On periodic solutions of Mackey-Glass hematopoiesis model via concave and increasing operator

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Abstract. The paper is concerned with a Mackey-Glass hematopoiesis model. By employing the fixed point theorem of u_0 concave and increasing operator, we provide easily verifiable sufficient conditions for the existence of a unique positive periodic solution for the considered model. We provide numerical examples along with illustrative figures to demonstrate the theory. Our approach is new and it is different from previously considered methods.

Keywords: Mackey-Glass hematopoiesis model; Periodic solution; Concave and increasing operator.

1. Introduction

One of the most important models in field of biomathematics is the celebrated hematopoiesis model which has been introduced and thus referred to by Mackey and Glass in their pioneering paper [1]. The model deals with the physiological processes that study the regulation of hematopoiesis in which time delays play a significant role. The proposed model not only exhibits a wide range of periodic behaviors but also exposes chaotic attitude. Indeed its importance lies in the

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fact that the early detection of some diseases are associated with alterations in the periodicity of certain physiological variables [2, 3, 4, 5, 6].

Due to its widespread applications, the Mackey-Glass hematopoiesis model has been the object of many researchers who significantly contributed abundant number of papers which study its dynamic behavior. Researchers have provided their results by the help of several methods and different techniques such as the Banach contraction fixed point theorem, decreasing operator fixed point theorem, the method of Hilbert projective metric in a cone, the fixed point theory and Lyapunov functional and the Mawhin's coincidence degree theory [7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19].

In this paper, we investigate Mackey-Glass hematopoiesis model described by the the following equation

$$x'(t) = -\alpha(t)x(t) + \frac{\beta(t)x^n(t-\tau)}{1+x^n(t-\tau)},\ n \in \mathbb{R}^+, \tag{1}$$

where $\alpha \in C(\mathbb{R}, \mathbb{R})$, $\beta \in C(\mathbb{R}, \mathbb{R}^+)$, α and β are $\omega-$periodic functions with $\int_0^\omega \alpha(t)\mathrm{d}t > 0$ and τ and ω are positive constants. Here $\mathbb{R}$ indicates the set of all real numbers while $\mathbb{R}^+$ denotes the set of all positive real numbers. Due to biological reasonings, we restrict our attention to positive solutions of equation (1). The associated initial condition is $x(t) = \phi(t) > 0$, $t \in [-\tau, 0]$.

Unlike previous methods used in the literature, we employ a novel approach based on the u_0 concave and increasing operator fixed point theorem to prove the existence of a unique $\omega-$ periodic positive solution for (1). The main results are proved for the cases when $0 < n < 1$, $n = 1$ and $n > 1$. Throughout the proofs, we accommodate some easily verifiable algebraic computations to complete the steps. Numerical examples along with illustrative figures are provided to demonstrate consistency with the theory.

2. Preliminaries and essential results

In this part, we assemble some notations, fundamental definitions and lemmas which will be served as underpinning framework prior to proving the main results. Meanwhile, the u_0 concave and increasing fixed point theorem is stated.

Definition 2.1 ([20])**.** *Let X be a Banach space and P be a closed and nonempty subset of X. Then P is called a cone if*

(*i*) $x \in P$, $\lambda \geq 0$, *it implies that* $\lambda x \in P$;

(*ii*) $x \in P$ *and* $-x \in P$, *it implies that* $x = 0$.

Every cone $P \subset X$ induces an ordering in X. We define " $\leq$ " with respect to P by $x \leq y$ if and only if $y - x \in P$.

