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Periodic Solutions of Nonautonomous Mackey-type Systems with Delays

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Abstract
Nonautonomous systems of delay differential equations, that model classical Mackey-type hematopoietic stem cell dynamics and Mackey-type circuit systems, are under study. Explicit sufficient and necessary conditions for the existence of positive periodic solutions were obtained via topological methods. Numerical simulations have also been presented to demonstrate the theoretical analysis.

Keywords: Hematopoiesis, Delayed feedback, Nonlinear nonautonomous delay differential equations, Existence of positive periodic solutions, Leray-Schauder degree methods.

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1. Introduction

A wide class of models in Mathematical Biology and Engineering can be described by the equation

$$\dot{x}(t) = A(t)x(t) + B(t)x(t - \tau) + f_1(t, x(t)) + f_2(t, x(t - \tau)).$$

(1)

Possible applications of system (1): Mathematical Biology: population dynamics, neurophysiology, hematopoiesis, periodic chronic myelogenous leukemia, metabolic regulation, respiration, etc. See, for example, [5], [8], [9], [12],...
One of the most celebrated classical model of hematopoietic stem cell dynamics \([5]-[6]\), or the \(G_0\) model of the cell cycle, can be expressed as

\[
\begin{align*}
\frac{dx}{dt} &= -\delta x(t) - \beta(x(t))x(t) + 2e^{-\delta \tau} \beta(x(t - \tau))x(t - \tau) \\
\frac{dy}{dt} &= -\gamma y(t) + \beta(x(t))x(t) - e^{-\delta \tau} \beta(x(t - \tau))x(t - \tau),
\end{align*}
\]

where

\[
\beta(x) = \frac{\beta_0 \theta^n}{\theta^n + x^n(t)}.
\]

This model consists of a proliferating phase cellular population \(y(t)\) and a \(G_0\) resting phase with a population of cells \(x(t)\). \(\gamma\) is the death rate due to apoptosis, where \(\beta_0\) is the maximal rate of cell movement from the resting phase \(G_0\) into proliferation, \(\theta\) is the \(G_0\) stem cell population at which the rate of cell movement from \(G_0\) into proliferation is one-half of its maximal value \(\beta_0\) and \(n\) controls the sensitivity of the mitotic reentry rate \(\beta\) to changes in the size of \(G_0\), and \(n\) is a positive real number. For a different set of constant parameters, this model is capable of producing steady-state solutions, periodic oscillations and chaos. For example, in \([8]\) it was shown that for some values of \(\gamma\) the model exhibits self-sustained oscillations, whose periods are in good agreement with the observed clinical results. The global existence of self-sustained periodic oscillations was established in \([18]\) by using the contraction mapping theorem. For more details, see, for example \([1]-[6]\), \([8]\) and \([12]\).

It is well-known that control of dynamical systems is a classical subject in engineering science. Time delayed-feedback control is an efficient method for stabilizing unstable periodic orbits of chaotic systems. The method is based on applying feedback proportional to the deviation of the current state of the system from its state one period in the past so that the control signal vanishes when the stabilization of the desired orbit is attained \([21]-[25]\), \([29]\) and
The purpose of feedback control is to assure the system asymptotically converges to the stationary point with only extremely small force $F(x)$; in other words, we seek not to change the position of the stationary point and change only its local properties in such a way as to make it stable. Thus the main requirement for the force is that it has to vanish when the system is on the stationary point. To satisfy this main requirement for the perturbations, two adaptive control models were studied numerically in [23] (see also [31]): If the controlling force is proportional to the deviation of the system from the equilibrium

$$
\frac{dx}{dt} = -ax(t) + \frac{bx(t - \tau)}{1 + x^n(t - \tau)}
\frac{dy}{dt} = -ay(t) + \frac{by(t - \tau)}{1 + y^n(t - \tau)} + D[y^* - y(t)]
$$

where $x^* = y^* = (b/a - 1)^{1/n}$ is a nontrivial equilibrium; and the delayed feedback

$$
\frac{dx}{dt} = -ax(t) + \frac{bx(t - \tau)}{1 + x^n(t - \tau)}
\frac{dy}{dt} = -ry(t) + \frac{by(t - \tau)}{1 + y^n(t - \tau)} + D[y(t - T) - y(t)].
$$

where $T$ is the feedback time delay.

The following system [15] can be also used for control

$$
\frac{dx}{dt} = -ax(t) + \frac{bx(t - \tau)}{1 + x^n(t - \tau)}
\frac{dy}{dt} = -ry(t) + \frac{by(t - \tau)}{1 + y^n(t - \tau)} + D[x(t) - y(t)]
$$

In all models a nonnegative coefficient $D$ is the coupling rate between the driver $x$ and the response system $y$.

Systems (2)–(5) have been extensively studied, and to the best of our knowledge, only autonomous systems were studied in literature. The first attempt to introduce a more complex model was made recently in 2010 [13], where a periodic treatment is incorporated in the hematopoietic stem cells
model
\[
\frac{dx}{dt} = -\delta x(t) - \frac{bx(t)}{1 + x^n(t)} + 2e^{-\delta \tau} \frac{bx(t - \tau)}{1 + x^n(t - \tau)} - q(t)x(t)
\]
\[
\frac{dy}{dt} = -\beta y(t) + \frac{bx(t)}{1 + x^n(t)} - e^{-\delta \tau} \frac{bx(t - \tau)}{1 + x^n(t - \tau)} - g(t)y(t),
\]
and sufficient conditions for the stability of the trivial equilibrium were obtained.

