EXISTENCE, UNIQUENESS AND STABILITY OF SOLUTIONS TO A DELAY HEMATOPOIESIS MODEL

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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.

1. INTRODUCTION

Consider the following delay hematopoiesis model :

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

where $x(t)$ is the density of mature cells in blood circulation at time t, $a(t)$ is the rate of lost cells from the circulation, $p(t)$ is the production rate, H is the harvesting function and the delay τ describes the duration of the proliferative phase.

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.

To incorporate this biological information, we need to revisit the previous model as follows :

$$x'(t) = -a(t)x(t) + p(t)\frac{x(t-\tau(t,x(t)))}{1+x(t-\tau(t,x(t)))} - H(t,x(t),x(t-\tau(t,x(t)))). \tag{2}$$

In this work, we assume that the delay in equation (2) takes the form $\tau(t,x(t)) = t - x(t)$. Under this assumption, equation (2) becomes the following iterative differential equation :

$$x'(t) = -a(t)x(t) + p(t)\frac{x^{[2]}(t)}{1+x^{[2]}(t)} - H\left(t,x(t),x^{[2]}(t)\right), \tag{3}$$

where $x^{[2]}(t) = x(x(t))$, $a \in \mathscr{C}(\mathbb{R},(0,\infty))$, $p \in \mathscr{C}(\mathbb{R},[0,\infty))$ and $H \in \mathscr{C}\left([0,\omega]\times\mathbb{R}^2,(0,\infty)\right)$.

2. PRELIMINARIES

We set the following assumptions :

$$a(t+\omega) = a(t),\ p(t+\omega) = p(t),\ H(t+\omega,x,y) = H(t,x,y),\ \text{for all } t,x,y \in \mathbb{R}, \tag{4}$$

and

$$\left|H\left(t,x_1,y_1\right)-H\left(t,x_2,y_2\right)\right|\leq k_1\left|x_1-x_2\right|+k_2\left|y_1-y_2\right|,\ k_1,k_2>0. \tag{5}$$

For proving the existence of at least one positive periodic solution of (3), we will convert this equation into an integral one before employing the Schauder's fixed point theorem.

For $L,M>0$, let

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

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

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

and

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

Furthermore, we assume that

$$\omega\beta\left(H_0+\|p\|+\left(k_1+k_2\left(1+L\right)\right)M\right)\leq M, \tag{6}$$

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

$$\beta\left(H_0+\|p\|+\left(k_1+k_2\left(1+L\right)\right)M\right)\left(2+\omega\|a\|\right)\leq L. \tag{7}$$

We begin our study by the following result which ensures the conversion of our problem into an equivalent integral equation :

Lemma 1 *If the condition (4) holds, then $x\in\mathbb{K}$ is a solution of (3) if and only if x is a solution of the following integral equation :*

$$x\left(t\right)=\int_t^{t+\omega}\left[p\left(s\right)\frac{x^{[2]}(s)}{1+x^{[2]}(s)}-H\left(s,x(s),x^{[2]}(s)\right)\right]G\left(t,s\right)ds, \tag{8}$$

where

$$G\left(t,s\right)=\frac{e^{\int_t^s a(v)dv}}{e^{\int_0^\omega a(v)dv}-1}. \tag{9}$$

Remark 1 *Let*

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

then

$$G(t+\omega,s+\omega)=G(t,s), \tag{10}$$

$$0<\alpha\leq G\left(t,s\right)\leq\beta, \tag{11}$$

and

$$\int_{t_1}^{t_1+w}\left|G\left(t_2,s\right)-G\left(t_1,s\right)\right|ds\leq\beta w\|a\|\left|t_2-t_1\right|. \tag{12}$$

3. MAIN RESULTS

3.1. Existence

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

$$(\mathscr{A}\varphi)(t) = \int_t^{t+\omega} \left[p(s) \frac{\varphi^{[2]}(s)}{1+\varphi^{[2]}(s)} - H\left(s, \varphi(s), \varphi^{[2]}(s)\right) \right] G(t,s)\, ds. \tag{13}$$

From Lemma 1, fixed points of operator $\mathscr{A}$ are solutions of equation (3) and vice versa.

Remark 2 *For all $t \in [0, \omega]$ and $\varphi \in \mathbb{K}$ we have*

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

so $\mathscr{A}$ is well defined.

Lemma 2 *If condition (5) holds, then operator $\mathscr{A}$ is continuous.*

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

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

By using (5), (11) and [Lemma 2.1, [12]], we obtain

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

Consequently, $\mathscr{A}$ is continuous. ■

Lemma 3 *Let conditions (5)-(7) hold and suppose that*

$$p(t) \frac{\varphi^{[2]}(t)}{1+\varphi^{[2]}(t)} - H\left(s, \varphi(t), \varphi^{[2]}(t)\right) \geq 0, \ \forall t \in [0, \omega]. \tag{14}$$

Then

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

Proof.
<u>**Step 1 :**</u> If $\varphi \in \mathbb{K}$, then

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

From (6), we obtain

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

and from (14) we get

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

Then

$$0 \leq (\mathscr{A}\varphi)(t) \leq M, \ \forall t \in [0,\omega], \ \forall \varphi \in \mathbb{K}. \tag{15}$$

Step 2 : Let $\varphi \in \mathbb{K}$ and $t_1, t_2 \in [0,\omega]$. Taking into account the assumptions (5), (11), (12) and [Lemma 2.1, [12]], we arrive at

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

By virtue of (7), we get

$$|(\mathscr{A}\varphi)(t_2) - (\mathscr{A}\varphi)(t_1)| \leq L|t_2 - t_1|. \tag{16}$$

Thanks to (15) and (16), we get

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

which completes the proof. ■

Now, we can formulate our existence result as follows :

Theorem 4 *If the assumptions (4)-(7) and (14) are fulfilled, then equation (3) has at least one positive periodic solution in* $\mathbb{K}$.

Proof. As a consequence of Lemmas 2 and 3, all conditions of Schauder's fixed point theorem are staisfied. So, we conclude that $\mathscr{A}$ has at least one fixed point which is a solution of equation (3). ■

3.2. Uniqueness

Theorem 5 *Besides the assumptions (4)-(7), we suppose that*

$$\beta\omega((\|p\| + k_2)(1+L) + k_1) < 1.$$

Then equation (3) has one and only one solution $x \in \mathbb{K}$.

Proof. The proof is based on using the Banach contraction principle. ■

3.3. Continuous dependence on parameters

Theorem 6 *Under the hypothesis of Theorem 2, the unique solution of equation (3) depends continuously on parameters.*

4. REFERENCES

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