Definition 2.2 ([20])**.** *A cone P of X is called normal cone if there exists a positive constant σ such that $\|x + y\| \geq \sigma$ for any $x, y \in P$ and $\|x\| = \|y\| = 1$.*

Definition 2.3. *Let $A : P \to P$ be an operator where P is a cone of X. Then, A is said to be an increasing operator if for $y \geq x \geq 0$, it implies that $Ay \geq Ax$.*

Let $P = \{x \in X : \ x(t) \geq 0\}$ and assume that $u_0 \in P$, $u_0 > 0$, that is, u_0 is not identically vanishing. Define

$$P_{u_0} = \{x : \ x \in X, \text{ there exist } \mu_1 > 0 \text{ and } \mu_2 > 0, \text{ such that } \mu_1 u_0 \leq x(t) \leq \mu_2 u_0\}.$$

Definition 2.4 ([20])**.** *Let $A : P \to P$ and $u_0 > 0$. Then A is said to be u_0 concave operator if A satisfies:*

(*i*) *For all $x > 0$, it implies that $Ax \in P_{u_0}$;*

(*ii*) *There exists $\eta = \eta(\lambda, x) > 0$ such that $A(\lambda x) \geq \lambda[1 + \eta(\lambda, x)]Ax$, for all $x \in P_{u_0}$ and $0 < \lambda < 1$.*

Our approach is based on the following fixed point theorem of u_0 concave and increasing operator [21].

Theorem 2.1 ([21])**.** *Suppose that*

(*i*) *P is a normal cone of Banach space X, $u_0 > 0$ and the operator $A : P_{u_0} \to P_{u_0}$ is increasing;*

(*ii*) *there exists $\eta = \eta(\lambda) > 0$ such that $A(\lambda x) \geq \lambda[1+\eta(\lambda)]Ax$, for all $x \in P_{u_0}$ and $0 < \lambda < 1$.*

Then, A has a unique fixed point $x^* \in P_{u_0}$ if and only if there exist w_0 and v_0 in P_{u_0} such that $w_0 \leq Aw_0 \leq Av_0 \leq v_0$.

Remark. The fixed point x^* can be approximated by the help of an iterative scheme. That is, $x_k \to x^*$ as $k \to \infty$ where $x_k = Ax_{k-1}$, $k = 1, 2, \dots$ for any initial point $x_0 \in [w_0, v_0]$.

Let $X = \{x(t) : \ x \in C(\mathbb{R}, \mathbb{R}), \ x(t + \omega) = x(t)\}$ with the norm $\|x\| = \sup_{t\in[0,\omega]} |x(t)|$. Then, X is a Banach space.

Notations: We make use of the following notations

$$\begin{aligned} G(t, s) &= \frac{\exp\{\int_t^s \alpha(t)\xi)\mathrm{d}\xi\}}{\exp\{\int_t^s \alpha(t)\xi)\mathrm{d}\xi\} - 1}, \\ H &= [t, t + \omega], \ H_1 = \{t :\in H : \ \alpha(t) \geq 0\}, \ H_2 = \{t :\in H : \ \alpha(t) < 0\}, \\ \overline{\alpha} &= \max\{0, \alpha(t)\}, \ \underline{\alpha} = \min\{0, \alpha(t)\} \end{aligned}$$

and

$$B = \frac{\exp\{\int_0^\omega \overline{\alpha}(\xi)\mathrm{d}\xi\}}{\exp\{\int_0^\omega \alpha(t)\xi)\mathrm{d}\xi\} - 1}, m = \frac{\exp\{\int_0^\omega \underline{\alpha}(\xi)\mathrm{d}\xi\}}{\exp\{\int_0^\omega \alpha(t)\xi)\mathrm{d}\xi\} - 1}.$$