Nonautonomous systems are more realistic since real-world models often require to incorporate temporal inhomogeneity in the models. In some cases a periodic oscillation is a desirable feature of the system and we must be able to decide with certainty whether a closed orbit exists. For example, the oscillatory insulin delivery with some periodicity is more efficient in reducing blood glucose levels than constant-dose drug administration. In population dynamics, the environments of most of the natural populations undergo temporal variation, causing changes in the growth characteristics of populations. One of the methods of incorporating temporal non-uniformity of the environments in models is to assume that the parameters are periodic with the same period of the time variable.

In this paper we assume that all mechanisms involved are time-dependent, and study nonautonomous models that belong to Mackey-type systems with feedback, i.e., models described by systems (2)–(5). Unfortunately, nonautonomous dynamical systems are more difficult technically than autonomous ones, especially if they are nonlinear, as realistic real-world models always are. Moreover, the conditions for the existence of periodic solutions of nonlinear systems are often implicit, unnecessarily numerous and difficult to verify. Several methods are used for the first order periodic systems; the best known among them is based on the use of the Poincaré operator, defined in terms of the solutions of the associated initial value problem. This requires some information about the flow of the differential equation, e.g., to know in advance if, for some choice of the initial data, solutions starting at \( t = 0 \) are defined over \([0, T]\). In contrast, topological degree methods are less restrictive and more direct. In particular, the original problem is transformed in an equivalent functional equation in such a way that no \textit{a priori} consideration about the flow is required.

Our main goal is to obtain necessary and sufficient conditions for the existence of nonconstant periodic solutions that require a set of natural and
easily verifiable conditions. In Section 2 we introduce the basics of the topological degree theory and the notations that will be used throughout the paper. In Section 3 we study classical Mackey model of hematopoietic stem cell dynamics model with variable parameters. Lemma 3.1 proved in Section 3, generalizes the existence result established for model (2) with constant parameters in [18]. In Section 4, we study nonautonomous models that controls chaos via Mackey-type system. Finally, we give numerical examples to show the stabilization of the unstable oscillations for model (4).

2. Preliminaries

For the reader’s convenience, we present the basic facts of the degree theory that are used in this paper. Roughly speaking, the topological degree is an algebraic count of the zeros of a continuous function \( f : \overline{U} \to E \) where \( U \) is an open and bounded subset of a Banach space \( E \), and \( f \) does not vanish on \( \partial U \). Let us firstly introduce the degree when \( \text{dim}(E) < \infty \). With this aim, recall that if \( A \subset \mathbb{R}^n \) is an open set and \( f : A \to \mathbb{R}^m \) is a \( C^1 \) function, then a point \( p \in \mathbb{R}^m \) is called a regular value of \( f \) if for each \( x \in f^{-1}(p) \) the differential \( Df(x) : \mathbb{R}^n \to \mathbb{R}^m \) is an epimorphism. In particular, when \( m = n \), the inverse mapping theorem implies that \( f^{-1}(p) \) is a discrete set.

**Definition 2.1** Let \( U \) be an open and bounded subset of \( \mathbb{R}^n \) and let \( f \in C^1(\overline{U}, \mathbb{R}^n) \) such that \( f \neq 0 \) on \( \partial U \) and \( 0 \) is a regular value of \( f \). We define Brouwer degree of \( f \) as

\[
\text{deg}_B(f, U, 0) := \sum_{x \in f^{-1}(0) \cap U} \text{sgn}Jf(x),
\]

where \( Jf \) denotes the Jacobian of \( f \), namely \( Jf(x) = \text{det}Df(x) \).

This definition can be extended in an appropriate way for \( f \in C(\overline{U}, \mathbb{R}^n) \) with \( f \neq 0 \) on \( \partial U \). In particular, when \( n = 1 \) and \( U = (a, b) \) the degree of \( f \) is simply given by

\[
\text{deg}_B(f, (a, b), 0) = \frac{\text{sgn}(f(b)) - \text{sgn}(f(a))}{2}.
\]

Further generalization for infinite dimensional spaces is given by the Leray-Schauder degree, which is defined for Fredholm operators \( f : \overline{U} \to E \) of
the type \( f = I - K \) with \( K \) compact. In particular, when the range of \( K \) is contained in a finite dimensional subspace \( V \subset E \), the Leray-Schauder degree is defined by

\[
\text{deg}_{LS}(f, U, 0) := \text{deg}_B(f|_V, U \cap V, 0).
\]

(8)

More remarkable properties of the degree can be found, for example, in [10] and [17]. However, in the present work, we will only use two of them:

1. If \( \text{deg}(f, U, 0) \neq 0 \), then \( f \) vanishes in \( U \).
2. Homotopy invariance: if \( F : \overline{U} \times [0,1] \to E \) is continuous such that \( I - F(\cdot, \lambda) \) is compact for all \( \lambda \) and \( F(u, \lambda) \neq 0 \) for \( u \in \partial U \) and \( \lambda \in [0, 1] \), then \( \text{deg}_{LS}(F(\cdot, \lambda), U, 0) \) does not depend on \( \lambda \).

