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Mackey-Glass Model of Respiratory Dynamics: Review and New Results ^{☆☆}

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Abstract

Since the celebrated Mackey-Glass model of respiratory dynamics was introduced in 1977, many results on its qualitative behavior have been obtained, including oscillation, stability and chaos. The paper reviews some known properties and presents new results for more general models: equations with time-dependent parameters, several delays, a positive periodic equilibrium and distributed delays. The problems considered in the paper involve existence, positivity and permanence of solutions, oscillation and global asymptotic stability. In addition, some general approaches to the study of nonlinear nonautonomous scalar delay equations are outlined. The paper generalizes and unifies existing results and provides an outlook on further studies.

Keywords: Nonlinear delay equations, Mackey-Glass equation, global asymptotic stability, permanence, oscillation and non-oscillation

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1. Preliminaries

To explain dynamic diseases, such as Cheyne-Stokes phenomenon (periodic breathing), the classical model

$$\frac{dy}{dt} = \lambda - \frac{\alpha_0 V_m y(t) y^n(t - \tau)}{\theta^n + y^n(t - \tau)} \quad (1.1)$$

was introduced by M. C. Mackey and L. Glass in 1977 [16]. Here $y(t)$ denotes the arterial concentration of CO_2 , λ is the CO_2 production rate, V_m denotes the maximum ventilation rate of CO_2 , and τ is the time between oxygenation of blood in the lungs and stimulation of chemoreceptors in the brainstem. According to [16], the ventilation function

$$V(y) = \frac{\alpha_0 V_m y^n}{\theta^n + y^n}$$

is a sigmoidal function of y with the parameters $\theta > 0$ and $n > 0$ to be adjusted to fit the experimental data. A more detailed description of the nature of model (1.1) and its applications can be found in [14, 16, 18], mathematical results for (1.1) were presented in [8, 10, 12, 14, 15, 17, 19].

Let $y(t) = \theta x(t)$, then (1.1) can be rewritten as

$$\frac{dx}{dt} = \alpha - \frac{\beta x(t) x^n(t - \tau)}{1 + x^n(t - \tau)}, \quad (1.2)$$

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with the initial function $x(t) = \varphi(t)$ for $-\tau \leq t \leq 0$, $\varphi \in C[[-\tau, 0], \mathbb{R}^+]$ and $\varphi(0) > 0$, where $\alpha = \lambda/\theta$ and $\beta = \alpha_0 V_m$. We consider a modification of (1.2) with variable nonnegative parameters

$$\frac{dx}{dt} = \alpha(t) - \beta(t)x(t) \frac{x^n(h(t))}{1 + x^n(h(t))}, \quad t \geq 0 \quad (1.3)$$

and the initial condition

$$x(t) = \varphi(t), \quad t \leq 0. \quad (1.4)$$

Here $\alpha(t)$ and $\beta(t)$ are Lebesgue measurable locally essentially bounded functions satisfying

$$\alpha(t) \geq 0 \quad \text{and} \quad \beta(t) \geq 0. \quad (1.5)$$

Henceforth we assume $h(t)$ is a Lebesgue measurable locally bounded function satisfying

$$h(t) \leq t \quad \text{and} \quad \lim_{t \rightarrow \infty} h(t) = \infty. \quad (1.6)$$

Also assume $\varphi(t)$ is nonnegative, $\varphi(0) > 0$, and $\varphi(t)$ is a Borel measurable bounded function. To study oscillation and global stability of model (1.3), we will use the substitution $x = e^u$ that transforms equation (1.3) into

$$\frac{du}{dt} = \alpha(t)e^{-u(t)} - \beta(t) \frac{e^{nu(h(t))}}{1 + e^{nu(h(t))}}, \quad t \geq 0. \quad (1.7)$$

Equation (1.7) belongs to a general class of nonlinear nonautonomous equations with variable delays

$$\frac{du}{dt} + f_1(t, u(t)) + f_2(t, u(h(t))) = 0. \quad (1.8)$$

For example, equation (1.8) is more general than the autonomous equation

$$\frac{du}{dt} = -au(t) + f(u(h(t)))$$

which is a mainstay for the classical production-destruction or delayed recruitment models.

We begin our study with the abstract model (1.8) and obtain new global stability results, which are later used to prove several new theorems for Mackey-Glass equation (1.3) and its generalizations.

The paper is organized as follows. Section 2 includes a brief review of some known stability and oscillation results for model (1.1). In Section 3, for a nonautonomous model, we examine existence, positivity and permanence of global solutions. Section 4 deals with oscillation properties of solutions. Global stability of nonautonomous equations is examined in Section 5. For the autonomous case we compare sufficient stability conditions to the results recently obtained in [12], and demonstrate that even for the autonomous model our results are novel. In Section 6 we extend our results and techniques to more general models, including equations with several delays, periodic parameters and distributed delays. For equations with periodic parameters we study global stability and oscillation about the positive periodic solution. It is noteworthy to mention that, compared with previous results, sufficient explicit conditions of our theorems do not contain unknown periodic solutions. For the equations with distributed delays we study permanence, global stability and oscillation. Finally, a list of open problems and conjectures is presented. In the Appendix we present several proofs omitted in the main part of the paper.

2. Review of Known Results

Provided that α and β are positive, equation (1.2) has a unique positive equilibrium K determined by the equation

$$\beta K^{n+1} = \alpha(1 + K^n). \quad (2.1)$$

The standard linearization of equation (1.2) for $y = x - K$ produces

$$\frac{dy}{dt} = -ay(t) - by(t - \tau), \quad (2.2)$$

where $a = \frac{\alpha}{K}$ and $b = \frac{\alpha n}{K(1+K^n)}$. Based on a classical result [9], any solution of equation (2.2) is asymptotically stable if $a > b > 0$. We will say that a delay equation is *absolutely stable* if it is stable for any delay.

Theorem 2.1. *If $0 < n < 1 + K^n$ then (1.2) is absolutely locally asymptotically stable (LAS).*

Lemma 2.2. *[13] If $a_k > 0$, $\tau_k \geq 0$ and $\sum_{k=1}^m a_k \tau_k < 3/2$ then the equation*

$$\frac{dx}{dt} + \sum_{k=1}^m a_k x(t - \tau_k) = 0$$

is asymptotically stable.

Thus, the linear equation (2.2) is LAS if $b\tau < 3/2$. Lemma 2.2 immediately implies a delay dependent condition for model (1.2).

Theorem 2.3. *If $\frac{n\alpha\tau}{K(1+K^n)} < 3/2$ then (1.2) is LAS.*

Theorem 2.3 is also true for a variable delay $\tau(t) \leq \tau$.

Definition 2.4. *An equilibrium K is **globally asymptotically stable (GAS)** for initial conditions in the open set $Q_0 \subset \mathbb{R}$ if it is an attractor for all solutions with the initial conditions in Q_0 , and it is also locally uniformly stable.*

The next result is due to [14].

Theorem 2.5. *[14, Corollary 8.3] Let one of the following two conditions hold:*

- (i) $0 < n \leq 1$ and $\beta < 2\alpha K$;
- (ii) $n > 1$ and

$$\frac{\beta}{4n}(n+1)^{(n+1)/n}(n-1)^{(n-1)/n} < \alpha.$$

Then the unique positive equilibrium K of (1.2) is absolutely GAS. If $n > 1$ and

$$\left[\alpha + \frac{\beta}{4n}(n+1)^{(n+1)/n}(n-1)^{(n-1)/n} \right] \frac{\beta\tau}{\alpha} < 1,$$

then K is GAS.

Most interesting global attractivity results for (1.2) were recently obtained in [12].

Theorem 2.6. *[12, Corollary 4] If either $0 < n \leq 1$ or $n > 1$ and $\alpha > \frac{(n-1)^{\frac{n+1}{n}}}{n}$ then the unique positive equilibrium K of (1.2) is absolutely GAS. If*

$$\left(1 - e^{-\tau\alpha/K} \right) \frac{n\alpha}{\beta K^{n+1}} < 1 \quad (2.3)$$

then K is GAS.

Condition (2.3) provides a sharper estimate compared to the results of [10, 14], as demonstrated in [12].

Theorem 2.7. [11, p.40, Corollary 2.2.1] Consider

$$\frac{dx}{dt} = -ax(t) - bx(t - \tau). \quad (2.4)$$

where $a, b, \tau \in \mathbb{R}$. Then

$$b\tau e^{a\tau} > \frac{1}{e} \quad (2.5)$$

is a necessary and sufficient condition for the oscillation of all solutions of equation (2.4).

Based on inequality (2.5) and [11, Theorem 4.1.1], the following result is valid (see also [15]).

Theorem 2.8. If

$$\frac{n\tau\alpha}{K(1+K^n)} \exp\left(\frac{\alpha\tau}{K}\right) < \frac{1}{e}$$

then there exists a positive nonoscillatory about K solution of (1.2). Every positive solution of (1.2) oscillates about K if

$$\frac{n\tau\alpha}{K(1+K^n)} \exp\left(\frac{\alpha\tau}{K}\right) > 1/e.$$

In [8], the authors considered the nonautonomous version of (1.2)

$$\frac{dx}{dt} = \alpha(t) - \frac{\beta(t)x(t)x^n(t - \tau(t))}{1 + x^n(t - \tau(t))}, \quad (2.6)$$

with ω -periodic functions $\alpha, \beta \in C(\mathbb{R}, (0, \infty))$ and $\tau \in C(\mathbb{R}, [0, \infty))$.

