(1+L) + k_1\right) < 1. \tag{3.5}$$

Then equation (1.3) has one and only one positive periodic solution $x \in \mathbb{K}$.

Proof. Similarly as in the proof of Lemmas 3.2 we have

$$\|\mathcal{A}\varphi - \mathcal{A}\theta\| \leq \beta\omega\left((\|p\| + k_2)(1+L) + k_1\right)\|\varphi - \theta\|,$$

for all $\varphi, \theta \in \mathbb{K}$.
It follows from (3.5) and the Banach fixed point theorem that $\mathcal{A}$ is a contraction and hence $\mathcal{A}$ has a unique fixed point in $\mathbb{K}$ which is the unique solution of equation (1.3). □

3.3 Continuous dependence on parameters

Theorem 3.6. *Under the hypotheses of Theorem 3.5, the unique solution of equation (1.3) depends continuously on parameters.*

Proof. Let

$$z_1(t) = \int_t^{t+\omega} \left[p_1(s) \frac{z_1^{[2]}(s)}{1+z_1^{[2]}(s)} - H_1\left(s, z_1(s), z_1^{[2]}(s)\right) \right] G_1(t,s)\, ds,$$

and

$$z_2(t) = \int_t^{t+\omega} \left[p_2(s) \frac{z_2^{[2]}(s)}{1+z_2^{[2]}(s)} - H_2\left(s, z_2(s), z_2^{[2]}(s)\right) \right] G_2(t,s)\, ds,$$

where

$$G_1(t,s) = \frac{e^{\int_t^s a_1(v)dv}}{e^{\int_0^\omega a_1(v)dv} - 1},\; G_2(t,s) = \frac{e^{\int_t^s a_2(v)dv}}{e^{\int_0^\omega a_2(v)dv} - 1},$$

are two different solutions of equation (1.3).
We have

$$\left| (G_1(t,s) - G_2(t,s))\, ds \right| \leq \mu \left\| a_1 - a_2 \right\|,$$

where

$$\mu = w^2 e^{w \max(\|a_1\|, \|a_2\|)} \left(\frac{1}{e^{\int_0^\omega a_1(v)dv} - 1} + \frac{e^{w\|a_2\|}}{\left(e^{\int_0^\omega a_1(v)dv} - 1\right)\left(e^{\int_0^\omega a_2 dv} - 1\right)} \right).$$

From (1.3) we get

$$\begin{aligned}\|z_1 - z_2\| \leq & \frac{1}{1 - \beta\omega\left(\left(\|p_2\| + k_2\right)(1+L) + k_1\right)} \left\{ \beta\omega\left(\left(\left(\|p_2\| + k_2\right)(L+1) + k_1\right)\|z_1 - z_2\|\right.\right. \\ & \left. +M\|p_1 - p_2\| + \|H_1 - H_2\|\right) + \left(H_0 + M\left(k_1 + k_2 + \|p_2\|\omega + Lk_2\right)\right)\|a_1 - a_2\| \right\}.\end{aligned}$$

This completes the proof. □

Acknowledgments

This paper has been presented in the International Conference on Mathematics and Applications (ICMA'2021), December 7-8, 2021, Blida1 University, Algeria.

Conflict of Interest

The authors have no conflicts of interest to declare.

References

[1] V. Berinde, *Existence and approximation of solutions of some first order iterative differential equations*, Miskolc Math. **11**(1) (2010), 13–26.

[2] A. Bouakkaz, A. Ardjouni and A. Djoudi, *Periodic solutions for a second order nonlinear functional differential equation with iterative terms by Schauder fixed point theorem*, Acta Math. Univ. Comen. **87**(2) (2018), 223–235.

[3] A. Bouakkaz, A. Ardjouni, R. Khemis and A. Djoudi, *Periodic solutions of a class of third-order functional differential equations with iterative source terms*, Bol. Soc. Mat. Mex. **26**(2) (2020), 443–458.

[4] A. Bouakkaz, *Bounded solutions to a three-point fourth-order iterative boundary value problem*, Rocky Mountain J. Math. **52**(3) (2022), 793–803. DOI

[5] A. Bouakkaz, *Positive periodic solutions for a class of first-order iterative differential equations with an application to a Hematopoiesis model*, Carpathian J. Math. **38**(2) (2022), 347–355.

[6] A. Bouakkaz and R. Khemis, *Positive periodic solutions for a class of second-order differential equations with state-dependent delays*, Turkish J. Math. **44**(4) (2020), 1412–1426. DOI

[7] A. Bouakkaz and R. Khemis, *Positive periodic solutions for revisited Nicholson's blowflies equation with iterative harvesting term*, J. Math. Anal. Appl. **494**(2) (2021), 124663.

[8] S. Cheraiet, A. Bouakkaz and R. Khemis, *Bounded positive solutions of an iterative three-point boundary-value problem with integral boundary conditions*, J. Appl. Math. Comput. **65**(1) (2020), 597–610.

[9] S. Chouaf, A. Bouakkaz and R. Khemis, *On bounded solutions of a second-order iterative boundary value problem*, Turkish J. Math. **46**(SI-1) (2022), 453–464.

[10] S. Chouaf, R. Khemis and A. Bouakkaz, *Some existence results on positive solutions for an iterative second-order boundary-value problem with integral boundary conditions*, Bol. Soc. Parana. Mat. (3) **4** (2022), 01–10. DOI

[11] E-R. Kaufmann, *Existence and uniqueness of solutions for asecond-order iterative boundary-value problem functional differential equation*, Electron. J. Differ. Equ. **2018**:150 (2018) (2018), 1-6. URL

[12] R. Khemis, A. Ardjouni, A. Bouakkaz and A. Djoudi, *Periodic solutions of a class of third-order differential equations with two delays depending on time and state*, Comment. Math. Univ. Carolin. **60**(3) (2019), 379–399.

[13] M. C. Mackey and L. Glass, *Oscillation and chaos in physiological control systems*, Science. **197**(4300) (1977), 287–289.

[14] E. Schröder, *Über iterate funktionen*, Math. Ann. **3** (1871), 295–322.

[15] D. Yang and W. Zhang, *Solutions of equivariance for iterative differential equations*, Appl. Math. Lett. **17**(7) (2004), 759–765.

[16] H-Y. Zhao and M. Fečkan, *Periodic solutions for a class of differential equations with delays depending on state*, Math. Commun. **23**(7) (2018), 29–42.

[17] H-Y. Zhao andJ. Liu, *Periodic solutions of an iterative functional differential equation with variable coefficients*, Math. Meth. Appl. **40** (2011), 286–292.