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# Existence of Three Nonnegative Periodic Solutions for Functional Differential Equations and Applications to Hematopoiesis 

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#### Abstract

Using the Leggett-Wiliams fixed point theorem, we show the existence of at least three solutions to a system of first-order nonlinear functional differential equations. These solutions have non-negative components which makes them suitable for hematopoiesis models. AMS (MOS) Subject Classification: 34C25, 34K13 Key words: Periodic solutions; functional differential equation.


## 1 Introduction

We prove the existence of at least three periodic solutions, with nonnegative components, to the system of differential equations

$$
\begin{equation*}
\left.u^{\prime}(t)=A(t, u) u(t)+\lambda f\left(t, u_{t}\right)\right) \tag{1.1}
\end{equation*}
$$

Here $A$ is a diagonal $n \times n$ matrix whose entries depend on $t$ and on the unknown function $u=\left(u_{1}, u_{2}, \ldots, u_{n}\right)^{T}$. We assume that the diagonal entries $a_{i}(t, u) \in C(\mathbb{R}, \mathbb{R})$ are periodic in

[^0]$t$, with a common period $T$ ( $T$-periodic for short). The parameter $\lambda$ is positive and assumed to be known, or at least its range. The function $f=\left(f_{1}, f_{2}, \ldots, f_{n}\right)^{T}$ has each component in $C(\mathbb{R}, \mathbb{R})$ and is $T$-periodic whenever $u$ is $T$-periodic. Here $u_{t}$ denotes a functional that depends on $t$ and satisfies the conditions stated below. Typical examples of such functionals are evaluations $u(h(t))$, and memory terms $\int_{-\infty}^{t} k(s) u(s) d s$.

The above system includes the scalar differential equations

$$
\begin{gathered}
u^{\prime}(t)=a(t) g(u) u(t)-\lambda b(t) f(t, u(t-\tau)), \\
u^{\prime}(t)=\mp a(t) u(t) \pm \lambda f(t, u(t-\tau))
\end{gathered}
$$

that have been studied by several authors $[1,2,11,14]$. For $A(t, u)=A(t)$ in (1.1), Jiang et al [3] proved the existence and non-existence of a nonnegative periodic solution. Zhang et al [14] used Krasnoselskii fixed point theorem to show the existence of two solutions for the above equation. Padhi et al [8] obtained the existence of three nonnegative periodic solutions to the scalar equation

$$
\begin{equation*}
u^{\prime}(t)=-a(t) u(t)-\lambda b(t) f(t, u(h(t))) \tag{1.2}
\end{equation*}
$$

Motivated by these studies, we set up (1.1) to include all of the above equations, and show the existence of three nonnegative periodic solutions.

## 2 Preliminaries

All functions in this article are assumed to be in the space of continuous functions, equipped the supremum norm $\|u\|=\max _{1 \leq i \leq n} \sup _{t}\left|u_{i}(t)\right|$. We shall use the following as general assumptions throughout this paper.
(A1) There exist continuous $T$-periodic functions $b, c$ such that $0 \leq b(t) \leq\left|a_{i}(t, u)\right| \leq c(t)$ for $1 \leq i \leq n$ and all $T$-periodic functions $u$. Furthermore, $\int_{0}^{T} b(t) d t>0$.
(A2) $f_{i}\left(t, u_{t}\right) \int_{0}^{T} a_{i}\left(s, u_{s}\right) d s \leq 0$ for $1 \leq i \leq n$ and $0 \leq t \leq T$.
(A3) $f\left(t, u_{t}\right)$ is a continuous function of $u$, when $u$ is bounded and continuous; i.e., for each $\epsilon>0$ there exists $\delta>0$ such that $\|\phi-\psi\|<\delta$ implies $\left\|f\left(t, \phi_{t}\right)-f\left(t, \psi_{t}\right)\right\|<\epsilon$.
From the periodicity of the solution and the assumption that $u$ is known in the non-linear parts of (1.1), we can construct a Green's kernel. In fact the solutions of (1.1) satisfy the integral equation