Theorem 2.9. [8] Equation (2.6) has a positive ω -periodic solution.

A particular case of Theorem 2.9 was obtained in [17]. For the integro-differential version of model (1.2)

$$\frac{dx}{dt} = a(t) - b(t)x(t) \int_0^t k(s) \frac{x^n(t-s)}{1+x^n(t-s)} ds, \quad t \geq 0,$$

sufficient conditions for the existence of a positive periodic solution were obtained, and the global attractivity and oscillation about this periodic solution were examined in [19].

3. Existence, Positivity and Permanence of Global Solutions

Lemma 3.1. There exists a unique positive global solution of model (1.3), (1.4) on the interval $[0, \infty)$.

Proof. Observe (see, for example, [9]) that there exists a local solution on $[0, c)$ for some $c > 0$. Since $x(0) > 0$, the continuous solution $x(t)$ is positive on $[0, \varepsilon)$ for some $\varepsilon > 0$. We proceed by contradiction. To prove that $x(t) > 0$ for any $t \in [0, c)$, assume that, on the contrary, $x(t) \leq 0$ for some $t \in [0, c)$. Define $t^* = \inf\{t \in [0, c) : x(t) \leq 0\} > 0$. For $t \in [0, t^*]$, we have $x(t) > 0$ and $x(t^*) = 0$. The function $f(x) = \frac{x^n}{1+x^n}$ satisfies $0 < f(x) < 1$ for $x > 0$, thus

$$\frac{dx}{dt} \geq -\beta(t)x(t), \quad t \in [0, t^*],$$

which implies

$$x(t^*) \geq x(0)e^{-\int_0^{t^*} \beta(s) ds} > 0.$$

But this violates our assumption $x(t^*) = 0$, therefore the solution is positive for any $t \in [0, c)$. Moreover, the left limit of the positive solution satisfies $\lim_{t \rightarrow c^-} x(t) \geq x(0)e^{-\int_0^c \beta(s) ds} > 0$. This also yields that $x'(t) \leq \alpha(t)$, or

$$x(t) \leq x(0)e^{\int_0^t \alpha(s) ds},$$

which excludes the possibility that $\lim_{t \rightarrow c^-} x(t) = \infty$ for some $c > 0$. Thus, we obtain the existence of the unique global positive solution of problem (1.3), (1.4) on $[0, \infty)$. $\square$

Definition 3.2. All positive solutions of a given equation are **permanent** if there exist $m > 0$ and $M > 0$ such that for any solution $x(t)$ we have

$$m \leq \liminf_{t \rightarrow \infty} x(t) \leq \limsup_{t \rightarrow \infty} x(t) \leq M. \quad (3.1)$$

Theorem 3.3. Suppose there exist positive numbers a, A, b and B such that

$$0 < a \leq \alpha(t) \leq A < \infty, \quad 0 < b \leq \beta(t) \leq B < \infty. \quad (3.2)$$

Then solutions of (1.3), (1.4) are permanent for $t \geq 0$, with

$$m = \frac{a}{B}, \quad M = \frac{A}{b} \left[1 + \left(\frac{B}{a} \right)^n \right]. \quad (3.3)$$

Proof. By Lemma 3.1, $x(t) > 0$ for $t \geq 0$, thus the inequality

$$\dot{x}(t) \geq a - Bx(t)$$

holds, and the solution $x(t)$ of the problem (1.3), (1.4) is not less than the solution of the initial value problem $\dot{y}(t) = a - By(t)$, $y(0) = x(0)$. Since

$$y(t) = x(0)e^{-Bt} + \frac{a}{B} (1 - e^{-Bt}),$$

we have

$$\liminf_{t \rightarrow \infty} x(t) \geq \liminf_{t \rightarrow \infty} y(t) = m = \frac{a}{B}.$$

Suppose that $x(t)$ is a fixed solution of (1.3), (1.4), then for any $\varepsilon > 0$ there exists $t_0 > 0$ such that $x(t) \geq m - \varepsilon$, $t \geq t_0$, and there is t_1 such that $h(t) > t_0$ for $t > t_1$. Therefore,

$$\frac{x^n(h(t))}{1 + x^n(h(t))} \geq \frac{(m - \varepsilon)^n}{1 + (m - \varepsilon)^n} \quad \text{and} \quad \dot{x}(t) \leq A - b \frac{(m - \varepsilon)^n}{1 + (m - \varepsilon)^n} x(t), \quad t \geq t_1.$$

Similar calculations yield

$$\limsup_{t \rightarrow \infty} x(t) \leq \frac{A(1 + (m - \varepsilon)^n)}{b(m - \varepsilon)^n}.$$

Since $\varepsilon > 0$ is an arbitrary number, we have

$$\limsup_{t \rightarrow \infty} x(t) \leq \frac{A(1 + m^n)}{bm^n} = \frac{A}{b} \left[1 + \left(\frac{B}{a} \right)^n \right].$$

Thus, both the lower and the upper bounds in (3.1) are valid, which completes the proof. $\square$

Example 3.4. Consider the equation

$$\frac{dx}{dt} = \alpha(t) - \beta(t) \frac{x^{n+1}(t)}{1 + x^n(t)}, \quad (3.4)$$

with $\beta(t) \equiv 1$ and $\alpha(t) = \frac{t^{n+1} + t^n + 1}{t^n + 1}$. Then $x(t) = t$ is an exact solution of equation (3.4), therefore, boundedness of $\alpha(t)$ is necessary for permanence (more exactly, for boundedness) of the solution.

Example 3.5. The equation (3.4) with $n = 1$, $\alpha(t) = (1 + t)^{-2}$, $\beta(t) = \frac{2(t + 2)}{t + 1}$ has the exact solution $x(t) = (1 + t)^{-1}$ that tends to zero as $t \rightarrow \infty$ and thus is not permanent. Here $\beta(t)$ and other functions but $\alpha(t)$ satisfy all the conditions of the Theorem 3.3. Therefore, the positive lower bound for $\alpha(t)$ is necessary for permanence (more exactly, for persistence) of the solution.

Example 3.6. The equation (3.4) with $\alpha(t) \equiv 1$, $\beta(t) = (1 + e^t)(1 + e^{nt})$ has the exact solution $x(t) = e^{-t}$ which tends to zero as $t \rightarrow \infty$, and, thus, it is not permanent. Therefore, boundedness of $\beta(t)$ is necessary for permanence (more exactly, for persistence) of the solution.

Example 3.7. Equation (3.4) with $\alpha(t) \equiv 1$, $\beta(t) = \frac{1 + (t + e^{-t})^n}{(t + e^{-t})^{n+1}} e^{-t}$ has the exact solution $x(t) = t + e^{-t}$, therefore, the positive lower bound for $\beta(t)$ is necessary for permanence (more exactly, for boundedness) of the solution.

4. Oscillation about a Positive Equilibrium

Consider equation (1.3) with proportional coefficients

$$\frac{dx}{dt} = r(t) \left[\alpha - \frac{\beta x(t) x^n(h(t))}{1 + x^n(h(t))} \right], \quad (4.1)$$

where $\alpha > 0$ and $\beta > 0$ are positive constants, $r(t) \geq r_0 > 0$ is a measurable essentially bounded function on $[0, \infty)$. Equation (4.1) has a nontrivial equilibrium $K > 0$ determined by equation (2.1); also by Lemma 3.1, (4.1) with initial conditions (1.4) has a unique positive solution $x(t)$. The proof of Theorem 3.3 is readily adapted to obtain the bounds of the eventual solution of (1.2) with

$$m = \frac{\alpha}{\beta}, \quad M = \frac{\alpha}{\beta} \left[1 + \left(\frac{\beta}{\alpha} \right)^n \right]. \quad (4.2)$$

We quote here some useful Lemmas.

Lemma 4.1. [1, 11] If $a_k(t) \geq 0$, $h_k(t) \leq t$, $\lim_{t \rightarrow \infty} h_k(t) = \infty$, and $\limsup_{t \rightarrow \infty} \int_{\min_k \{h_k(t)\}}^t \sum_{j=1}^m a_j(s) ds < \frac{1}{e}$, then there exists a nonoscillatory solution of the linear delay equation

$$\dot{x}(t) + \sum_{k=1}^m a_k(t) x(h_k(t)) = 0. \quad (4.3)$$

If $\liminf_{t \rightarrow \infty} \sum_{k=1}^m \int_{h_k(t)}^t a_k(s) ds > \frac{1}{e}$, then all solutions of (4.3) are oscillatory.

Lemma 4.2. [2, 11] Consider the nonlinear delay differential equation

$$\dot{x}(t) + \sum_{k=1}^m a_k(t) f_k(x(h_k(t))) = 0, \quad (4.4)$$

where $a_k(t) \geq 0$, $h_k(t) \leq t$, $\lim_{t \rightarrow \infty} h_k(t) = \infty$, f_k are continuous functions, $x f_k(x) > 0$, $x \neq 0$ and $f_k(0) = 0$. If $0 < f_k(x) \leq x$, $x > 0$ or $0 > f_k(x) \geq x$, $x < 0$, and the linear equation

$$\dot{x}(t) + \sum_{k=1}^m a_k(t) x(h_k(t)) = 0$$

has a nonoscillatory solution, then equation (4.4) also has a nonoscillatory solution.