Moreover, we observe that

$$G(t,s)=\frac{\exp\{\big(\int_{[t,s]\cap H_1}\alpha(t)\xi)\mathrm{d}\xi+\int_{[t,s]\cap H_2}\alpha(t)\xi)\mathrm{d}\xi\big)\}}{\exp\{\int_0^\omega\alpha(t)\xi)\mathrm{d}\xi\}-1}$$
$$\leq\frac{\exp\{\int_{[t,s]\cap H_1}\alpha(t)\xi)\mathrm{d}\xi\}}{\exp\{\int_0^\omega\alpha(t)\xi)\mathrm{d}\xi\}-1}\leq\frac{\exp\{\int_0^\omega\overline{\alpha}(\xi)\mathrm{d}\xi\}}{\exp\{\int_0^\omega\alpha(t)\xi)\mathrm{d}\xi\}-1}=B,$$

and

$$G(t,s)\geq\frac{\exp\{\int_{[t,s]\cap H_2}\alpha(t)\xi)\mathrm{d}\xi\}}{\exp\{\int_0^\omega\alpha(t)\xi)\mathrm{d}\xi\}-1}\geq\frac{\exp\{\int_0^\omega\underline{\alpha}(\xi)\mathrm{d}\xi\}}{\exp\{\int_0^\omega\alpha(t)\xi)\mathrm{d}\xi\}-1}=m.$$

Therefore, we conclude that $0<m\leq G(t,s)\leq B$, $s\in[t,t+\omega]$.

It is easy to verify that x is the $\omega-$periodic solution of equation (1) if and only if x is the $\omega-$periodic solution of the integral equation

$$x(t)=\int_t^{t+\omega}G(t,s)\frac{\beta(s)x^n(s-\tau)}{1+x^n(s-\tau)}\mathrm{d}s.$$

We define the operator $A:X\to X$ by

$$(Ax)(t)=\int_t^{t+\omega}G(t,s)\frac{\beta(s)x^n(s-\tau)}{1+x^n(s-\tau)}\mathrm{d}s.$$

Clearly, $x\in C(\mathbb{R},\mathbb{R})$ is the the $\omega-$periodic solution of equation (1) if and only if x is the fixed point of the operator A.

We refer to β^- and β^+ as follows:

$$\beta^-=\min_{t\in[0,\omega]}\{\beta(t)\}\ \text{ and }\ \beta^+=\max_{t\in[0,\omega]}\{\beta(t)\}.$$

Let $f(x)=\frac{x^n}{1+x^n}$ and $g(x)=\frac{1}{\beta^-m\omega}x$. In order to prove the main results, we first consider the existence of roots for the algebraic equation $\frac{c^n}{1+c^n}=\frac{1}{\beta^-m\omega}c$. We discuss this in the following three lemmas whose proofs are entirely based on calculus background.

Lemma 2.1. *Let $0<n<1$. Then there exists a unique positive constant $c>0$ such that $\frac{c^n}{1+c^n}=\frac{1}{\beta^-mw}c$.*

Proof. Since $0<n<1$, we have $f'(x)=\frac{n}{x^{1-n}(1+x^n)^2}$, $\lim_{x\to0^+}f'(x)=+\infty$, $\lim_{x\to\infty}f(x)=1$ and $f''(x)=\frac{nx^{n-2}[n-1-(n+1)x^n]}{(1+x^n)^3}<0$ for $x\in(0,+\infty)$. Then, the curve of $f(x)$ is convex on $(0,+\infty)$. We conclude that the curve of f and the straight line g has a unique intersection point on $(0,+\infty)$. Thus, there exists a unique positive constant $c>0$ such that $\frac{c^n}{1+c^n}=\frac{1}{\beta^-mw}c$. □

Lemma 2.2. *Let $n=1$, and $\frac{1}{\beta^-mw}<1$. Then there exists a unique positive constant $c>0$ such that $\frac{c^n}{1+c^n}=\frac{1}{\beta^-mw}c$.*

Proof. Since $n = 1$, we have $f'(x) = \frac{1}{(1+x^n)^2}$, $f'(0) = 1$, $\lim_{x\to\infty} f(x) = 1$ and $f''(x) = \frac{-2}{(1+x)^2} < 0$, for $x \in (0, +\infty)$. Then, the curve of $f(x)$ is convex on $(0, +\infty)$. From the assumption $\frac{1}{\beta^- mw} < 1$, we know the curve of f and the straight line g has a unique intersection point on $(0, +\infty)$. Thus, there exists a unique positive constant $c > 0$ such that $\frac{c^n}{1+c^n} = \frac{1}{\beta^- mw} c$. □