According to the standard continuation method [10], [20], we shall convert each of the problems under study into an equivalent equation \( F(z) = 0 \) for some continuous \( F : E \to E \); and embed it in a continuous one-parameter family of problems \( F_\lambda(z) = 0 \), where \( F_1 = F \), and each \( F_\lambda \) has the form \( F_\lambda = I - K_\lambda \), with \( K_\lambda : E \to E \) compact. Thus, using the homotopy invariance of the degree, it will suffice to find a bounded domain \( \Omega \subset E \) such that

1. \( F_\lambda \) does not vanish on \( \partial \Omega \) for \( 0 \leq \lambda < 1 \).
2. \( \text{deg}_{LS}(F_0, \Omega, 0) \neq 0 \).

The following notation will be used throughout the paper. The space of continuous \( T \)-periodic functions will be denoted by \( C_T \), namely

\[
C_T := \{ u \in C(\mathbb{R}, \mathbb{R}) : u(t + T) = u(t) \text{ for all } t \}.
\]

Given a function \( u \in C_T \), the maximum and minimum values and its average \( \frac{1}{T} \int_0^T u(t) \, dt \) will be denoted respectively by \( u_{\max}, u_{\min} \) and \( \overline{u} \).

3. Mackey Models of Hematopoietic Stem Cell Dynamics

Consider the following nonautonomous model:

\[
\begin{align*}
\frac{dx}{dt} &= -\alpha(t)x(t) - \frac{b(t)x(t)}{A(t) + x^n(t)} + 2e^{-\delta(t)\tau} \frac{b(t)x(t - \tau)}{A(t) + x^n(t - \tau)}, \\
\frac{dy}{dt} &= -\beta(t)y(t) + \frac{b(t)x(t)}{A(t) + x^n(t)} - e^{-\delta(t)\tau} \frac{b(t)x(t - \tau)}{A(t) + x^n(t - \tau)},
\end{align*}
\]

(9)
Here \( A(t), \alpha(t), \beta(t), \delta(t) \) and \( b(t) : \mathbb{R} \to (0, +\infty) \) are continuous and \( T \)-periodic functions, \( \tau \) is a positive constant. By ‘positive \( T \)-periodic solution’ we mean a solution \((x, y)\) that is globally defined and for all \( t \) satisfies

\[
x(t + T) = x(t) > 0, \quad y(t + T) = y(t) > 0.
\]

**Remark 3.1** Setting \( A(t) \equiv 1, b(t) \equiv b, \delta(t) \equiv \delta, \alpha(t) = \delta + q(t) \) and \( \beta(t) = \beta + g(t) \) reduces system (9) to model (6).

Before establishing the results of this section, let us observe the following facts related to system (9):

1. For any fixed \( T \)-periodic function \( x \), the second equation is linear on \( y \). As \( \beta > 0 \), it has a unique \( T \)-periodic solution \( y(t) \). In particular, for \( \tau = 0 \) the second equation reduces to \( y'(t) = -\beta(t)y(t) \), so \( y(t) \equiv 0 \) and the system has no positive \( T \)-periodic solutions. As we shall see, when \( \tau \) is large enough the system admits no positive \( T \)-periodic solutions either.

2. When \( 0 < n \leq 1 \), the function \( f(t, x) := \frac{x}{A(t) + x^\tau} \) is nondecreasing in \( x \) for each fixed \( t \). For \( n > 1 \), \( f(t, \cdot) \) is initially strictly nondecreasing up to \( x_t := \left( \frac{A(t)}{n-1} \right)^{1/n} \) and strictly nonincreasing after \( x_t \). Furthermore,

\[
f(t, \cdot)_{max} = f(t, x_t) = \gamma(t),
\]

where

\[
\gamma(t) := \frac{1}{n} \left( \frac{n-1}{A(t)} \right)^{\frac{n-1}{n}}.
\]

In order to state our results, we define the function

\[
\psi(t) := \frac{b(t)}{\alpha(t)} \left( 2e^{-\delta(t)\tau} - 1 \right) - A(t),
\]

and formulate the following Theorem.

**Theorem 3.1** Assume that \( 0 < n < 2 \) and \( \psi(t) > 0 \) for all \( t \). Then (9) admits at least one \( T \)-periodic positive solution, provided that

\[
\frac{A(t) + \psi_{\text{min}}}{A(t) + \psi_{\text{max}}} < e^{\delta(t)\tau} \left( \frac{\psi_{\text{min}}}{\psi_{\text{max}}} \right)^{1/n}
\]

(10)
and
\[ 2(n - 1) \frac{b(t)}{\alpha(t)} \leq nA(t)e^{\delta(t)\tau} \quad (11) \]
for all \( t \).