If $\lim_{x \rightarrow 0} \frac{f_k(x)}{x} = 1$, and for some $\varepsilon > 0$ all solutions of the equation

$$\dot{x}(t) + \sum_{k=1}^m (a_k(t) - \varepsilon) x(h_k(t)) = 0$$

are oscillatory, then all solutions of equation (4.4) are oscillatory.

Denote

$$\beta_n = \frac{\beta n K^n}{(1 + K^n)^2}. \quad (4.5)$$

Theorem 4.3. *If*

$$\beta_n \limsup_{t \rightarrow \infty} \int_{h(t)}^t e^{\frac{\alpha}{K} \int_{h(s)}^s r(\tau) d\tau} r(s) ds < \frac{1}{e}, \quad (4.6)$$

then equation (4.1) has a nonoscillatory about K solution. If

$$\beta_n \liminf_{t \rightarrow \infty} \int_{h(t)}^t e^{\frac{\alpha}{K} \int_{h(s)}^s r(\tau) d\tau} r(s) ds > \frac{1}{e}, \quad (4.7)$$

then all solutions of equation (4.1) are oscillatory about K .

Proof. Let $x = e^u$, then equation (4.1) has the form

$$\frac{du}{dt} = r(t) \left[\alpha e^{-u(t)} - \frac{\beta e^{nu(h(t))}}{1 + e^{nu(h(t))}} \right]. \quad (4.8)$$

Equation (4.8) has the unique equilibrium $u_0 = \ln K$. Evidently (4.1) is oscillatory/nonoscillatory about K if and only if (4.8) is oscillatory/nonoscillatory about u_0 . Since u_0 is the equilibrium of (4.8), it satisfies

$$\alpha e^{-u_0} = \frac{\beta e^{nu_0}}{1 + e^{nu_0}}. \quad (4.9)$$

Let $u = y + u_0$, then equation (4.8) has the form

$$\frac{dy}{dt} = r(t) \left[\alpha e^{-u_0} e^{-y(t)} - \frac{\beta e^{nu_0} e^{ny(h(t))}}{1 + e^{nu_0} e^{ny(h(t))}} \right].$$

Hence by (4.9) we have the equation

$$\begin{aligned} \frac{dy}{dt} = r(t) & \left[-\alpha e^{-u_0} (1 - e^{-y(t)}) - \frac{\beta n e^{nu_0}}{(1 + e^{nu_0})^2} \times \right. \\ & \left. \times \frac{(1 + e^{nu_0})^2}{n} \left(\frac{e^{ny(h(t))}}{1 + e^{nu_0} e^{ny(h(t))}} - \frac{1}{1 + e^{nu_0}} \right) \right] \end{aligned} \quad (4.10)$$

with the zero equilibrium. Denote

$$a_1(t) = \alpha e^{-u_0} r(t), \quad f_1(x) = 1 - e^{-x}, \quad a_2(t) = \frac{\beta n e^{nu_0}}{(1 + e^{nu_0})^2} r(t),$$

$$f_2(x) = \frac{(1 + e^{nu_0})^2}{n} \left(\frac{e^{nx}}{1 + e^{nu_0} e^{nx}} - \frac{1}{1 + e^{nu_0}} \right).$$

Then equation (4.10) has form (4.4) with $m = 2$, where functions f_1 and f_2 satisfy the conditions of Lemma 4.2 with $f_k(x) \leq x$, $x > 0$, $k = 1, 2$; therefore equation (4.10) has a nonoscillatory solution if the linear equation

$$\frac{dx}{dt} + \alpha e^{-u_0} r(t) x(t) + \frac{\beta n e^{nu_0}}{(1 + e^{nu_0})^2} r(t) x(h(t)) = 0 \quad (4.11)$$

has a non-oscillatory solution. Next, all solutions of equation (4.10) are oscillatory, if for some $\varepsilon > 0$ all solutions of the equation

$$\frac{dx}{dt} + \alpha e^{-u_0} r(t) x(t) + \left(\frac{\beta n e^{nu_0}}{(1 + e^{nu_0})^2} - \varepsilon \right) r(t) x(h(t)) = 0 \quad (4.12)$$

are oscillatory. For $u_0 = \ln K$, equations (4.11) and (4.12) have the forms

$$\frac{dx}{dt} + \frac{\alpha}{K}r(t)x(t) + \beta_n r(t)x(h(t)) = 0, \quad (4.13)$$

$$\frac{dx}{dt} + \frac{\alpha}{K}r(t)x(t) + (\beta_n - \varepsilon)r(t)x(h(t)) = 0, \quad (4.14)$$

respectively. After the substitution $x(t) = e^{-\frac{\alpha}{K} \int_0^t r(s)ds} v(t)$, which does not change oscillation properties of equations (4.13) and (4.14), these equations can be written as

$$\frac{dv}{dt} + \beta_n e^{\frac{\alpha}{K} \int_{h(t)}^t r(s)ds} r(t)v(h(t)) = 0, \quad (4.15)$$

$$\frac{dv}{dt} + (\beta_n - \varepsilon) e^{\frac{\alpha}{K} \int_{h(t)}^t r(s)ds} r(t)v(h(t)) = 0. \quad (4.16)$$

Condition (4.6) and Lemma 4.1 imply that equation (4.15) has a nonoscillatory solution, whereas condition (4.7) and Lemma 4.1 imply that for small $\varepsilon > 0$ all solutions of (4.16) are oscillatory, and the statement of the theorem follows from Lemma 4.2. $\square$

Theorem 2.8 is an immediate corollary of Theorem 4.3 for autonomous model (1.2).

5. Global Stability

5.1. Delay-dependent stability

The following Lemma is the key to the proofs of basic results of this section.

Lemma 5.1. [4, 5] *Consider the nonlinear delay differential equation*

$$\dot{x}(t) + f_0(t, x(t)) + \sum_{k=1}^m f_k(t, x(h_k(t))) + f(t, x(t), x(g(t))) = 0, \quad (5.1)$$

where $f_k(t, \cdot)$ and $f(t, \cdot, \cdot)$ are continuous functions, $f_k(\cdot, x)$ and $f(\cdot, u, v)$ are locally essentially bounded functions, and $f_k(t, 0) = 0$, $|f(t, u, v)| \leq c(t)$, $\lim_{t \rightarrow \infty} c(t) = 0$.

Suppose that for some given numbers x_1 and x_2 such that $x_1 < 0 < x_2$, there exist positive numbers a_k and positive essentially bounded on $[0, \infty)$ functions $a_0(t)$ and $b_k(t)$, $k = 0, 1, \dots, m$ such that at least one of the following conditions holds:

$$1) \ 0 < a_k \leq \frac{f_k(t, x)}{x} \leq b_k(t), \ k = 0, 1, \dots, m, \ x_1 \leq x \leq x_2,$$

$$\limsup_{t \rightarrow \infty} \frac{\sum_{k=1}^m b_k(t)}{\sum_{k=0}^m b_k(t)} \int_{\min_k h_k(t)}^t \sum_{k=0}^m b_k(s) ds < 1 + \frac{1}{e};$$

$$2) \ 0 < a_0 \leq a_0(t) \leq \frac{f_0(t, x)}{x} \leq b_0(t), \ \left| \frac{f_k(t, x)}{x} \right| \leq b_k(t), \ k = 1, \dots, m, \ x_1 \leq x \leq x_2, \text{ and there exists } \lambda \in (0, 1) \text{ such that}$$

$$\limsup_{t \rightarrow \infty} \frac{\sum_{k=1}^m b_k(t)}{a_0(t)} \leq \lambda.$$

Then all solutions of equation (5.1) satisfying the inequality $x_1 \leq x(t) \leq x_2$ tend to zero.

Remark 5.2. Lemma 5.1 is based on [4, Theorem 1] which was proven for the case $f(t, u, v) \equiv 0$; however the proof remains valid for a more general equation (5.1).

In the proof of Theorems 5.4 and 5.10, the following elementary Lemma will be used.

Lemma 5.3. 1) Let $f(x)$ be an increasing twice differentiable function on $[a, b]$, where $a < 0 < b$, $f(0) = 0$ and $f''(x) < 0$. Then

$$\frac{f(x)}{x} \leq \frac{f(a)}{a}, \quad x \in [a, b].$$

2) Let $f(x)$ be a decreasing twice differentiable function on $[0, b]$, $f(K) = K$ and $f''(x) > 0$. Then

$$\left| \frac{f(x) - K}{x - K} \right| \leq \left| \frac{f(0) - K}{K} \right|, \quad x \in [0, b].$$

3) Let $f(x)$ be an increasing twice differentiable function on $[a, b]$, where $a < 0 < b$, $f(0) = 0$, $f''(x) > 0$ for $a \leq 0 \leq x < c$, $f''(c) = 0$ and $f''(x) < 0$ for $c < x \leq b$. Then

$$\frac{f(x)}{x} \leq f'(c), \quad x \in [a, b].$$

4) Let $f(x)$ be a continuous function on $[a, b]$, where $a < 0 < b$, $f(0) = 0$, $xf(x) > 0$, $x \neq 0$, and $\lim_{x \rightarrow 0} \frac{f(x)}{x} = \alpha > 0$ exists. Then there exists $a_0 > 0$ such that

$$\frac{f(x)}{x} \geq a_0, \quad x \in [a, b].$$

The proof is presented in the Appendix.