Lemma 2.3. *Let $n > 1$, and $\frac{1}{\beta^- m\omega} \leq \frac{\frac{n-1}{2n}}{\sqrt[n]{\frac{n-1}{n+1}}}$. Then there exists a unique positive constant $c > 0$ such that $\frac{c^n}{1+c^n} = \frac{1}{\beta^- m\omega} c$.*

Proof. Since $n > 1$, we have $f''(x) = \frac{nx^{n-2}[n-1-(n+1)x^n]}{(1+x^n)^3}$. Thus, $f''(x) > 0$ for $0 < x < \sqrt[n]{\frac{n-1}{n+1}}$ and $f''(x) < 0$ for $x > \sqrt[n]{\frac{n-1}{n+1}}$. Then, the curve of $f(x)$ is convex on $(\sqrt[n]{\frac{n-1}{n+1}}, +\infty)$, and concave on $(0, \sqrt[n]{\frac{n-1}{n+1}})$. Moreover, $f'(0) = 0$, $\lim_{x\to\infty} f(x) = 1$ and $f(\sqrt[n]{\frac{n-1}{n+1}}) = \frac{n-1}{2n}$. By the assumption $\frac{1}{\beta^- mw} \leq \frac{\frac{n-1}{2n}}{\sqrt[n]{\frac{n-1}{n+1}}}$, it is clear that the curve of f and the straight line g has at least one intersection point on $(0, +\infty)$. Thus, the desired conclusion holds. □

3. Existence results

The existence of a unique positive periodic solution for equation (1) is discussed in this section. We prove the main results by the help of Theorem 2.1.

Theorem 3.1. *Let $0 < n < 1$. Then equation (1) has a unique $\omega-$periodic positive solution.*

Proof. Let $X = \{x(t) : x \in C(\mathbb{R}, \mathbb{R}), x(t + \omega) = x(t)\}$ with the norm $\|x\| = \sup_{t\in[0,\omega]} |x(t)|$, then X is a Banach space. Define $P = \{x \in X : x(t) \geq 0\}$, then P is a normal cone of the Banach space X. Let $u_0 = 1$ then $P_{u_0} = \{x : x \in X$, there exist $\mu_1 > 0$ and $\mu_2 > 0$, such that $\mu_1 \leq x(t) \leq \mu_2\}$. Thus, we have

$$(Ax)(t) = \int_t^{t+\omega} G(t,s) \frac{\beta(s)x^n(s-\tau)}{1 + x^n(s-\tau)} ds \leq \int_t^{t+\omega} G(t,s)\beta(s) ds \leq \beta^+ B\omega$$

and

$$\begin{aligned}(Ax)(t) &= \int_t^{t+\omega} G(t,s) \frac{\beta(s)x^n(s-\tau)}{1 + x^n(s-\tau)} ds \geq \int_t^{t+\omega} G(t,s)\beta(s) \frac{\mu_1^n}{1+\mu_1^n} ds \\ &\geq mb^- B\omega \frac{\mu_1^n}{1+\mu_1^n}.\end{aligned}$$

The above two inequalities yield $m\beta^- B\omega \frac{\mu_1^n}{1+\mu_1^n} \leq (Ax)(t) \leq \beta^+ B\omega$, which implies that $Ax \in P_{u_0}$. Therefore, we get $A : P_{u_0} \to P_{u_0}$. In addition, it is clear that A is an increasing operator.