$$
u(t)=\lambda \int_{t}^{t+T} G(t, s) f\left(s, u_{s}\right) d s
$$

where $G(t, s)$ is a diagonal matrix of entries

$$
G_{i}(t, s)=\frac{\exp \left(\int_{s}^{t} a_{i}\left(\theta, u_{\theta}\right) d \theta\right)}{\exp \left(-\int_{0}^{T} a_{i}\left(\theta, u_{\theta}\right) d \theta\right)-1}
$$

These entries are bounded as follows:

$$
\begin{equation*}
\alpha:=\frac{\exp \left(-\int_{0}^{T} c(\theta) d \theta\right)}{\exp \left(-\int_{0}^{T} b(\theta) d \theta\right)-1} \leq\left|G_{i}(t, s)\right| \leq \frac{\exp \left(\int_{0}^{T} c(\theta) d \theta\right)}{\exp \left(-\int_{0}^{T} c(\theta) d \theta\right)-1}=: \beta \tag{2.1}
\end{equation*}
$$

Note that $G(t, s)$ is $T$-periodic in both variables and that $G_{i}$ and $\int_{0}^{T} a_{i}$ have opposite signs. Therefore, by (A2), $f_{i}$ and $G_{i}$ have the same sign.

The following concept will be used in the statement of the Leggett-Williams fixed point theorem. Let $E$ be a Banach space and $K$ be a cone in $E$. A mapping $\psi$ is said to be a concave nonnegative continuous functional on $K$ if $\psi: K \rightarrow[0, \infty)$ is continuous and

$$
\psi(\mu x+(1-\mu) y) \geq \mu \psi(x)+(1-\mu) \psi(y), \quad x, y \in K, \mu \in[0,1] .
$$

Let $c_{1}, c_{2}, c_{3}$ be positive constants. With $K$ and $E$ as defined above, we define

$$
K_{c_{1}}=\left\{y \in K:\|y\|<c_{1}\right\}, \quad K\left(\psi, c_{2}, c_{3}\right)=\left\{y \in K: c_{2} \leq \psi(y),\|y\|<c_{3}\right\}
$$

Theorem 2.1 (Leggett-Williams fixed point theorem [5]). Let $(E,\|\cdot\|)$ be a $B a$ nach space and $K \subset E$ a cone, and $c_{4}$ a positive constant. Suppose there exists a concave nonnegative continuous functional $\psi$ on $K$ with $\psi(u) \leq\|u\|$ for $u \in \bar{K}_{c_{4}}$ and let $A: \bar{K}_{c_{4}} \rightarrow \bar{K}_{c_{4}}$ be a completely continuous mapping. Assume that there are numbers $c_{1}, c_{2}, c_{3}, c_{4}$ with $0<c_{1}<c_{2}<c_{3} \leq c_{4}$ such that
(i) $\left\{u \in K\left(\psi, c_{2}, c_{3}\right): \psi(u)>c_{2}\right\} \neq \phi$, and $\psi(A u)>c_{2}$ for all $u \in K\left(\psi, c_{2}, c_{3}\right)$;
(ii) $\|A u\|<c_{1}$ for all $u \in \bar{K}_{c_{1}}$;
(iii) $\psi(A u)>c_{2}$ for all $u \in K\left(\psi, c_{2}, c_{4}\right)$ with $\|A u\|>c_{3}$.

Then $A$ has at least three fixed points $u_{1}, u_{2}, u_{3}$ in $\bar{K}_{c_{4}}$. Furthermore, $\left\|u_{1}\right\| \leq c_{1}<\left\|u_{2}\right\|$, and $\psi\left(u_{2}\right)<c_{2}<\psi\left(u_{3}\right)$.