Henceforth we assume that $r(t)$ satisfies

$$r(t) \geq 0 \quad \text{and} \quad \int_0^\infty r(t) dt = \infty. \quad (5.2)$$

Theorem 5.4. Suppose

$$\limsup_{t \rightarrow \infty} \frac{\beta n}{4} \int_{h(t)}^t r(s) ds < 1 + \frac{1}{e}. \quad (5.3)$$

Then the positive equilibrium K of equation (4.1) is GAS.

Proof. We apply Lemma 5.1 with $m = 1$ and $f(t, u, v) \equiv 0$. Suppose that $x(t)$ is a solution of equation (4.1) and let $y(t) = \ln \frac{x(t)}{K}$, then (4.1) has the form

$$\frac{dy}{dt} = -r(t)\alpha e^{-u_0}(1 - e^{-y(t)}) - \beta e^{nu_0}r(t) \left(\frac{e^{ny(h(t))}}{1 + e^{nu_0}e^{ny(h(t))}} - \frac{1}{1 + e^{nu_0}} \right), \quad (5.4)$$

where $u_0 = \ln K$. Clearly, the equilibrium K is an attractor for all solutions of equation (4.1) if and only if $y = 0$ is an attractor for all solutions of (5.4). To continue, recall Theorem 3.3 and assume $x(t) \geq \frac{\alpha}{\beta} - \varepsilon$, $t \geq 0$ for some $\varepsilon > 0$, or $y(t) \geq c_0$, where $c_0 := \ln \left(\left(\frac{\alpha}{\beta} - \varepsilon \right) / K \right) < 0$. If for $y \geq c_0$ we set

$$f_0(t, y) = r(t) \frac{\alpha}{K} (1 - e^{-y}), \quad f_1(t, y) = \beta K^n r(t) \left(\frac{1}{K^n + e^{-ny}} - \frac{1}{1 + K^n} \right), \quad (5.5)$$

then equation (5.4) has form (5.1). By Theorem 3.3 positive solutions of equation (5.4) are bounded: $y(t) < C_0$, where $C_0 = \ln[(M + \varepsilon)/K]$, where M is defined in (4.2). Denote

$$g_0(y) = 1 - e^{-y}, \quad g_1(y) = \frac{1}{K^n + e^{-ny}} - \frac{1}{1 + K^n}, \quad c_0 \leq y \leq C_0.$$

We have $g_0(0) = 0$, $g_0'(y) > 0$, $g_0'' < 0$ for any x , then by Lemma 5.3 for $c_0 \leq y \leq C_0$ there exists $\alpha_1 > 0$ such that

$$\alpha_1 \leq \frac{g_0(y)}{y} \leq \frac{g_0(c_0)}{c_0},$$

therefore

$$\frac{\alpha_1 \alpha}{K} r_0 \leq \frac{f_0(t, y)}{y} \leq \frac{\alpha}{K} \frac{g_0(c_0)}{c_0} r(t).$$

For the function $g_1(y)$ we have

$$g_1'' > 0 \text{ for } c_0 < y < \ln K^{-1}, \quad g_1'' < 0 \text{ for } \ln K^{-1} < y < M + \varepsilon, \quad \text{and } g_1''(\ln K^{-1}) = 0.$$

By Parts 3 and 4 of Lemma 5.3 there exists $\alpha_2 > 0$ such that

$$\alpha_2 \leq \frac{g_1(y)}{y} \leq g_1'(\ln K^{-1}) = \frac{n}{4K^n},$$

hence

$$\alpha_2 \beta K^n r_0 \leq \frac{f_1(t, y)}{y} \leq \frac{\beta n}{4} r(t).$$

Finally, by Lemma 5.1, Part 1), all solutions of equation (5.4) tend to zero. To conclude the proof of the theorem, let us verify that condition (5.3) also implies the local stability of (5.4). To accomplish this, we consider the linearization of equation (5.4)

$$\dot{y}(t) = -\frac{\alpha}{K} g_0'(0) r(t) y(t) - \beta K^n g_1'(0) r(t) y(h(t)). \quad (5.6)$$

By [5, Corollary 3.8], equation (5.6) is exponentially stable if

$$\limsup_{t \rightarrow \infty} \beta K^n g_1'(0) \int_{h(t)}^t r(s) ds < 1 + \frac{1}{e}.$$

Observe that

$$\beta K^n g_1'(0) = \frac{\beta K^n n}{(1 + K^n)^2} \leq \frac{\beta n}{4}.$$

Hence, inequality (5.3) implies that equation (5.6) is exponentially stable; the zero solution of (5.4) is locally stable, thus (4.1) is GAS. $\square$

Corollary 5.5. *If*

$$\frac{\beta \tau n}{4} < 1 + \frac{1}{e}, \quad (5.7)$$

then the positive equilibrium K of equation (1.2) is GAS.

Let us compare Corollary 5.5 with the global stability conditions obtained in [12, 14] for autonomous equation (1.2). The following example illustrates that for certain values of parameters the results of Corollary 5.5 are sharper than Theorems 2.5 and 2.6.

Example 5.6. *Let $K = 1$, then by (2.1) for any n we have $\beta = 2\alpha$. Further, let $n > 1$, then the delay-dependent GAS condition in Theorem 2.5 holds if*

$$\tau < \frac{1}{2} \left(\alpha + \frac{\alpha}{2n} (n+1)^{1+1/n} (n-1)^{1-1/n} \right)^{-1}. \quad (5.8)$$

Theorem 2.6 implies global asymptotic stability for

$$\tau < -\frac{K}{\alpha} \ln \left(1 - \frac{\beta}{\alpha n} \right) = -\frac{1}{\alpha} \ln \left(1 - \frac{2}{n} \right), \quad n > 2, \quad (5.9)$$

while inequality (5.7) in Corollary 5.5 becomes

$$\tau < \left(1 + \frac{1}{e}\right) \frac{4}{\beta n} = \frac{2}{\alpha n} \left(1 + \frac{1}{e}\right). \quad (5.10)$$

Let $n = 8$ and $\alpha = 1$. Then condition (5.8) implies stability for $\tau < 0.09875$, whereas condition (5.9) improves significantly the estimate to $\tau < 0.28768$, and (5.10) gives even better estimate of $\tau < 0.341969$. In Fig. 1 we observe that the estimate of (5.10) is sharper than (5.9), while (5.9) is better than (5.8).

Figure 1: The domain of values (α, τ) satisfying inequalities (5.10) (the upper line), (5.9) (the middle line) and (5.8) for $n = 8$ and $K = 1$.

We will conclude this part with the following theorem for the general nonautonomous equation (1.3).

Theorem 5.7. Consider nonautonomous equation (1.3) and let

$$\lim_{t \rightarrow \infty} \alpha(t) = \alpha > 0, \quad \lim_{t \rightarrow \infty} \beta(t) = \beta > 0,$$

and conditions of Corollary 5.5 hold for autonomous equation (1.2). Then the number K defined by (2.1) is a global attractor for all solutions of nonautonomous equation (1.3).

Proof. We apply Part 1 of Lemma 5.1 with $m = 1$. Equation (1.3) takes the same form as (5.1) upon substituting $y(t) = \ln \frac{x(t)}{K}$, where

$$f_0(t, y) = r(t) \frac{\alpha}{K} (1 - e^{-y}), \quad f_1(t, y) = \beta K^n r(t) \left(\frac{1}{K^n + e^{-ny}} - \frac{1}{1 + K^n} \right),$$

$$f(t, u, v) = r(t) \frac{\alpha(t) - \alpha}{K} (1 - e^{-u}) + (\beta(t) - \beta) K^n r(t) \left(\frac{1}{K^n + e^{-nv}} - \frac{1}{1 + K^n} \right).$$

Evidently there exists $A > 0$ such that for $u, v \in [c_0, C_0]$

$$|f(t, u, v)| \leq C(t) := A(|\alpha(t) - \alpha| + |\beta(t) - \beta|),$$

where $\lim_{t \rightarrow \infty} C(t) = 0$. The end of the proof is similar to the proof of Theorem 5.4. $\square$

5.2. Delay-independent (absolute) stability

The following Lemmas provide a key tool for this section.

Lemma 5.8. *Let $f : (0, \infty) \rightarrow \mathbb{R}$ be a continuous function, $g : (0, \infty) \rightarrow \mathbb{R}$ be a strictly increasing continuous function, K be the unique point such that $g(K) = f(K)$, $[g(x) - f(x)](x - K) > 0$ for any $x \neq K$ and*

$$|g^{-1}(f(y)) - K| < |y - K|, \quad y > 0, \quad y \neq K. \quad (5.11)$$

Then the steady state K of the equation

$$\dot{y}(t) = r(t)y(t)[f(y(h(t))) - g(y(t))] \quad (5.12)$$

is GAS.