For all $x \in P_{u_0}$, there exists $\mu_1 > 0$ and $\mu_2 > 0$ such that $\mu_1 \leq x(t) \leq \mu_2$. Let $0 < \lambda < 1$, then

$$\begin{aligned} A(\lambda x)(t) &= \int_t^{t+\omega} G(t,s)\frac{\beta(s)\lambda^n x^n(s-\tau)}{1+\lambda^n x^n(s-\tau)}ds \\ &= \int_t^{t+\omega} G(t,s)\frac{\beta(s)x^n(s-\tau)}{1+x^n(s-\tau)}.\frac{\lambda^n[1+x^n(s-\tau)]}{1+\lambda^n x^n(s-\tau)}ds. \end{aligned} \tag{2}$$

However, we observe that $\frac{\lambda^n[1+x^n(s-\tau)]}{1+\lambda^n x^n(s-\tau)} = 1 + \frac{\lambda^n - 1}{1+\lambda^n x^n(s-\tau)} \geq 1 + \frac{\lambda^n-1}{1+\lambda^n\mu_1^n} = \frac{\lambda^n(1+\mu_1^n)}{1+\lambda^n\mu_1^n}$. It follows from (2) that

$$\begin{aligned} A(\lambda x)(t) &\geq \int_t^{t+\omega} G(t,s)\frac{\beta(s)\lambda^n x^n(s-\tau)}{1+x^n(s-\tau)}\frac{\lambda^n(1+\mu_1^n)}{1+\lambda^n\mu_1^n}ds \\ &= \lambda\frac{\lambda^{n-1}(1+\mu_1^n)}{1+\lambda^n\mu_1^n}\int_t^{t+\omega} G(t,s)\frac{\beta(s)x^n(s-\tau)}{1+x^n(s-\tau)}ds \\ &= \lambda\Big(1+\frac{\lambda^{n-1}+\lambda^{n-1}\mu_1^n - 1 - \lambda^n\mu_1^n}{1+\lambda^n\mu_1^n}\Big)Ax(t) = \lambda(1+\eta)Ax(t), \end{aligned}$$

in which $\eta := \eta(\lambda) = \frac{\lambda^{n-1}+\lambda^{n-1}\mu_1^n-1-\lambda^n\mu_1^n}{1+\lambda^n\mu_1^n}$. Consider the function $h(x) = x^{n-1} + x^{n-1}\mu_1^n - 1 - \lambda^n\mu_1^n$. It follows that $h'(x) = x^{n-2}[n-1+(n-1)\mu_1^n - nx\mu_1^n]$, and thus $h'(x) < 0$ for $x \in (0,+\infty)$, which means that $h(x)$ is decreasing on $(0,+\infty)$. So we have $h(\lambda) > h(1) = 0$. From this, we conclude that $\eta(\lambda) > 0$.

By Lemma 2.1, there exists a unique positive constant $c > 0$ such that $\frac{c^n}{1+c^n} = \frac{1}{\beta^- mw}c$. Let

$$w_0 = \int_t^{t+\omega} G(t,s)\frac{\beta(s)c^n}{1+c^n}ds, v_0 = \int_t^{t+\omega} G(t,s)\beta(s)ds.$$

Then, $w_0 < v_0$, thus we have $Aw_0 < Av_0$. From this, we deduce that

$$\begin{aligned} w_0 &\leq \int_t^{t+\omega} G(t,s)\beta(s)ds \leq \beta^+ B\omega, \\ w_0 &\geq \int_t^{t+\omega} m\beta^- \frac{c_n}{1+c^n}ds = \omega m\beta^- \frac{c_n}{1+c^n} = c, \end{aligned}$$

and

$$\begin{aligned} v_0 &\leq \int_t^{t+\omega} B\beta^+ ds = B\beta^+\omega, \\ v_0 &\geq \int_t^{t+\omega} m\beta^- ds = \omega m\beta^- > \frac{c_n}{1+c^n}\omega m\beta^- = c. \end{aligned}$$

Hence, we obtain that

$$w_0(t) \leq Aw_0(t) < Av_0(t) < v_0(t).$$

By Theorem 2.1, the operator A has a unique fixed point $x^* \in P_{u_0}$, which means that equation (1) has a unique $\omega-$periodic positive solution x^*. The proof is complete. □

By the help of Lemma 2.2 and Lemma 2.3, we can prove the following theorems by applying the same arguments done in the proof of Theorem 3.1.