In this article, let $E$ be the set of continuous $T$-periodic functions, which forms a Banach space under the norm $\|u\|=\max _{1 \leq i \leq n} \sup _{0 \leq t \leq T}\left|u_{i}(t)\right|$. Then we define the operator $A$ on $E$ by

$$
(A u)(t)=\lambda \int_{t}^{t+T} G(t, s) f\left(s, u_{s}\right) d s
$$

Recall that by (A2), the functions $G_{i}$ and $f_{i}$ have the same sign so that $A u_{i}$ is non-negative. Furthermore,

$$
\left(A u_{i}\right)(t)=\lambda \int_{t}^{t+T}\left|G_{i}(t, s) \| f_{i}\left(s, u_{s}\right)\right| d s \leq \lambda \beta \int_{0}^{T}\left|f_{i}\left(s, u_{s}\right)\right| d s
$$

Taking the supremum on $t$,

$$
\left\|\left(A u_{i}\right)(t)\right\| \leq \lambda \beta \int_{0}^{T}\left|f_{i}\left(s, u_{s}\right)\right| d s
$$

Also we have

$$
\left(A u_{i}\right)(t) \geq \lambda \alpha \int_{0}^{T}\left|f_{i}\left(s, u_{s}\right)\right| d s
$$

Combining the two inequalities above,

$$
\begin{equation*}
\left(A u_{i}\right)(t) \geq \frac{\alpha}{\beta}\left\|\left(A u_{i}\right)(t)\right\| \tag{2.2}
\end{equation*}
$$

Motivated by this inequality, we define the cone $K$ in $E$ as

$$
K=\left\{u \in E: u_{i}(t) \geq \frac{\alpha}{\beta}\left\|u_{i}\right\|, \text { for } t \in[0, T] \text { and } 1 \leq i \leq n\right\}
$$

so that $A(K) \subset K$. From assumptions (A1)-(A3), it is also clear that $A$ is a completely continuous operator on $K$; see [4, Lemma 2.3]. Furthermore the existence of solutions of (1.1), with nonnegative components, is equivalent to the existence of fixed points for $A$ in $K$. On the cone $K$, we define concave functional

$$
\psi(u)=\min _{1 \leq i \leq n} \inf _{0 \leq t \leq T} u_{i}(t)
$$

## 3 Main results

To prove our main result, we state the following conditions in terms of the bounds $\alpha$ and $\beta$ defined by (2.1).
(H1) There exists a positive constant $c_{1}$ such that

$$
\begin{equation*}
\lambda \beta \int_{0}^{T}\left|f_{i}\left(t, u_{t}\right)\right| d t<c_{1} \quad \text { for } 1 \leq i \leq n \text { and } u \in K \text { with }\|u\| \leq c_{1} \tag{3.1}
\end{equation*}
$$

(H2) There exists a positive constant $c_{2}>c_{1}$ such that

$$
\begin{equation*}
c_{2}<\lambda \alpha \int_{0}^{T}\left|f_{i}\left(t, u_{t}\right)\right| d t \quad \text { for } 1 \leq i \leq n \text { and } u \in K \text { with } c_{2} \leq\|u\| \leq \beta c_{2} / \alpha \tag{3.2}
\end{equation*}
$$

(H3) There exists a constant $c_{4} \geq \beta c_{2} / \alpha=: c_{3}$ such that

$$
\begin{equation*}
\lambda \beta \int_{0}^{T}\left|f_{i}\left(t, u_{t}\right)\right| d t \leq c_{4} \quad \text { for } 1 \leq i \leq n \text { and } u \in K \text { with }\|u\| \leq c_{4} \tag{3.3}
\end{equation*}
$$

Theorem 3.1. Assuming (H1)-(H3), the conditions for the Leggett-Williams theorem are satisfied and therefore (1.1) has at least three nonnegative periodic solutions.