**Corollary 3.1** Let \( 0 < n < 2 \) and \( b_0, \alpha_0, \delta_0 \) and \( A_0 \) be positive constants satisfying
\[ 2e^{-\delta_0\tau} - 1 > \frac{\alpha_0A_0}{b_0} > \frac{2(n - 1)}{n}e^{-\delta_0\tau}. \quad (12) \]
Then there exists a constant \( \varepsilon > 0 \) such that (9) admits at least one \( T \)-periodic positive solution, provided that
\[ \| b - b_0 \|_\infty < \varepsilon, \quad \| \alpha - \alpha_0 \|_\infty < \varepsilon, \quad \| \delta - \delta_0 \|_\infty < \varepsilon, \quad \| A - A_0 \|_\infty < \varepsilon. \]

When \( 0 < n \leq 1 \), it is clear that condition (11) and the second inequality of (12) are trivially satisfied. For \( n > 1 \), Theorem 3.1 can be regarded as a consequence of a more general existence result for system (9), stated in terms of a function \( X(t) \) and defined implicitly as the largest zero of the function \( M : [0, +\infty) \to [0, +\infty) \) given by
\[ M(X) := X \left( \frac{\alpha(t)}{b(t)} + \frac{1}{A(t) + X^n} \right) - 2\gamma(t)e^{-\delta(t)\tau}. \]

**Theorem 3.2** Assume that \( n > 1 \) and \( \psi(t) > 0 \) for all \( t \). Then (9) admits at least one positive \( T \)-periodic solution if one of the following conditions is satisfied:
1. \( X^n(t) \leq \frac{A(t)}{n-1} \) and (10) holds for all \( t \),
or
2. \( X^n(t) > \frac{A(t)}{n-1} \) for some \( t \) and
\[ \gamma(t) < e^{\delta(t)\tau} \min \left\{ \frac{X_{\text{max}}}{A(t) + X_{\text{max}}^n}, \frac{\psi_{\text{min}}^{1/n}}{A(t) + \psi_{\text{min}}} \right\} \]
for all \( t \).

The following lemma is used for a proof of Theorems 3.1 and 3.2:

**Lemma 3.1** Assume that \( \psi(t) > 0 \) for all \( t \). Then the first equation of (9) admits at least one positive \( T \)-periodic solution.
Proof:
Setting \( u = \ln x \), the problem can be written as \( u'(t) = Nu(t) \), where

\[
Nu(t) := -\alpha(t) + b(t) \left( \frac{2e^{-\delta(t)\tau}e^{u(t-\tau)-u(t)}}{A(t) + e^{nu(t-\tau)}} - \frac{1}{A(t) + e^{nu(t)}} \right).
\]

We shall apply a degree argument on \( C_T \). For \( \lambda \in [0, 1] \), let \( F_\lambda : C_T \to C_T \) be given by

\[
F_\lambda(u) := u - \bar{u} - Nu - \lambda K(Nu - \bar{u}),
\]
where \( K \) is a right inverse of the operator \( Lu := u' \); namely, for \( \varphi \in C_T \) such that \( \varphi = 0 \). Define

\[
K\varphi(t) := \varphi(t) - \bar{\varphi},
\]
where \( \varphi(t) = \int_0^t \varphi(t) \, dt \). Finally, for some \( R \) to be specified, let

\[
\Omega := \{ u \in C_T : -R < u(t) < R \text{ for all } t \in \mathbb{R} \}.
\]

**Remark 3.2** For \( u \in C_T \) and \( \lambda > 0 \), it is easy to see that \( u \) is a zero of \( F_\lambda \) if and only if \( u'(t) = \lambda Nu(t) \).

In view of the preceding remark, we shall prove that \( F_1 \) vanishes in \( \overline{\Omega} \). If \( u \in \mathbb{R} \), then

\[
F_0(u) = \overline{u} - \frac{1}{T} \int_0^T \left( 2e^{-\delta(t)\tau} - 1 \right) \frac{b(t)}{A(t) + e^{nu}} \, dt,
\]
and it follows that

\[
\lim_{u \to -\infty} F_0(u) = \overline{u} - \frac{1}{T} \int_0^T \left( 2e^{-\delta(t)\tau} - 1 \right) \frac{b(t)}{A(t) + e^{nu}} \, dt < 0,
\]
\[
\lim_{u \to +\infty} F_0(u) = \overline{u} > 0.
\]
Thus, if \( R \) is large enough we obtain:

\[
\deg_{LS}(F_0, \Omega, 0) = \deg_B(F_0|_{\mathbb{R}}, (-R, R), 0) = 1.
\]
It remains to prove that if \( \lambda \in (0, 1) \) and \( u \in \partial \Omega \) then \( F_\lambda(u) \neq 0 \) or, equivalently, that \( u' \neq \lambda Nu \). Indeed, suppose that \( F_\lambda(u) = 0 \) for some \( \lambda \in (0, 1) \) and consider two different cases:

**Case** \( 0 < n \leq 1 \):
For each fixed \( t \), the function \( f(t, \cdot) \) is strictly nondecreasing. If \( \xi \) is an absolute maximum of \( u \), then \( Nu(\xi) = 0 \) and hence

\[
\alpha(\xi) \leq b(\xi) \left( 2e^{-\delta(\xi)\tau} - 1 \right) \frac{1}{A(\xi) + e^{nu_{\text{max}}}},
\]

which implies:

\[
e^{nu_{\text{max}}} \leq \frac{b(\xi)}{\alpha(\xi)} \left( 2e^{-\delta(\xi)\tau} - 1 \right) A(\xi) = \psi(\xi).
\]

Thus,

\[
e^{nu_{\text{max}}} \leq \psi_{\text{max}}.
\]

On the other hand, if \( \xi \) is now an absolute minimum, then

\[
\alpha(\xi) = b(\xi) \left( 2e^{-\delta(\xi)\tau} \frac{e^{u(\xi-\tau)-u_{\text{min}}}}{A(\xi) + e^{nu(\xi-\tau)}} - \frac{1}{A(\xi) + e^{nu_{\text{min}}}} \right)
\geq b(\xi) \left( 2e^{-\delta(\xi)\tau} - 1 \right) \frac{1}{A(\xi) + e^{nu_{\text{min}}}},
\]