Theorem 3.2. *Let $n = 1$, and $\frac{1}{\beta^- mw} < 1$. Then equation (1) has a unique $\omega-$ periodic positive solution.*

Theorem 3.3. *Let $n > 1$, and $\frac{1}{\beta^- m\omega} \leq \frac{\frac{n-1}{2n}}{\sqrt[n]{\frac{n-1}{n+1}}}$. Then equation (1) has a unique $\omega-$ periodic positive solution.*

4. Illustrative examples

Example 1. For $n = \frac{1}{2}$, consider the equation

$$x'(t) = -(0.5 + \sin(2t))x(t) + \frac{650\,(1.2 + \cos(2t))x^{\frac{1}{2}}(t-2)}{1 + x^{\frac{1}{2}}(t-2)}, \tag{3}$$

where the initial condition can be defined as $x(t) = 5t$ on $[-2, 0]$. The parameters $0.5 + \sin(2t)$ and $650(1.2 + \cos(2t))$ are $\pi-$periodic continuous functions on $\mathbb{R}$. It is clear that $\int_0^\pi (0.5 + \sin(2t))dt = \frac{\pi}{2} > 0$. By the conclusion of Theorem 3.1, equation (3) has a unique $\pi-$periodic solution. Figure 1 illustrates the the solution behavior of equation (3).

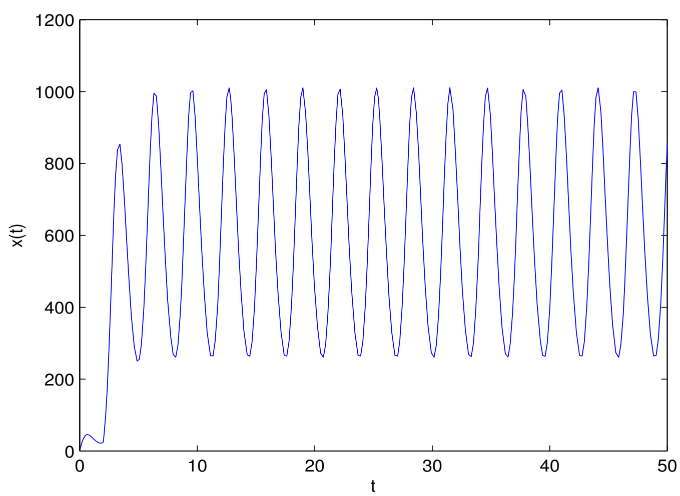

Figure 1: Behavior of the solution of Example 1 for the case $n = 0.5$.

Example 2. For $n = 1$, consider the equation

$$x'(t) = -(1+\sin(2t))x(t) + \frac{700\,(1.5+\cos(2t))x(t-3\pi)}{1+x(t-3\pi)}, \tag{4}$$

where the initial condition can be defined as $x(t) = \frac{t}{4}$ on $[-3\pi, 0]$. One can easily see that the parameters $1+\sin(2t)$ and $700(1.5+\cos(2t))$ are $\pi-$periodic continuous functions on $\mathbb{R}$ and the integral $\int_0^\pi (1+\sin(2t))dt = \pi > 0$. Besides, the assumption $\frac{1}{\beta^- mw} < 1$ is preserved since $m = \frac{1}{e^\pi - 1}$, $\omega = \pi$ and $\beta^- = 350$. By the conclusion of Theorem 3.2, equation (4) has a unique $\pi-$periodic solution which is described in the following figure.