Proof. First we show that $A$ maps $\bar{K}_{c_{4}}$ into $\bar{K}_{c_{4}}$. For $u$ in $\bar{K}_{c_{4}}$, using (2.1) and (3.3), we have

$$
\left\|A u_{i}\right\| \leq \lambda \int_{t}^{t+T}\left|G_{i}(t, s) \| f_{i}\left(s, u_{s}\right)\right| d s \leq \lambda \beta \int_{0}^{T}\left|f_{i}\left(s, u_{s}\right)\right| d s \leq c_{4}
$$

which proves that $A\left(\bar{K}_{c_{4}}\right) \subset \bar{K}_{c_{4}}$. Now, we prove (i) in Theorem 2.1. The set $\{u \in$ $\left.K\left(\psi, c_{2}, c_{3}\right): \psi(u)>c_{2}\right\}$ is not empty because the constant function $u_{i}(t)=\left(c_{2}+c_{3}\right) / 2$ is in this set. For each function $u$ in $K\left(\psi, c_{2}, c_{3}\right)$, we have $c_{2} \leq\|u\| \leq c_{3}=\beta c_{2} / \alpha$. Then using the definition of $\psi$, that $G_{i}$ and $f_{i}$ have the same sign, (2.1), and (3.2), we have

$$
\psi(A u)=\min _{i} \inf _{t} \lambda \int_{t}^{t+T}\left|G_{i}(t, s)\right|\left|f_{i}\left(s, u_{s}\right)\right| d s \geq \min _{i} \lambda \alpha \int_{0}^{T}\left|f_{i}\left(s, u_{s}\right)\right| d s>c_{2}
$$

which implies (i). Now, we prove (ii) in Theorem 2.1. For $u$ in $\bar{K}_{c_{1}}$, using (2.1) and (3.1), we have

$$
\left\|A u_{i}\right\| \leq \lambda \int_{t}^{t+T}\left|G_{i}(t, s) \| f_{i}\left(s, u_{s}\right)\right| d s \leq \lambda \beta \int_{0}^{T}\left|f_{i}\left(s, u_{s}\right)\right| d s<c_{1}
$$

which proves (ii). Now, we prove (iii) in Theorem 2.1. From the definition of $\psi$ and (2.1),

$$
\psi(A u)=\min _{i} \inf _{t} \lambda \int_{t}^{t+T}\left|G_{i}(t, s)\right|\left|f_{i}\left(s, u_{s}\right)\right| d s \geq \min _{i} \lambda \alpha \int_{0}^{T}\left|f_{i}\left(s, u_{s}\right)\right| d s
$$

From $\|A u\|>c_{3}=\beta c_{2} / \alpha$ and (2.1), we have

$$
c_{3}<\left\|A u_{i}\right\| \leq \lambda \beta \int_{0}^{T}\left|f_{i}\left(s, u_{s}\right)\right| d s
$$

Combining the two inequalities above, $\psi(A u)>c_{2}$, which proves (iii). Once the conditions for the Leggett-Williams theorem are satisfied, the operator $A$ has at least three fixed points that correspond to solutions of (1.1).

## Related results

Several versions of Theorem 3.1 can be stated (and have been stated for particular cases) using the following four lemmas.

Lemma 3.2. Condition (3.1) in (H1) is implied by

$$
\beta \lambda \limsup _{\|u\| \rightarrow 0} \int_{0}^{T}\left|f_{i}\left(t, u_{t}\right)\right| d t /\|u\|<1, \quad \forall i
$$

In turn, this condition is implied by

$$
\beta \lambda T \limsup _{\|u\| \rightarrow 0} \max _{0 \leq t \leq T}\left|f_{i}\left(t, u_{t}\right)\right| /\|u\|<1, \quad \forall i
$$

Proof. From the definition of limit superior, for each $0<\epsilon<1$, there exists a $\delta>0$ such that

$$
\beta \lambda \int_{0}^{T}\left|f_{i}\left(t, u_{t}\right)\right| d t<\epsilon\|u\| \quad \text { for }\|u\|<\delta, \quad \forall i
$$