Proof. To begin, note that any nonoscillatory solution tends to K . In fact, a nonoscillatory solution is monotone and thus has a finite limit $\lim_{t \rightarrow \infty} y(t) = d$. Assuming $d < K$, we have $\dot{y} \geq 0.5r(t)d[f(d) - g(d)] \geq 0$ for t large enough and the integral of the right hand side diverges by (5.2), so $\lim_{t \rightarrow \infty} x(t) = \infty$, which is a contradiction. Similarly, inequality $d > K$ leads to $\lim_{t \rightarrow \infty} y(t) = -\infty$. Thus $\lim_{t \rightarrow \infty} y(t) = K$, and we have to examine only oscillatory about K solutions. Denote $u = \limsup_{t \rightarrow \infty} |y(t) - K|$. If $u = 0$, then K is globally exponentially stable. Let $u \neq 0$. The function $\psi(x) = |g^{-1}(f(x)) - K|$ is continuous and nonnegative on $[c, d] = [\max\{0, K - u\}, K + u]$ and thus attains its maximum M on $[c, d]$, which by inequality (5.11) is less than u . Moreover, $\psi(x)$ is continuous on $(0, \infty)$, so there exists $\varepsilon_1 > 0$ such that $\psi(x) < (u + M)/2$ for $x \in [c - \varepsilon_1, d + \varepsilon_1]$, $x > 0$. If we choose $\varepsilon = \min\{(u - M)/2, \varepsilon_1\}$, then

$$|g^{-1}(f(x)) - K| < u - \varepsilon, \quad |x - K| < u + \varepsilon, \quad x > 0. \quad (5.13)$$

Further, there exists $t_2 \geq t_1 > 0$ such that $0 \leq |y(t) - K| < u + \varepsilon$, $t \geq t_1$ and $h(t) \geq t_1$ for $t \geq t_2$. Since the solution oscillates, there is a $t_3 > t_2$ such that $|y(t_3) - K| > u - \varepsilon$ and either $y(t_3) > K$, $\dot{y}(t_3) \geq 0$, or $y(t_3) < K$, $\dot{y}(t_3) \leq 0$. Assume that $y(t_3) > K$, $\dot{y}(t_3) > 0$ (the second set of inequalities is considered similarly). Then $\dot{y}(t_3) = r(t)y(t_3)[f(y(h(t_3))) - g(y(t_3))] \geq 0$ implies $f(y(h(t_3))) \geq g(y(t_3))$ and, due to monotonicity of g , $g^{-1}(f(y(h(t_3)))) \geq y(t_3)$, so

$$|g^{-1}(f(y(h(t_3)))) - K| \geq |y(t_3) - K| > u - \varepsilon,$$

while $|y(h(t_3)) - K| < u + \varepsilon$. But by (5.13) the inequality $|g^{-1}(f(y(h(t_3)))) - K| < u - \varepsilon$ holds. The contradiction proves that $u = 0$, which implies $\lim_{t \rightarrow \infty} y(t) = K$. $\square$

Consider the equation

$$\frac{dx}{dt} = -r(t) \left[f_0(x(t)) + \sum_{k=1}^m f_k(x(h_k(t))) \right], \quad (5.14)$$

where f_i are continuous functions, f_0 is a monotone increasing function, $f_i(0) = 0$, and $xf_i(x) > 0$ for $x \neq 0$. We assume that the initial value problem for equation (5.14) has a unique global solution.

Lemma 5.9. *If for some $a < 0 < b$ and $\alpha \in (0, 1)$*

$$\sup_{x \in [a, b], x \neq 0} \frac{\sum_{k=1}^m f_k(x)}{f_0(x)} \leq \alpha < 1,$$

then for any solution $x(t)$ of equation (5.14) such that $a \leq x(t) \leq b$, we have $\lim_{t \rightarrow \infty} x(t) = 0$.

The proof is given in the Appendix.

Let us go back to equation (4.1). The substitution $y(t) = 1/x(t)$ yields

$$\frac{dy}{dt} = r(t)y(t) \left[\frac{\beta}{1 + y^n(h(t))} - \alpha y(t) \right].$$

Theorem 5.10. *If*

$$\text{either } n \leq 1 \text{ and } \frac{\beta}{\alpha} < 2K, \text{ or } n > 1 \text{ and } \frac{\beta}{4n\alpha}(n-1)^{(n-1)/n}(n+1)^{(n+1)/n} < 1, \quad (5.15)$$

then equation (4.1) is GAS.

The proof is based on Lemma 5.8 and repeats the justification of the relevant result in [14] and is given in the Appendix; it can also be deduced from Lemma 5.9.

Remark 5.11. *Let us compare Theorem 2.5 in [14] (in the autonomous case it coincides with Theorem 5.10) and Theorem 5 in [12] that claims that the autonomous equation is stable whenever either $n \leq 1$ or $n > 1$ and $\frac{\beta}{\alpha n}(n-1)^{(n+1)/n} \leq 1$. Thus, for $n \leq 1$ Theorem 5 in [12] gives the best possible result, and the condition for $n > 1$, say, for $n < 1.22$, is better in [12, Theorem 5] than in Theorem 5.10.*

The following theorem gives an absolute global attractivity result for general nonautonomous equation (1.3).

Theorem 5.12. *Consider nonautonomous equation (1.3), and let*

$$\lim_{t \rightarrow \infty} \alpha(t) = \alpha > 0, \quad \lim_{t \rightarrow \infty} \beta(t) = \beta > 0,$$

and conditions of Theorem 5.10 hold for autonomous equation (1.2). Then the number K defined by (2.1) is a global attractor for all solutions of nonautonomous equation (1.3).

The proof is based on Part 2 of Lemma 5.1, and is similar to the proof of Theorem 5.4.

6. Generalizations of the Mackey-Glass Equation

6.1. Equations with Several Delays

Our results are readily adapted to equations with several delays. We assume that the previous restrictions on the parameters and the initial function are satisfied.

Theorem 6.1. *There exists a unique global positive solution of the equation*

$$\frac{dy}{dt} = \sum_{j=1}^m \left[\alpha_j(t) - \frac{\beta_j(t)y(t)y^{n_j}(h_j(t))}{1 + y^{n_j}(h_j(t))} \right] \quad (6.1)$$

with initial condition (1.4). If there exist positive numbers a_j, A_j, b_j and B_j such that

$$0 < a_j \leq \alpha_j(t) \leq A_j < \infty, \quad 0 < b_j \leq \beta_j(t) \leq B_j < \infty, \quad j = 1, \dots, m, \quad (6.2)$$

then solutions of (6.1), (1.4) are permanent.

Theorem 6.2. *Assume that inequalities (6.2) hold and K satisfies*

$$\sum_{j=1}^m \beta_j K^{n_j+1} = \sum_{j=1}^m \alpha_j (1 + K^{n_j}),$$

where β_j are defined by (4.5).

If

$$\limsup_{t \rightarrow \infty} \sum_{j=1}^m \frac{\beta_j n_j K^{n_j}}{(1 + K^{n_j})^2} \int_{\min_j h_j(t)}^t e^{(\alpha_j/K) \int_{h_j(s)}^s r(\tau) d\tau} r(s) ds < \frac{1}{e}$$

then the equation

$$\frac{dy}{dt} = r(t) \sum_{j=1}^m \left[\alpha_j - \frac{\beta_j y(t) y^{n_j}(h_j(t))}{1 + y^{n_j}(h_j(t))} \right] \quad (6.3)$$

has a nonoscillatory about the equilibrium K solution. If

$$\liminf_{t \rightarrow \infty} \sum_{j=1}^m \frac{\beta_j n_j K^{n_j}}{(1 + K^{n_j})^2} \int_{\max_j h_j(t)}^t e^{(\alpha_j/K) \int_{h_j(s)}^s r(\tau) d\tau} r(s) ds > \frac{1}{e}$$

then all solutions of equation (6.3) are oscillatory about K .

Lemmas 5.1 and 5.9 can be used to obtain the following theorems.

Theorem 6.3. *If inequalities (6.2) hold and*

$$\sum_{j=1}^m \frac{\beta_j n_j}{4} \limsup_{t \rightarrow \infty} \int_{\min_k h_k(t)}^t r(s) ds < 1 + \frac{1}{e}$$

then the nontrivial equilibrium K of equation (6.3) is GAS.

Theorem 6.4. *If inequalities (6.2) and (5.2) hold, and either all $n_j \leq 1$ and $\sum_{j=1}^m \frac{\beta_j}{\alpha_j} < 2K$, or all $n_j > 1$ and $\sum_{j=1}^m \frac{\beta_j}{4n_j \alpha_j} (n_j - 1)^{(n_j-1)/n_j} (n_j + 1)^{(n_j+1)/n_j} < 1$, then the solution of equation (6.3) is GAS.*

6.2. Equations with periodic parameters

In this section, we will study oscillation and stability of model (2.6), where $\alpha(t), \beta(t) \in C(\mathbb{R}, (0, \infty))$ and $\tau(t) \in C(\mathbb{R}, [0, \infty))$ are ω -periodic functions. By Theorem 2.9, there exists a positive ω -periodic solution $\tilde{x}(t)$ of equation (2.6).

Theorem 6.5. *Let inequalities (3.2) hold. If*

$$\limsup_{t \rightarrow \infty} \frac{n\beta(t)}{4\gamma\alpha(t) + n\beta(t)} \int_{t-\tau(t)}^t \left[\gamma\alpha(s) + \frac{1}{4}n\beta(s) \right] ds < 1 + \frac{1}{e},$$

where

$$\gamma = \frac{M - m}{m(\ln M - \ln m)} \quad (6.4)$$

and constants m and M are defined by (3.3), then the positive periodic solution $\tilde{x}(t)$ of equation (2.6) is GAS.

Proof. The proof is following the main steps of the proof of Theorem 5.4.