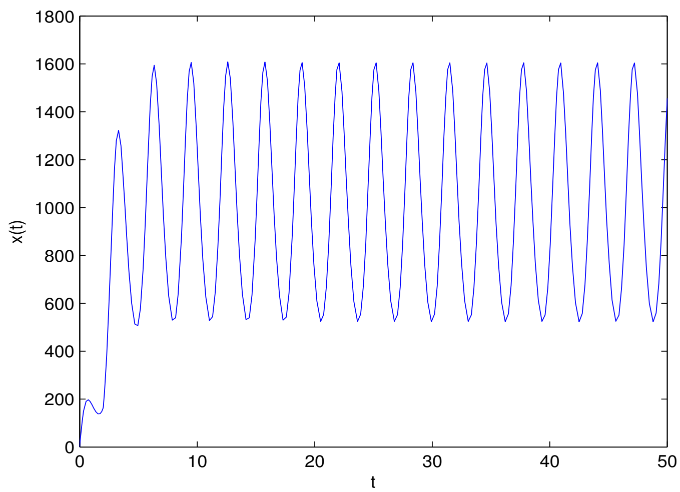

Figure 2: Behavior of the solution of Example 2 for the case $n = 1$.

Example 3. For $n = 3$, consider the equation

$$x'(t) = -(1+\sin(2t))x(t) + \frac{600\,(1.1+\cos(2t))x^3(t-5.82)}{1+x^3(t-5.82)}, \tag{5}$$

where the initial condition can be chosen as $x(t) = |t|$ on $[-5.82, 0]$. The assumptions of Theorem 3.3 are clearly satisfied. Moreover, that $\frac{1}{\beta^- m\omega} \leq \frac{\frac{n-1}{2n}}{\sqrt[n]{\frac{n-1}{n+1}}}$ holds since $n = 3$, $m = \frac{1}{e^\pi - 1}$, $\omega = \pi$ and $\beta^- = 60$. Therefore, Theorem 3.3 guarantees the existence of a unique $\pi-$periodic solution for equation (5). Figure 3 depicts the solution behavior.

Conclusion

In this paper, we prove the existence and uniqueness of $\omega-$periodic positive solution of a Mackey-Glass hematopoiesis model. Different from the methods

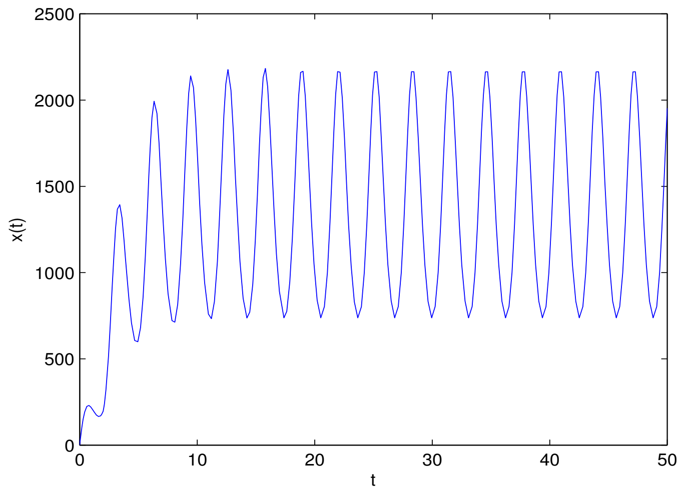

Figure 3: Behavior of the solution of Example 3 for the case $n = 3$.

used in the previous works, easily variable technique is utilized to prove the main results. We conclude here some features that make this research distinctive:

1. The proofs of the main results are given by the help of a novel approach depending on u_0 concave and increasing operator fixed point theorem that has not been employed before.

2. The main theorems exhibit that the periodic coefficients of the addressed model admit a unique positive periodic solution without additional restrictions.

3. The provided examples are illustrative and demonstrate consistency to the theoretical findings.

The approach employed in this paper can be used to prove existence results for more general population models.

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