This implies that

\[
e^{nu_{\text{min}}} \geq \psi_{\text{min}}.
\]

**Case \( n > 1 \):**

If \( \xi \) is an absolute maximum of \( u \), then

\[
\frac{\alpha(\xi)}{b(\xi)} = 2e^{-\delta(\xi)\tau} \frac{e^{u(\xi-\tau)-u_{\text{max}}}}{A(\xi) + e^{nu(\xi-\tau)}} - \frac{1}{A(\xi) + e^{nu_{\text{max}}}}
\leq 2e^{-\delta(\xi)\tau} \gamma(\xi)e^{-u_{\text{max}}} - \frac{1}{A(\xi) + e^{nu_{\text{max}}}}.
\]

Thus,

\[
e^{u_{\text{max}}} \left( \frac{\alpha(\xi)}{b(\xi)} + \frac{1}{A(\xi) + e^{nu_{\text{max}}}} \right) \leq 2\gamma(\xi)e^{-\delta(\xi)\tau}
\]

and hence \( e^{u_{\text{max}}} \leq X(\xi) \leq X_{\text{max}} \). In particular, if \( X^n(\xi) \leq \frac{A(\xi)}{\alpha - 1} \), we deduce as in the case \( n \leq 1 \) that \( e^{nu_{\text{max}}} \leq \psi_{\text{max}} \). Next, if \( \xi \) is an absolute minimum, define \( k(t) \) as the smallest of the two positive solutions of the equation

\[
\frac{k}{A(t) + k^n} = \frac{X(t)}{A(t) + X(t)^n}.
\]
If $e^{u_{\min}} < k_{\min}$, then from the fact that $e^{u_{\min}} \leq e^{u(\xi - \tau)} \leq X_{\max}$ we deduce that

$$\frac{e^{u_{\min}}}{A(\xi) + e^{u_{\min}}} \leq \frac{e^{u(\xi - \tau)}}{A(\xi) + e^{u(\xi - \tau)}}$$

and hence

$$\alpha(\xi) \geq b(\xi) \left(2e^{-\delta(\xi)\tau} - 1\right) \frac{1}{A(\xi) + e^{u_{\min}}}.$$ 

Thus,

$$e^{u_{\min}} \geq \min\{k_{\min}^n, \psi_{\min}\}.$$

In both cases, we conclude that $u \notin \partial \Omega$ if $R$ is large enough and the proof is complete.

**Remark 3.3** Lemma 3.1 generalizes the existence result obtained in [18, section 4] for

$$\alpha(t) \equiv \delta, \quad \beta(t) \equiv \beta_0, \quad A(t) \equiv 1, \quad \delta(t) \equiv \gamma.$$ 

Note that the condition

$$\tau < -\frac{1}{\gamma} \ln \frac{\delta + \beta_0}{2\beta_0},$$

required in [18, p. 169], is exactly the same as our condition $\psi(t) > 0$ applied to this particular case. The main tool in [18] is the contraction mapping theorem, which allows to prove uniqueness as well, but is more restrictive, e.g., can be applied only for sufficiently large $n$. In contrast, application of the degree method yields the existence of the periodic solutions for all values of $n > 0$, although this technique does not guarantee uniqueness of the solutions. The problem of proving uniqueness (or multiplicity) of positive $T$-periodic solutions for arbitrary $n$ remains open.

**Remark 3.4** It follows from the previous proof that, if $\tau$ is large, then the first equation of (9) has no positive $T$-periodic solutions. Indeed, existence of a $T$-periodic solution $x(t) = e^{u(t)}$ for $0 < n \leq 1$ implies $0 < e^{nu_{\max}} \leq \psi_{\max}$. The latter inequality yields

$$2e^{-n_{\min} \tau} > \left(\frac{\alpha A}{b}\right)_{\min} + 1.$$ 

On the other hand, if $n > 1$, for $\tau$ sufficiently large $X^n(t) \leq \frac{A(t)}{n-1}$ therefore, $0 < e^{nu_{\max}} \leq \psi_{\max}$. 

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**Proof of Theorems 3.1 and 3.2:**

From Lemma 3.1, the first equation of (9) has a positive $T$-periodic solution $x$. Once $x$ is fixed, the second equation has a unique $T$-periodic solution $y$. It remains to prove that $y > 0$. Let $\xi$ be an absolute minimum of $y$, then

$$\beta(\xi)y(\xi) = \frac{b(\xi)e^{-\delta(\xi)\tau}x(\xi - \tau)}{A(\xi) + x^n(\xi)} \left( \frac{x(\xi)}{x(\xi - \tau)}e^{\delta(\xi)\tau} - \frac{A(\xi) + x^n(\xi)}{A(\xi) + x^n(\xi - \tau)} \right).$$