Select $c_{1}<\delta$. Then for $u$ in $\bar{K}_{c_{1}}$,

$$
\beta \lambda \int_{0}^{T}\left|f_{i}\left(t, u_{t}\right)\right| d t<\epsilon\|u\|<\|u\| \leq c_{1}, \quad \forall i
$$

which implies (3.1).
Lemma 3.3. Condition (3.2) in (H2) is implied by

$$
c_{2}<\lambda \alpha T\left|f_{i}\left(t, u_{t}\right)\right| \quad \text { for } t \in[0, T], \forall i, u \in K \text { with } c_{2} \leq\|u\| \leq \beta c_{2} / \alpha
$$

Lemma 3.4. Condition (3.3) in (H3) is implied by

$$
\beta \lambda \limsup _{\|u\| \rightarrow \infty} \int_{0}^{T}\left|f\left(t, u_{t}\right)\right| d t /\|u\|<1, \quad \forall i
$$

In turn, this condition is implied by

$$
\beta \lambda T \limsup _{\|u\| \rightarrow \infty} \max _{0 \leq t \leq T}\left|f\left(t, u_{t}\right)\right| /\|u\|<1, \quad \forall i
$$

Proof. From the definition of limit superior, there exist positive constants $\epsilon<1$ and $\delta>0$ such that

$$
\beta \lambda \int_{0}^{T}\left|f\left(t, u_{t}\right)\right| d t<\epsilon\|u\| \quad \text { for }\|u\| \geq \delta, \quad \forall i
$$

From (A3), when $\|u\| \leq \delta, \beta \lambda \int_{0}^{T}\left\|f\left(t, u_{t}\right)\right\|$ is bounded by a positive constant $r$. Select $c_{4}=r /(1-\epsilon)$. Then for $u$ in $\bar{K}_{c_{4}}$,

$$
\beta \lambda \int_{0}^{T}\left|f_{i}\left(t, u_{t}\right)\right| d t \leq \epsilon\|u\|+r \leq \epsilon c_{4}+r \leq c_{4}
$$

which implies (H3).
When we know only the range of $\lambda$, rather than its value, Hypotheses (H1)-(H3) need to be modified as follows.

Theorem 3.5. When $\lambda_{1} \leq \lambda \leq \lambda_{2}$, Theorem 3.1 remains valid if we replace (3.1)-(3.3), respectively, by

$$
\begin{gather*}
\lambda_{2} \beta \int_{0}^{T}\left|f_{i}\left(t, u_{t}\right)\right| d t<c_{1} \quad \text { for } 1 \leq i \leq n \text { and } u \in K \text { with }\|u\| \leq c_{1}  \tag{3.4}\\
c_{2}<\lambda_{1} \alpha \int_{0}^{T}\left|f_{i}\left(t, u_{t}\right)\right| d t \quad \text { for } u \in K \text { with } c_{2} \leq\|u\| \leq \beta c_{2} / \alpha  \tag{3.5}\\
\lambda_{2} \beta \int_{0}^{T}\left|f_{i}\left(t, u_{t}\right)\right| d t \leq c_{4} \quad \text { for } 1 \leq i \leq n \text { and } u \in K \text { with }\|u\| \leq c_{4} \tag{3.6}
\end{gather*}
$$

Table 1 shows some choices of $\lambda_{1}$ and $\lambda_{2}$ found in the indicated references.