Suppose that $x(t)$ is a solution of equation (2.6) and let $y(t) = \ln \frac{x(t)}{\tilde{x}(t)}$, then (2.6) has the form

$$\frac{dy}{dt} = -f_1(t, y(t)) - f_2(t, y(t - \tau(t))), \quad (6.5)$$

where

$$\begin{aligned} f_1(t, y) &= \frac{\alpha(t)}{\tilde{x}(t)} (1 - e^{-y}), \\ f_2(t, y) &= \beta(t) \tilde{x}^n(t - \tau(t)) \left(\frac{1}{\tilde{x}^n(t - \tau(t)) + e^{-ny}} - \frac{1}{1 + \tilde{x}^n(t - \tau(t))} \right). \end{aligned}$$

Clearly, the periodic solution $\tilde{x}$ attracts all solutions of equation (2.6) if and only if $y = 0$ is an attractor for all solutions of equation (6.5). To continue, recall Theorem 3.3 and assume $x(t) \geq m - \varepsilon$, $t \geq 0$ for some

$\varepsilon > 0$, or $y(t) \geq c_0$, where $c_0 := \ln\left(\frac{m-\varepsilon}{M}\right) < 0$. By Theorem 3.3 positive solutions of equation (6.5) are bounded, i.e. for any small ε and t large enough

$$c_0 = \ln\left(\frac{m-\varepsilon}{M}\right) \leq y(t) \leq \ln\left(\frac{M}{\tilde{x}(t)} + \varepsilon\right) = C_0(t).$$

Denote

$$g_1(y) = 1 - e^{-y}, \quad g_2(t, y) = \frac{1}{\tilde{x}^n(t - \tau(t)) + e^{-ny}} - \frac{1}{1 + \tilde{x}^n(t - \tau(t))}, \quad c_0 \leq y \leq C_0(t). \quad (6.6)$$

We have $g_1(0) = 0$, $g_1'(x) > 0$, $g_1''(x) < 0$ for any x , then by Lemma 5.3 there exists $\alpha_1 > 0$ such that for any t

$$\alpha_1 \leq \frac{g_1(y)}{y} \leq \frac{g_1(c_0)}{c_0} = \frac{M - m + \varepsilon}{\ln M - \ln(m - \varepsilon)}.$$

Therefore

$$\frac{\alpha_1 a}{M} \leq \frac{f_1(t, y)}{y} \leq \frac{\alpha(t)}{\tilde{x}(t)} \frac{g_1(c_0)}{c_0} = \frac{(M - m + \varepsilon)\alpha(t)}{(\ln M - \ln(m - \varepsilon))\tilde{x}(t)} \leq \frac{(M - m + \varepsilon)\alpha(t)}{m(\ln M - \ln(m - \varepsilon))}$$

The function $\frac{\partial g_2(t, y)}{\partial y}$ attains its maximum $\frac{n}{4}\tilde{x}^{-n}(t - \tau(t))$ at $y = -\ln(\tilde{x}(t - \tau(t)))$ for each t . By Lemma 5.3, there exists $\alpha_2 > 0$ such that

$$\alpha_2 \leq \frac{g_2(x)}{y} \leq \frac{n}{4\tilde{x}^n(t - \tau(t))},$$

thus

$$\alpha_2 b m^n \leq \frac{f_2(t, y)}{y} \leq \frac{n\beta(t)}{4}.$$

The number ε is arbitrary, so for any $\delta > 0$

$$\frac{f_1(t, y)}{y} \leq \frac{(M - m)\alpha(t)}{m(\ln M - \ln m)} + \delta = \gamma\alpha(t) + \delta.$$

Finally, applying Lemma 5.1, Part 1, we obtain that, as far as the upper limit

$$\frac{\frac{n\beta(t)}{4}}{\gamma\alpha(t) + \frac{n\beta(t)}{4}} \int_{t-\tau(t)}^t \left[\gamma\alpha(s) + \frac{1}{4}n\beta(s) \right] ds = \frac{n\beta(t)}{4\gamma\alpha(t) + n\beta(t)} \int_{t-\tau(t)}^t \left[\gamma\alpha(s) + \frac{1}{4}n\beta(s) \right] ds$$

is less than $1 + \frac{1}{e}$, all solutions of equation (5.4) tend to zero. The proof of local stability of (6.5) is similar to that in Theorem 5.4. $\square$

Remark 6.6. The paper [8] also presents sufficient global attractivity conditions for a positive periodic solution of equation (2.6). Let us note that, unlike the results obtained in [8], Theorem 6.5 involves explicit conditions in terms of the parameters of the equation.

Theorem 6.7. If

$$\limsup_{t \rightarrow \infty} \int_{t-\tau(t)}^t \frac{n\beta(s)}{4} \exp \left\{ \int_{s-\tau(s)}^s \gamma\alpha(\zeta) d\zeta \right\} ds < \frac{1}{e},$$

where γ is defined in (6.4), then equation (2.6) has a nonoscillatory about $\tilde{x}(t)$ solution. If

$$\liminf_{t \rightarrow \infty} \int_{t-\tau(t)}^t \frac{nm^n}{M^n(m^n + 1)^2} \exp \left\{ \int_{s-\tau(s)}^s \frac{\alpha(\zeta)e^{-M}}{M} d\zeta \right\} ds > \frac{1}{e},$$

then all solutions of equation (2.6) are oscillatory about $\tilde{x}(t)$.

Proof. Let us note that (2.6) has a nonoscillatory (about the periodic equilibrium) solution if and only if the equation

$$\begin{aligned} \frac{dy}{dt} = & -\alpha(t)e^{-u_0(t)}(1 - e^{-y(t)}) \\ & -\beta(t)e^{nu_0(t-\tau(t))} \left(\frac{e^{ny(t-\tau(t))}}{1 + e^{nu_0(t-\tau(t))}e^{ny(t-\tau(t))}} - \frac{1}{1 + e^{nu_0(t-\tau(t))}} \right) \end{aligned} \quad (6.7)$$

has a nonoscillatory (about zero) solution. Further, any solution of the above equation also satisfies the linear equation

$$y'(t) = -a_1(t)y(t) - a_2(t)y(t - \tau(t)), \quad (6.8)$$

where for any $\delta > 0$ and t large enough

$$b_1(t) := \frac{\alpha(t)e^{-M}}{M} - \delta \leq a_1(t) \leq \gamma\alpha(t) + \delta =: B_1(t), \quad (6.9)$$

$$b_2(t) := \frac{nm^n}{M^n(m^n + 1)^2} - \delta \leq a_2(t) \leq \frac{n\beta(s)}{4} + \delta =: B_2(t). \quad (6.10)$$

Here the lower bound for $a_1(t)$ corresponds to the derivative at $y = M$, while for $a_2(t)$ the minimum of the derivative is attained at $y = m$. Without loss of generality, we can assume that for $\delta > 0$ small enough and $t \geq 0$, inequalities (6.9),(6.10) hold, and

$$\int_{t-\tau(t)}^t \left(\frac{n\beta(s)}{4} + \delta \right) \exp \left\{ \int_{s-\tau(s)}^s (\gamma\alpha(\zeta) + \delta) d\zeta \right\} ds < \frac{1}{e}, \quad t \geq 0,$$

which immediately implies that the linear equation $x'(t) = -B_1(t)x(t) - B_2(t)x(t - \tau(t))$ has a nonoscillatory solution; moreover, any solution of the corresponding inequality

$$y'(t) \geq -B_1(t)y(t) - B_2(t)y(t - \tau(t)) \quad (6.11)$$

with the same initial conditions satisfies $y(t) \geq x(t) > 0$. Let $y(t)$ be a solution of (6.8) with the same initial conditions as for a positive solution x . Then $y(t) > 0$ on some interval $[0, c]$. From above, as far as $y(t) > 0$, the solution of (6.8) is also a solution of inequality (6.11), so $y(t) \geq x(t) > 0$ on $[0, c]$, and c can be any positive number. Thus, (2.6) has a solution which is nonoscillatory about the periodic solution.

Next, let y be a nonoscillatory solution of (6.7), then it also satisfies (6.8). Assuming that for $\delta > 0$ small and $t \geq t_1$, we have estimates (6.9),(6.10) and

$$\int_{t-\tau(t)}^t \frac{nm^n}{M^n(m^n + 1)^2} \exp \left\{ \int_{s-\tau(s)}^s \frac{\alpha(\zeta)e^{-M}}{M} d\zeta \right\} ds > \frac{1}{e}, \quad t \geq t_1,$$

we obtain that linear equation (6.8) with $a_a(t) \geq 0$, $a_2(t) \geq 0$ has a nonoscillatory solution, while

$$\liminf_{t \geq t_1} \int_{t-\tau(t)}^t a_2(t) \exp \left\{ \int_{s-\tau(s)}^s a_2(\zeta) d\zeta \right\} ds > \frac{1}{e}.$$

The contradiction with Lemma 4.1 completes the proof of the theorem. $\square$

6.3. Equations with a Distributed Delay

Consider model (1.2) with a distributed delay

$$\frac{dx}{dt} = \alpha(t) - x(t) \int_{h(t)}^t \frac{x^n(s)}{1 + x^n(s)} d_s R(t, s), \quad t \geq 0. \quad (6.12)$$

If $R(t, s) = \chi_{(h(t), \infty)}(s)$, where χ_I is the characteristic function of set I , then (6.12) becomes (1.3), and for $R(t, s) = \chi_{(t-\tau, \infty)}(s)$, we obtain equation (1.2). If $R(t, s) = \int_{h(t)}^s K(t, \tau) d\tau$, then (6.12) is the integro-differential equation

$$\frac{dx}{dt} = \alpha(t) - x(t) \int_{h(t)}^t \frac{K(t, s)x^n(s)}{1 + x^n(s)} ds. \quad (6.13)$$

Assume that for any $t \geq 0$ the function $R(t, s) \geq 0$ is left continuous and nondecreasing in s , $R(t, h(t)) = 0$,

$$\beta(t) = \int_{h(t)}^t d_s R(t, s)$$

is a Lebesgue measurable locally bounded function, $K(t, s) \geq 0$ in (6.13) and

$$\beta(t) = \int_{h(t)}^t K(t, s) ds$$

is a locally bounded function. We require that the integral in (6.12) exists when we substitute the initial function for $s < 0$, this is satisfied for any continuous function $\varphi(t)$ for $t \leq 0$, we also assume that $\varphi(t) \geq 0$ and $x(0) > 0$. The proofs of the following statements are similar to the proofs of Lemma 3.1 and Theorem 3.3.