Thus, it suffices to prove that $\frac{A(t) + x^n(t)}{A(t) + e^{n\alpha(t-t)}} < \frac{x(t)}{x(t-\tau)}e^{\delta(t)\tau}$ for all $t$ or, equivalently, that

$$\frac{A(t) + e^{nu(t)}}{A(t) + e^{nu(t-\tau)}}e^{u(t-\tau) - u(t)} \leq \left( \frac{\psi_{\text{max}}}{\psi_{\text{min}}} \right)^{1/n} \frac{A(t) + \psi_{\text{min}}}{A(t) + \psi_{\text{max}}} < e^{\delta(t)\tau},$$

so (13) holds. When $n > 1$, it is clear that the left-hand side of (13) would achieve its maximum if $u(t) = u_{\text{min}}$ and $u(t-\tau) = u_{\text{max}}$. From the computations in Lemma 3.1 and (10),

$$\frac{A(t) + e^{nu(t)}}{A(t) + e^{nu(t-\tau)}}e^{u(t-\tau) - u(t)} \leq \left( \frac{\psi_{\text{max}}}{\psi_{\text{min}}} \right)^{1/n} \frac{A(t) + \psi_{\text{min}}}{A(t) + \psi_{\text{max}}} < e^{\delta(t)\tau},$$

so (13) holds. When $n > 1$, it is clear that the left-hand side of (13) would achieve its maximum if $u(t) = u_{\text{min}}$ and $u(t-\tau) = u_{\text{max}}$. From the computations in Lemma 3.1 and (10),

$$\frac{A(t) + e^{nu(t)}}{A(t) + e^{nu(t-\tau)}}e^{u(t-\tau) - u(t)} \leq \left( \frac{\psi_{\text{max}}}{\psi_{\text{min}}} \right)^{1/n} \frac{A(t) + \psi_{\text{min}}}{A(t) + \psi_{\text{max}}} < e^{\delta(t)\tau},$$

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so (13) holds. When $n > 1$, it is clear that the left-hand side of (13) would achieve its maximum if $u(t) = u_{\text{min}}$ and $u(t-\tau) = u_{\text{max}}$. From the computations in Lemma 3.1 and (10),

$$\frac{A(t) + e^{nu(t)}}{A(t) + e^{nu(t-\tau)}}e^{u(t-\tau) - u(t)} \leq \left( \frac{\psi_{\text{max}}}{\psi_{\text{min}}} \right)^{1/n} \frac{A(t) + \psi_{\text{min}}}{A(t) + \psi_{\text{max}}} < e^{\delta(t)\tau},$$

so (13) holds. When $n > 1$, it is clear that the left-hand side of (13) would achieve its maximum if $u(t) = u_{\text{min}}$ and $u(t-\tau) = u_{\text{max}}$. From the computations in Lemma 3.1 and (10),
for all \( t \), and Theorem 3.2 applies. This completes the proof of Theorem 3.1, case \( n > 1 \).

\[ \blacksquare \]

**Proof of Corollary 3.1:**

If \( b \equiv b_0, \alpha \equiv \alpha_0, \delta \equiv \delta_0 \) and \( A \equiv A_0 \), then \( \psi \) is a positive constant and (10) holds. By continuity, if \( b, \alpha, \delta \) and \( A \) are sufficiently close to \( b_0, \alpha_0, \delta_0 \) and \( A_0 \) respectively, then \( \psi(t) > 0 \) for all \( t \), and (10) is satisfied. Finally, when \( n > 1 \) condition (11) holds strictly for \( b_0, \alpha_0, \delta_0 \) and \( A_0 \), and hence it still holds for \( \varepsilon \) small enough.

\[ \blacksquare \]

### 4. Delayed Feedback Control via Mackey-type Circuit System

Motivated by models (4)–(5), we study the following nonautonomous system

\[
\begin{align*}
\frac{dx}{dt} &= -a(t)x(t) + \frac{b(t)x(t - \tau_1)}{1 + x^n(t - \tau_1)} + c(t)x(t - \tau_2) + d(t)y(t), \\
\frac{dy}{dt} &= -r(t)y(t) + \frac{b(t)y(t - \tau_1)}{1 + y^n(t - \tau_1)} + s(t)y(t - \tau_2) + q(t)x(t).
\end{align*}
\]

(14)

Here \( n > 0 \) and \( a(t), b(t), c(t), d(t), q(t), r(t) \) and \( s(t) : \mathbb{R} \to [0, +\infty) \) are continuous and \( T \)-periodic. The constants \( \tau_{1,2} > 0 \) are fixed delays, although they might be replaced by arbitrary positive \( T \)-periodic functions. The main result of this section reads as follows:

**Theorem 4.1** Assume that

\[ b(t) > a(t) - c(t) - d(t) > 0 \]

and

\[ b(t) > r(t) - s(t) - q(t) > 0 \]

for all \( t \). Then problem (14) admits at least one positive \( T \)-periodic solution.