Table 1: Hypotheses when $\lambda_{1} \leq \lambda \leq \lambda_{2}$

| Theorem 3.5 | Ref. [8] | Ref. [8] | Ref. [8] |  |
| :---: | :---: | :---: | :---: | :---: |
| $\lambda_{1} \leq \lambda \leq \lambda_{2}$ | $\frac{1}{2 \beta} \leq \lambda \leq \frac{1}{\beta}$ | $\frac{\alpha}{\beta} \leq \lambda \leq 1$ | $1 \leq \lambda \leq \beta$ | $\frac{1}{2 T} \leq \lambda \leq \frac{1}{T}$ |
| $(3.4)$ | $\int_{0}^{T}\left\|f_{i}\right\|<c_{1}$ | $\beta \int_{0}^{T}\left\|f_{i}\right\|<c_{1}$ | $\beta^{2} \int_{0}^{T}\left\|f_{i}\right\|<c_{1}$ | $\frac{\beta}{T} \int_{0}^{T}\left\|f_{i}\right\|<c_{1}$ |
| $(3.5)$ | $c_{2}<\frac{\alpha}{2 \beta} \int_{0}^{T}\left\|f_{i}\right\|$ | $c_{2}<\frac{\alpha^{2}}{\beta} \int_{0}^{T}\left\|f_{i}\right\|$ | $c_{2}<\alpha \int_{0}^{T}\left\|f_{i}\right\|$ | $c_{2}<\frac{\alpha}{2 T} \int_{0}^{T}\left\|f_{i}\right\|$ |
| $(3.6)$ | $\int_{0}^{T}\left\|f_{i}\right\| \leq c_{4}$ | $\beta \int_{0}^{T}\left\|f_{i}\right\| \leq c_{4}$ | $\beta^{2} \int_{0}^{T}\left\|f_{i}\right\| \leq c_{4}$ | $\frac{\beta}{T} \int_{0}^{T}\left\|f_{i}\right\| \leq c_{4}$ |

## 4 Applications

As a particular case of (1.1), we have the scalar equation

$$
\begin{equation*}
u^{\prime}(t)=-\gamma(t) u(t)+p(t) \frac{u^{m}(t-\tau(t))}{1+u^{n}(t-\tau(t))} \tag{4.1}
\end{equation*}
$$

which is a hematopoiesis model; it describes the production of red blood cells. In this model it is realistic to assume the periodicity of some parameters, because of the periodic variations of the environment, which play an important role in many biological and ecological systems. Mackey and Glass [6] also used this equation, with a continuous function as initial condition, to describe some physiological control systems. Here $\gamma, p, \tau$ are continuous periodic positive functions with a common period $T$, and the constants $m, n, T$ are positive. Existence of a solution to (4.1) has been proved by Wan et al [10], while global attractivity has been studied by Wang and Li [12]. The Green's kernel for this equation is

$$
G(t, s)=\frac{\exp \left(\int_{t}^{s} \gamma(\theta) d \theta\right)}{\delta-1}, \quad \text { where } \delta=\exp \left(\int_{0}^{T} \gamma(\theta) d \theta\right)
$$

This kernel is bounded as

$$
\frac{1}{\delta-1} \leq G(t, s) \leq \frac{\delta}{\delta-1}
$$

The cone $K$ is defined by

$$
K=\left\{u \in E: u(t) \geq \frac{1}{\delta}\|u\|, \text { for } t \in[0, T]\right\}
$$

and the operator $A$ by

$$
(A u)(t)=\int_{t}^{t+T} G(t, s) p(s) \frac{u^{m}(s-\tau(s))}{1+u^{n}(s-\tau(s))} d s
$$

As explained in the proof of the next theorem, the condition (ii) of the Leggett-Williams theorem is satisfied if there exists a positive constant $c_{2}$ such that

$$
\frac{1}{\delta-1} \int_{t}^{t+T} p(s) d s \frac{\left(c_{2} / \delta\right)^{m}}{1+\left(\delta c_{2}\right)^{n}}>c_{2}
$$

We select $c_{2}$ as the minimizer of the function $f(c)=(\delta-1) c(c / \delta)^{-m}\left(1+(\delta c)^{n}\right)$. This choice of $c_{2}$ leads the assumption in the following result.