Lemma 6.8. *There exists a unique positive global solution of (6.12), (1.4).*

Theorem 6.9. *Suppose that there exist positive numbers a , A , b and B such that (3.2) holds. Then solutions of (6.12), (1.4), are permanent for $t \geq 0$, and inequality (3.1) holds with m and M defined by (3.3).*

Remark 6.10. *Observe that the lower solutions bound m defined by (3.3) is valid for any $h(t)$, not necessarily satisfying $\lim_{t \rightarrow \infty} h(t) = \infty$, while the upper bound may exceed M , if $\lim_{t \rightarrow \infty} h(t) \neq \infty$, as the following example demonstrates.*

Example 6.11. *Consider the equation*

$$\frac{dx}{dt} = 1 - \frac{x(t)x(h(t))}{1 + x(h(t))}, \quad (6.14)$$

where

$$h(t) = \begin{cases} 0, & t < 1, \\ \frac{1}{[t]}, & t \geq 1 \end{cases} \quad (6.15)$$

and $[t]$ is the integer part of t . Then $m = 1$, $M = 2$ in (3.3), however, for $x(0) < 1$ we have

$$\limsup_{t \rightarrow \infty} x(t) > 2,$$

see Figure 2 for illustration when $x(0) = 0.1$.

In addition to (6.12), consider the equation with a constant positive equilibrium

$$\frac{dx}{dt} = c(t) \left[\alpha - \beta x(t) \int_{h(t)}^t \frac{x^n(s)}{1 + x^n(s)} d_s R(t, s) \right], \quad t \geq 0, \quad (6.16)$$

where $\alpha > 0$, $\beta > 0$, $R(t, \cdot)$ is nondecreasing for any t , $R(t, t^+) = 1$,

$$c(t) \geq 0 \quad \text{and} \quad \int_0^\infty c(t) dt = \infty. \quad (6.17)$$

The proof of oscillation properties is based on the following Lemmas.

Figure 2: The solution of (6.14), where $h(t)$ is defined by (6.15), with the initial condition $x(0) = 0.1$, eventually exceeds $M = 2$.

Lemma 6.12. [3] Let $p(t) \geq 0$ and $c(t) \geq 0$. If

$$\limsup_{t \rightarrow \infty} \int_{h(t)}^t \left[c(\tau) \int_{h(\tau)}^{\tau} p(s) d_s R(\tau, s) \right] d\tau < \frac{1}{e}$$

then the equation

$$\dot{x}(t) + c(t) \int_{h(t)}^t p(s) x(s) d_s R(t, s) = 0, \quad t \geq 0 \quad (6.18)$$

has a nonoscillatory solution. If

$$\liminf_{t \rightarrow \infty} \int_{h(t)}^t \left[c(\tau) \int_{h(\tau)}^{\tau} p(s) d_s R(\tau, s) \right] d\tau > \frac{1}{e}$$

then all solutions of (6.18) are oscillatory.

Lemma 6.13. [6] Consider the equation

$$\dot{x}(t) + \sum_{k=1}^m c_k(t) \int_{h_k(t)}^t f_k(x(s)) d_s R_k(t, s) = 0, \quad (6.19)$$

where $c_k(t) \geq 0$, $h_k(t) \leq t$, $\lim_{t \rightarrow \infty} h_k(t) = \infty$, f_k are continuous differentiable functions and f'_k are locally essentially bounded functions.

If either $0 < f_k(x) \leq x$, $x > 0$ or $0 > f_k(x) \geq x$, $x < 0$, and the linear equation

$$\dot{x}(t) + \sum_{k=1}^m c_k(t) \int_{h_k(t)}^t x(s) d_s R_k(t, s) = 0$$

has a nonoscillatory solution, then equation (6.19) also has a nonoscillatory solution. If $\lim_{x \rightarrow 0} \frac{f_k(x)}{x} = 1$, $k = 1, \dots, m$, and for some $\varepsilon > 0$ all solutions of the equation

$$\dot{x}(t) + (1 - \varepsilon) \sum_{k=1}^m c_k(t) \int_{h_k(t)}^t x(s) d_s R_k(t, s) = 0$$

are oscillatory, then all solutions of the equation

$$\dot{x}(t) + \sum_{k=1}^m c_k(t) \int_{h_k(t)}^t f_k(x(s)) d_s R_k(t, s) = 0$$

are also oscillatory.

Theorem 6.14. *Let the function $c(t)$ satisfy condition (6.17). If*

$$\beta_n \limsup_{t \rightarrow \infty} \int_{h(t)}^t \left[c(\zeta) \int_{h(\zeta)}^\zeta e^{\frac{\alpha}{K} \int_{h(s)}^s c(\tau) d\tau} d_s R(\zeta, s) \right] d\zeta < \frac{1}{e},$$

where β_n is defined by (4.5), then equation (6.16) has a nonoscillatory about K solution. If

$$\beta_n \liminf_{t \rightarrow \infty} \int_{h(t)}^t \left[c(\zeta) \int_{h(\zeta)}^\zeta e^{\frac{\alpha}{K} \int_{h(s)}^s c(\tau) d\tau} d_s R(\zeta, s) \right] d\zeta > \frac{1}{e},$$

then all solutions of equation (6.16) are oscillatory about K .

Proof. We sketch the proof since it is similar to the proof of Theorem 4.3. The substitution $y = \ln(x/K) = \ln x - u_0$, where $u_0 = \ln K$, leads to the equation

$$\begin{aligned} \frac{dy}{dt} = c(t) & \left[-\alpha e^{-u_0} (1 - e^{-y(t)}) - \frac{\beta_n e^{nu_0}}{(1 + e^{nu_0})^2} \times \right. \\ & \left. \times \int_{h(t)}^t \frac{(1 + e^{nu_0})^2}{n} \left(\frac{e^{ny(s)}}{1 + e^{nu_0} e^{ny(s)}} - \frac{1}{1 + e^{nu_0}} \right) \right] d_s R(t, s) \end{aligned} \quad (6.20)$$

with the zero equilibrium. Denote

$$a_1(t) = \alpha e^{-u_0} c(t), \quad f_1(x) = 1 - e^{-x}, \quad a_2(t) = \frac{\beta_n e^{nu_0}}{(1 + e^{nu_0})^2} c(t),$$

$$f_2(x) = \frac{(1 + e^{nu_0})^2}{n} \left(\frac{e^{nx}}{1 + e^{nu_0} e^{nx}} - \frac{1}{1 + e^{nu_0}} \right).$$

The application of Lemma 6.13 proves that equation (6.16) has a nonoscillatory solution if the linear equation

$$\frac{dx}{dt} + \frac{\alpha}{K} c(t) x(t) + \beta_n c(t) \int_{h(t)}^t x(s) d_s R(t, s) = 0$$

has a nonoscillatory solution. All the solutions of equation (6.16) are oscillatory, if for some $\varepsilon > 0$ all solutions of the equation

$$\begin{aligned} \frac{dx}{dt} + \alpha e^{-u_0} c(t) x(t) + \left(\frac{\beta_n e^{nu_0}}{(1 + e^{nu_0})^2} - \varepsilon \right) c(t) \int_{h(t)}^t x(s) d_s R(t, s) \\ = \frac{dx}{dt} + \frac{\alpha}{K} c(t) x(t) + (\beta_n - \varepsilon) c(t) \int_{h(t)}^t x(s) d_s R(t, s) = 0 \end{aligned}$$

are oscillatory. The application of Lemma 6.12 completes the proof. $\square$

Similarly to Theorem 5.10, the following result can be justified.

Theorem 6.15. *If conditions (6.17) and (5.15) hold, then the positive equilibrium K of equation (6.16) is GAS.*

The absolute stability results can also be justified based on [7, Theorem 3.3] which claims that as far as the only positive equilibrium K of the difference equation $x_{n+1} = f(x_n)$ is globally asymptotically stable for any positive x_0 , the equilibrium K of the differential equation $x'(t) = c(t) [\int_{h(t)}^t f(x(s)) d_s R(t, s) - x(s)]$, with $c(t)$ satisfying (6.17), is also globally asymptotically stable.

Theorem 6.16. *If condition (6.17) holds, and in addition,*

$$\limsup_{t \rightarrow \infty} \frac{\beta n}{4} \int_{h(t)}^t c(s) ds < 1 + \frac{1}{e}, \quad (6.21)$$

then the positive equilibrium K of equation (6.16) is GAS.