**Proof:** Setting \( u = \ln x \), \( v = \ln y \), the system (14) becomes:

\[
\begin{align*}
u'(t) &= -a(t) + \frac{b(t)e^{u(t-\tau_1)-u(t)}}{1 + e^{nu(t-\tau_1)}} + c(t)e^{u(t-\tau_2)-u(t)} + d(t)e^{v(t)-u(t)}, \\
v'(t) &= -r(t) + \frac{b(t)e^{v(t-\tau_1)-v(t)}}{1 + e^{nv(t-\tau_1)}} + s(t)e^{v(t-\tau_2)-v(t)} + q(t)e^{u(t)-v(t)}.
\end{align*}
\]

(15)
We shall apply a degree argument on \((C_T)^2 := C_T \times C_T\). For \(\lambda \in [0, 1]\), let \(F_\lambda : (C_T)^2 \rightarrow (C_T)^2\) be given by

\[
F_\lambda(u, v) := (u, v) - (u, v) - N(u, v) - \lambda \widehat{K}(N(u, v) - N(u, v)),
\]

where \(N(u, v)\) denotes the right-hand side term of (15) and

\[
\widehat{K}(\varphi, \psi) := (K\varphi, K\psi)
\]

for \(\varphi, \psi \in C_T\) such that \(\overline{\varphi} = \overline{\psi} = 0\), with \(K\) as in Lemma 3.1. Let \(\Omega \subset (C_T)^2\) be defined as

\[
\Omega := \{(u, v) \in (C_T)^2 : |u(t)|, |v(t)| < R\}
\]

for some \(R\) to be specified. For \((u, v) \in \mathbb{R}^2\), it is verified that

\[
F_0(u, v) = \left(\frac{a - \overline{b}}{1 + e^{nu}} - \overline{c} - de^{u} - \overline{r} - \frac{b}{1 + e^{nv}} - \overline{s} - qe^{u-v}\right).
\]

For large enough \(R\), if \(|v| \leq R\) then the first coordinate of \(F_0\) is strictly positive for \(u = R\) and strictly negative for \(u = -R\). In the same way, when \(|u| \leq R\) the second coordinate of \(F_0\) is strictly positive for \(v = R\) and strictly negative for \(v = -R\). Thus, from the homotopy invariance of the degree we deduce that

\[
\text{deg}_{LS}(F_0, \Omega, 0) = \text{deg}_B(F_0|_{\mathbb{R}^2}, (-R, R)^2, 0) = \text{deg}_B(\text{Id}, (-R, R)^2, 0) = 1.
\]

**Remark 4.1** A simple computation shows that if \(F_0\) vanishes at some point \((u^*, v^*) \in \mathbb{R}^2\), then its Jacobian is positive; thus, we conclude that \(F_0\) has exactly one zero. In particular, if \(a, b, c, d, q\) and \(r\) are positive constants then (14) has exactly one positive equilibrium.

Next, suppose that \(F_\lambda(u, v) = (0, 0)\) for some \((u, v) \in \partial \Omega\) and \(\lambda \in (0, 1)\) or, equivalently, that

\[
(u', v') = \lambda N(u, v).
\]

**Case** \(n > 1\): As in the previous section (now with \(A \equiv 1\)), denote by \(\gamma_1\) the value for which the function \(\frac{e^x}{1 + e^x}\) achieves its maximum, namely \(\gamma_1 = \frac{1}{n}(n - 1)^{\frac{n-1}{n}}\). If \(\xi\) is an absolute maximum of \(u\), it follows from the first equation of system (16) that

\[
a(\xi) \leq \gamma_1 b(\xi) e^{-u_{\max}} + c(\xi) e^{u(\xi - \tau_2) - u_{\max}} + d(\xi) e^{v(\xi) - u_{\max}}.
\]
If \(u_{\text{max}} \geq v_{\text{max}}\), then it follows that
\[
a(\xi) \leq \gamma_1 b(\xi) e^{-u_{\text{max}}} + c(\xi) + d(\xi),
\]
and hence
\[
e^{u_{\text{max}}} \leq \gamma_1 \left( \frac{b}{a - c - d} \right)_{\text{max}}.
\]

Suppose, on the contrary, that \(u_{\text{max}} < v_{\text{max}}\) and let \(\eta\) be an absolute maximum of \(v\). Using now the second equation of (16) we deduce that
\[
r(\eta) \leq \gamma_1 b(\eta) e^{-v_{\text{max}}} + s(\eta) e^{v(\eta - \tau_2)} - v_{\text{max}} + d(\eta) e^{u(\eta) - v_{\text{max}}} < \gamma_1 b(\eta) e^{-v_{\text{max}}} + s(\eta) + q(\eta)
\]
and thus
\[
e^{v_{\text{max}}} < \gamma_1 \left( \frac{b}{r - s - q} \right)_{\text{max}}.
\]

We conclude that
\[
\max\{e^{u_{\text{max}}}, e^{v_{\text{max}}}\} \leq \gamma_1 \max\left\{ \left( \frac{b}{a - c - d} \right)_{\text{max}}, \left( \frac{b}{r - s - q} \right)_{\text{max}} \right\} := R_M.
\]

Next, assume that \(u\) achieves an absolute minimum at \(t = \xi\). Then
\[
a(\xi) \geq b(\xi) e^{u(\xi - \tau_1)} + c(\xi) + d(\xi) e^{v(\xi) - u_{\text{min}}}.
\]

As before, if \(u_{\text{min}} \leq v_{\text{min}}\) then it follows that
\[
a(\xi) \geq b(\xi) \frac{e^{u(\xi - \tau_1)}}{1 + e^{u(\xi - \tau_1)}} e^{-u_{\text{min}}} + c(\xi) + d(\xi).
\]

Let \(k\) be the smallest of the two positive solutions of the equation
\[
\frac{k}{1 + k^n} = \frac{R_M}{1 + R_M^n}.
\]