Theorem 4.1. Assume $n>m-1>0$ and

$$
\begin{equation*}
\int_{0}^{T} p(s) d s>\delta^{2 m-1}(\delta-1)\left(\frac{n}{1+n-m}\right)\left(\frac{1+n-m}{m-1}\right)^{(m-1) / n} \tag{4.2}
\end{equation*}
$$

Then the hypotheses of Theorem 2.1 are satisfied and, therefore, (4.1) has at least three nonnegative periodic solutions.

Proof. From the definition of the cone $K,\|u\| / \delta \leq u(s-\tau(s)) \leq\|u\|$ for $s \in[0, T]$. Then

$$
\frac{1}{\|u\|} \int_{0}^{T} G(t, s) p(s) \frac{u^{m}(s-\tau(s))}{1+u^{n}(s-\tau(s))} d s \leq \frac{\delta}{\delta-1} \int_{0}^{T} p(s) d s \frac{\|u\|^{m-1}}{1+(\|u\| / \delta)^{n}}
$$

Since $\lim _{x \rightarrow \infty} x^{m-1} /\left(1+x^{n}\right)=0$, the right-hand side of the above inequality approaches zero as $\|u\| \rightarrow \infty$. By Lemma 3.4, this implies (H3), for $c_{4}$ arbitrarily large, which in turn implies $A\left(\bar{K}_{c_{4}}\right) \subset \bar{K}_{c_{4}}$. On the other hand, since $\lim _{x \rightarrow 0} x^{m-1} /\left(1+x^{n}\right)=0$, the right-hand side of the above inequality approaches zero as $\|u\| \rightarrow 0$. By Lemma 3.2, this implies (H1), for $c_{1}$ arbitrarily small, which in turn implies (ii) of Theorem 2.1. To prove (i) of Theorem 2.1, we set

$$
c_{2}=\frac{1}{\delta}\left(\frac{m-1}{1+n-m}\right)^{1 / n}
$$

and $c_{3}=\delta c_{2}$. Note that the set $\left\{u \in K\left(\psi, c_{2}, c_{3}\right): \psi(u)>c_{2}\right\}$ is not empty because the constant function $u=\left(c_{2}+c_{3}\right) / 2$ is in this set. For each $u$ in the cone $K$ with $c_{2} \leq \psi(u)$ and $\|u\| \leq c_{3}$, we have $c_{2} \leq\|u\| \leq c_{3}$ and $c_{2} / \delta \leq u(s-\tau(s)) \leq c_{2} \delta$. Then

$$
\psi(A u) \geq \frac{1}{\delta-1} \int_{0}^{T} p(s) d s \frac{\left(c_{2} / \delta\right)^{m}}{1+\left(c_{2} \delta\right)^{n}}>c_{2}
$$

The above inequality follows from (4.2) and the choice of $c_{2}$. Here we have used that $1+$ $\left(c_{2} \delta\right)^{n}=n /(1+n-m)$ and that

$$
\left(c_{2} / \delta\right)^{m}=c_{2} \frac{1}{\delta^{2 m-1}}\left(\frac{m-1}{1+n-m}\right)^{(m-1) / n}
$$

The above inequality implies (i). Now, we prove (iii) in Theorem 2.1. Note that

$$
\psi(A u) \geq \frac{1}{\delta-1} \int_{t}^{t+T} p(s) \frac{u^{m}(s-\tau(s))}{1+u^{n}(s-\tau(s))} d s
$$

From $\|A u\|>c_{3}=\delta c_{2}$, we have

$$
c_{3}<\|A u\| \leq \frac{\delta}{\delta-1} \int_{t}^{t+T} p(s) \frac{u^{m}(s-\tau(s))}{1+u^{n}(s-\tau(s))} d s
$$

Combining the two inequalities above, $\psi(A u)>c_{2}$, which proves (iii). By the LeggettWilliams theorem, (4.1) has at least three nonnegative periodic solutions.