Proof. Let $x(t)$ be a continuous solution of (6.16). We recall that $R(t, \cdot)$ is nondecreasing for any t , $R(t, t^+) = 1$, thus by Mean Value Theorem for each t there exists $h_1(t)$ such that $h(t) \leq h_1(t) \leq t$, and

$$\int_{h(t)}^t \frac{x^n(s)}{1 + x^n(s)} d_s R(t, s) = \frac{x^n(h_1(t))}{1 + x^n(h_1(t))}.$$

Thus, equation (6.16) is GAS if the equation

$$\frac{dx}{dt} = c(t) \left[\alpha - \beta \frac{x(t)x^n(h_1(t))}{1 + x^n(h_1(t))} \right]$$

is GAS for any $h_1(t)$ satisfying $h(t) \leq h_1(t) \leq t$. Application of Theorem 5.4 and (6.21) completes the proof. $\square$

7. Open problems

Finally we state some open problems and topics for further research.

1. Prove or disprove:

Suppose $f_i : [a, b] \rightarrow \mathbb{R}$, $i = 1, 2$ are continuous functions such that

$$f_i(0) = 0, \quad x f_1(x) > 0 \quad \text{for } x \neq 0,$$

$$0 < a_1 \leq \inf_{x \in [a, b]} \frac{f_1(x)}{x} \leq \sup_{x \in [a, b]} \frac{f_1(x)}{x} < \infty, \quad \sup_{x \in [a, b]} \frac{|f_2(x)|}{f_1(x)} \leq a_2 < 1.$$

Then for any delay function such that $h(t) \leq t$, $\lim_{t \rightarrow \infty} h(t) = \infty$, all solutions of the equation

$$x'(t) + f_1(x(t)) + f_2(x(h(t))) = 0,$$

satisfying the inequality $a \leq x(t) \leq b$ for sufficiently large t , tend to zero.

If the conjecture is correct, consider it for an equation with several delays.

2. Prove or disprove:

If $n \leq 1$ and (5.2) is satisfied then equation (4.1) is absolutely GAS.

Note that for the autonomous equation (1.2) this result was obtained in [12].

3. Prove or disprove:

Let $\lim_{t \rightarrow \infty} \alpha(t) = \alpha > 0$, $\lim_{t \rightarrow \infty} \beta(t) = \beta > 0$, and conditions of Theorem 2.6 hold for autonomous equation (1.2). Then the number K defined by (2.1) is a global attractor for all solutions of nonautonomous equation (1.3).

4. Consider the following generalizations of equation (1.3):

$$\frac{dx}{dt} = \alpha(t) - \beta(t)x(t) \frac{x^n(h(t))}{1 + x^n(h(t))},$$

$$\frac{dx}{dt} = \alpha(t) - \beta(t)x(t) \frac{x^n(h(t))}{1 + x^n(g(t))},$$

$$\frac{dx}{dt} = \alpha(t) - \beta(t)x(g(t)) \frac{x^n(h(t))}{1 + x^n(h(t))}.$$

Study these and the original model with the “control” term added in the right hand side without a delay $\gamma(t)x(t)$ or with a delay $\gamma(t)x(h_0(t))$. Consider periodic impulsive perturbations and possibility of stabilization of equations with variable periodic parameters by periodic impulsive perturbations.

5. Note that condition $\lim_{t \rightarrow \infty} h(t) = \infty$ is not quite natural for equations with a distributed delay. Obtain sufficient permanence conditions, solutions estimates, nonoscillation and stability tests in the following two cases: $h(t) = 0$ and $h(t) = -\infty$.
6. For equations with an unbounded distributed delay and periodic parameters, obtain sufficient conditions for the existence of a positive periodic solution. Investigate stability and oscillation of a periodic positive equilibrium of equations with a distributed delay and a positive periodic solution.

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8. Appendix

Proof of Lemma 5.2. 1) Since

$$f(x) = \int_0^x f'(u) du,$$

after the substitution $u = tx$ we have

$$\frac{f(x)}{x} = \int_0^1 f'(tx) dt.$$

The function $\frac{f(x)}{x}$ is decreasing and

$$\frac{f(x)}{x} \leq \frac{f(a)}{a}.$$

2) Denote $x = t + K, g(t) = K - f(t + K), -K \leq t \leq b - K$. Then $g'(x) > 0, g''(x) < 0$ and $g(0) = 0$. Similarly to the proof of Part 1, we obtain

$$0 \leq \frac{g(t)}{t} \leq \frac{g(-K)}{-K}, \quad \left| \frac{f(x) - K}{x - K} \right| = \left| \frac{g(t)}{t} \right| \leq \left| \frac{g(-K)}{-K} \right| = \left| \frac{f(0) - K}{K} \right|.$$

3) For some ξ we have $f(x) = f'(\xi)x$, thus

$$\frac{f(x)}{x} \leq \max_{a \leq x \leq b} f'(x) = f'(c).$$

4) Denote

$$g(x) = \begin{cases} \frac{f(x)}{x}, & x \neq 0, \\ \alpha, & x = 0. \end{cases}$$

As g is a positive continuous function on $[a, b]$, there exists $\min_{x \in [a, b]} g(x) = a_0 > 0$ and $\frac{f(x)}{x} \geq a_0$ for $x \in [a, b]$, which completes the proof.

Proof of Theorem 5.10. Denote

$$g(x) = \alpha x, \quad f(x) = \frac{\beta}{x^n + 1}, \tag{8.1}$$

then $\alpha K = f(K)$. Firstly, let $n \leq 1$. Then for $x > 0$ $g^{-1}(x) = \frac{1}{\alpha}x$, so the ratio $\frac{|\frac{1}{\alpha}f(x) - K|}{|x - K|}$ attains its maximum on $[0, \infty)$ at $x = 0$. Note also that $\frac{\beta}{\alpha K} - 1 > 0$, since $\frac{\beta}{\alpha K} = K^n + 1$. Thus, if

$$\frac{|g^{-1}(f(y)) - K|}{|x - K|} \leq \frac{|\frac{1}{\alpha}f(0) - K|}{K} = \frac{\beta}{\alpha K} - 1 < 1,$$

or $\beta < 2\alpha K$, then by Lemma 5.8, the equation (4.1) is GAS.

Let $n > 1$. Then $f''(\tilde{x}) = 0$ where $\tilde{x} = (\frac{n-1}{n+1})^{1/n}$. Clearly, $\tilde{x}$ is the only inflection point, where the maximum of the absolute value of the derivative is attained; hence

$$\frac{|\frac{1}{\alpha}f(x) - K|}{|x - K|} = \frac{1}{\alpha}f'(\zeta) \leq \frac{1}{\alpha}f' \left(\left(\frac{n-1}{n+1} \right)^{1/n} \right) = \frac{\beta}{4n\alpha} (n-1)^{1-1/n} (n+1)^{1+1/n} < 1,$$

and Lemma 5.8 implies that equation (4.1) is GAS.

Proof of Lemma 5.9. For simplicity suppose that $m = 1$, the proof in the general case is similar.

First, we prove that any non-oscillatory solution tends to zero. Assume that $x(t) > 0$. Then $\dot{x} < 0$ and thus x is monotone and there is $\lim_{t \rightarrow \infty} x(t) = d$. If $d > 0$ then

$$\lim_{t \rightarrow \infty} [f_0(x(t)) + f_1(x(h(t)))] = f_0(d) + f_1(d) > 0.$$

Hence the equality $x(t) = x(0) - \int_0^t r(s)(f_0(x(s)) + f_1(x(h(s))))ds$ implies $\lim_{t \rightarrow \infty} x(t) = -\infty$. The contradiction leads to $d = 0$. The case $x(t) < 0$ is considered similarly.

Next, suppose that $x(t)$, $a \leq x(t) \leq b$ is an oscillatory solution of (5.14) and $u = \limsup_{t \rightarrow \infty} |x(t)|$. We will prove that $u = 0$.

There are two options: $f_0(u) \geq -f_0(-u)$ or $f_0(u) \leq -f_0(-u)$. Suppose that $f_0(u) \geq -f_0(-u)$, then for any $\varepsilon > 0$ there exist t_1, t_2 such that $-u - \varepsilon < x(t) < u + \varepsilon$, $t \geq t_1$, and $h_1(t) \geq t_1, t \geq t_2 > t_1$. There exists $t_3 > t_2$ such that $x(t_3) > u - \varepsilon$, $\dot{x}(t_3) \geq 0$ or $x(t_3) < -u + \varepsilon$, $\dot{x}(t_3) \leq 0$. Suppose that $x(t_3) > u - \varepsilon$, $\dot{x}(t_3) \geq 0$, then

$$f_0(x(t_3)) + f_1(x(t_3)) \leq 0, \quad f_0(x(t_3)) > f_0(u - \varepsilon),$$

$$f_1(h(x(t_3))) < 0, \quad f_1(h(x(t_3))) \geq \alpha f_0(h(x(t_3))) > \alpha f_0(-u - \varepsilon),$$

which implies $f_0(u - \varepsilon) + \alpha f_0(-u - \varepsilon) \leq 0$. Hence $f_0(u - \varepsilon) \leq -\alpha f_0(-u - \varepsilon)$. Since $\varepsilon > 0$ is an arbitrary small number, $f_0(u) \leq -\alpha f_0(-u) < -f_0(-u)$. This contradiction proves the lemma. The proof for the case $f_0(u) \leq -f_0(-u)$ is similar.