If \(e^{u_{\text{min}}} < k\), then
\[
\frac{e^{u(\xi)}}{1 + e^{u(\xi - \tau_1)}} \geq \frac{e^{u_{\text{min}}}}{1 + e^{u_{\text{min}}}}
\]
and we obtain:
\[
a(\xi) \geq b(\xi) \frac{1}{1 + e^{u_{\text{min}}}} + c(\xi) + d(\xi).
\]

The latter implies
\[
e^{u_{\text{min}}} \geq \left( \frac{b}{a - c - d} \right)_{\text{min}} - 1.
\]
On the other hand, if $u_{\min} > v_{\min}$ and $\eta$ is an absolute minimum of $v$, then
\[ r(\eta) > b(\eta) \frac{e^{v(\xi - \tau_1)}}{1 + e^{n(\xi - \tau_1)}} e^{-v_{\min}} + s(\eta) + q(\eta) \]
and we deduce, as before, that if $e^{v_{\min}} < k$, then
\[ e^{n v_{\min}} \geq \left( \frac{b}{r - s - q} \right)_{\min} - 1. \]
Summarizing, we have proved that $\min\{e^{u_{\min}}, e^{v_{\min}}\} \geq R_m$, where
\[ R_m := \min \left\{ k^n, \left( \frac{b}{a - c - d} \right)_{\min} - 1, \left( \frac{b}{r - s - q} \right)_{\min} - 1 \right\}^{1/n}. \]
Thus, it suffices to take $R > \max\{\ln R_M, -\ln R_m\}$.

**Case** $0 < n \leq 1$: Now the function $e^{\frac{s}{1+e^{ax}}}$ is strictly increasing. If $\xi$ is an absolute maximum of $u$ and $u_{\max} \geq v_{\max}$ then we obtain:
\[ a(\xi) \leq \frac{b(\xi)}{1 + e^{n u_{\max}}} + c(\xi) + d(\xi), \]
and hence
\[ e^{n u_{\max}} \leq \left( \frac{b}{a - c - d} \right)_{\max} - 1. \]
In the same way, if $v_{\max} > u_{\max}$ then we get
\[ e^{n v_{\max}} < \left( \frac{b}{r - s - q} \right)_{\max} - 1 \]
and consequently
\[ \max\{e^{n u_{\max}}, e^{n v_{\max}}\} \leq \max\left\{ \left( \frac{b}{a - c - d} \right)_{\max}, \left( \frac{b}{r - s - q} \right)_{\max} \right\} - 1. \]
On the other hand, if $u$ achieves an absolute minimum at $t = \xi$ and $u_{\min} \leq v_{\min}$, then
\[ a(\xi) \geq \frac{b(\xi)}{1 + e^{n u_{\min}}} + c(\xi) + d(\xi), \]
and hence
\[ e^{n u_{\min}} \geq \left( \frac{b}{a - c - d} \right)_{\min} - 1. \]
In the same way, if \( v_{\min} < u_{\min} \) we obtain:

\[
e^{nu_{\min}} > \left( \frac{b}{r - s - q} \right)_{\min} - 1.
\]

We conclude that

\[
\min \{ e^{nu_{\min}}, e^{nv_{\min}} \} \geq \min \left\{ \left( \frac{b}{a - c - d} \right)_{\min}, \left( \frac{b}{r - s - q} \right)_{\min} \right\} - 1
\]

and the proof follows.

**Corollary 4.1** Assume that the problem (14) has a positive \( T \)-periodic solution. Then

\[
a(t) > c(t) + d(t) \quad \text{or} \quad r(t) > s(t) + q(t)
\]

for some \( t \).

**Proof:**

Let \((u, v)\) be a solution of (15). From the previous proof, if \( u_{\max} \geq v_{\max} \) then \( a(\xi) > c(\xi) + d(\xi) \) for some \( \xi \), and if \( u_{\max} < v_{\max} \), then \( r(\xi) > s(\xi) + t(\xi) \) for some \( \xi \).

**Remark 4.2** We may generalize the models given by the uncoupled system (4) and system (5) by considering arbitrary positive \( T \)-periodic functions \( a(t), b(t), r(t) \) and \( D(t) \). In this case, Theorem 4.1 yields the existence of at least one positive periodic solution if \( b(t) > a(t), r(t) \). When \( a, b, r \) and \( D \) are positive constants, existence of a positive constant solution follows trivially in (4) provided that \( b > a, r \) and also in (5), provided that \( b > a \). It is interesting to observe that no condition on \( r \) is required in this last case, which reveals that Theorem 4.1 is not sharp when applied to (5). Indeed, a direct application of the degree method for the first equation of (5) proves that a positive \( T \)-periodic solution \( x(t) \) exists when \( b(t) > a(t) \), and placing \( x(t) \) into the second equation a positive \( T \)-periodic solution \( y(t) \) is obtained for an arbitrary positive \( T \)-periodic function \( r(t) \).

The following graphs (Fig. 1) illustrate that if \( D = 0.31 \) then system (4) produces unstable periodic solutions; however, the choice \( D = 0.1 \) stabilizes the system.
Figure 1: Existence of positive periodic solutions with the parameters given by a) $D = 0.31$ and b) $D = 0.1$. Data set for Model: $n = 2; \tau_1 = 0.25; \tau_2 = 30.5; a = 0.2 \times \sin(2t) + 0.3; A = 1; b = 1.5 \times \sin(0.5t) + 2; r = 0.5 \times \sin(2t) + 0.6$
References