Note that a function in $K$ can not have zeros, unless it is identically zero. Therefore, the second and the third solutions obtained in Theorem 4.1 are positive. The first solution will be positive if for example $f(t, 0)$ is not identically zero, which seems to be very restrictive.

## Remark

The hematopoiesis model (4.1) with $m=1$ was considered in [8]. Unfortunately, [8, Theorems $3.8-3.11]$ are incorrect: The fact that

$$
\limsup _{u \rightarrow o} \max _{0 \leq s \leq T} \frac{p(s) u}{1+u^{n}}=0
$$

does not imply (ii) in Theorem 2.1.

## Second example

Consider the scalar delay differential equation

$$
\begin{equation*}
u^{\prime}(t)=-\gamma(t) u(t)+p(t) u^{m}(t-\tau(t)) \exp (-r u(t-\tau(t))) \tag{4.3}
\end{equation*}
$$

where $\gamma, p, \tau$ are continuous periodic positive functions with a common period $T$, and the constants $m, r, T$ are positive. The Green's kernel $G$, and the cone $K$ are the same as above. While the operator $A$ is

$$
(A u)(t)=\int_{t}^{t+T} G(t, s) p(s) u^{m}(s-\tau(s)) \exp (-r u(s-\tau(s))) d s
$$

For proving (ii) in the Leggett-Williams theorem, we need a positive constant $c_{2}$ such that

$$
\frac{1}{\delta-1} \int_{t}^{t+T} p(s) d s\left(c_{2} / \delta\right)^{m} \exp \left(-r \delta c_{2}\right)>c_{2}
$$

We select $c_{2}$ as the minimizer of the function $f(c)=(\delta-1) c(c / \delta)^{-m} e^{r \delta c}$. This choice of $c_{2}$ leads the assumption in the following result.

Theorem 4.2. Assume that $m>1$ and that

$$
\begin{equation*}
\int_{0}^{T} p(s) d s>\delta(\delta-1)\left(\frac{r \delta^{2} e}{m-1}\right)^{m-1} \tag{4.4}
\end{equation*}
$$

Then the hypotheses of Theorem 2.1 are satisfied and, therefore, (4.3) has at least three nonnegative periodic solutions.

Proof. This proof is similar to the one in Theorem 4.1; so we only sketch it. Since $\lim _{x \rightarrow \infty} x^{m-1} e^{-r x}=$ 0 , Lemma 3.4 implies (H3), for $c_{4}$ arbitrarily large, which in turn implies $A\left(\bar{K}_{c_{4}}\right) \subset \bar{K}_{c_{4}}$. Since $\lim _{x \rightarrow 0} x^{m-1} e^{-r x}=0$, Lemma 3.2 implies (H1), for $c_{1}$ arbitrarily small, which in turn implies (ii) of Theorem 2.1. To prove (i) of Theorem 2.1, we set

$$
c_{2}=\frac{m-1}{r \delta}
$$

and $c_{3}=\delta c_{2}$. For each $u$ in the cone $K$ with $c_{2} \leq \psi(u)$ and $\|u\| \leq c_{3}$, we have $c_{2} \leq\|u\| \leq c_{3}$ and $c_{2} / \delta \leq u(s-\tau(s)) \leq c_{2} \delta$. Then

$$
\psi(A u) \geq \frac{1}{\delta-1} \int_{0}^{T} p(s) d s\left(c_{2} / \delta\right)^{m} e^{-r c_{2} \delta}>c_{2}
$$

The above inequality follows from (4.4) and the choice of $c_{2}$. Therefore, (i) is satisfied. The proof of (iii) is the same as in Theorem 4.1. Then by the Leggett-Williams theorem, (4.1) has at least three nonnegative periodic solutions.

Equation (4.3) with $m=1$ was also considered in [8]. However, the conditions for applying the Leggett-Williams are not satisfied.

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