

ON THE PERMANENCE OF THE POSITIVE ABSOLUTELY CONTINUOUS SOLUTIONS OF THE GENERALIZED MACKEY-GLASS MODEL

H. Kiskinov, A. Zahariev, S. Zlatev

Abstract. The aim of the present paper is to study one of possible generalizations of the Mackey-Glass model of respiratory dynamics. Existence of unique global absolutely continuous positive solutions of the Cauchy problem, their boundedness and permanence are proved. Moreover, an example is given which shows that the conditions introduced in this paper are sharp and cannot be weakened even for ordinary differential equations of this type.

Key words: Nonlinear delay equations, Mackey-Glass equation, boundedness, permanence.

Mathematics Subject Classification 2000: 34K25, 34K11, 34K20, 92D25.

1. Introduction

The following classical model

$$(1.1) \quad \frac{dy(t)}{dt} = \lambda - \frac{aV_{max}y(t)y^n(t-\tau)}{b^n + y^n(t-\tau)}$$

is introduced by Mackey and Glass [1] to explain dynamic diseases, such as the Cheyne-Stokes phenomenon (periodic breathing). Here $y(t)$ denotes the arterial concentration of CO_2 , V_{max} denotes the maximum ventilation rate of CO_2 , λ is the CO_2 production rate, and the delay $\tau > 0$ is the time between oxygenation of blood in the lungs and stimulation of chemoreceptors in the brainstem.

According to [1], the ventilation function $\frac{aV_{max}y(t)y^n(t-\tau)}{b^n+y^n(t-\tau)}$ is a sigmoidal type function of y with parameters $b, n > 0$ to be adjusted to fit the experimental data. Detailed description of the nature of model (1.1) and its applications can be found in [1, 2]. Several mathematical results for (1.1) are established in [2–7].

In the remarkable work [8] the following generalization of equation (1.1)

$$(1.2) \quad \frac{dx(t)}{dt} = \alpha(t) - \beta(t)x(t) \frac{x^n(h(t))}{1 + x^n(h(t))}, \quad t \geq 0.$$

is considered.

In the same work for the equation (1.2) several results about existence of global absolutely continuous positive solutions and their permanence are obtained. The stability of the equilibrium and oscillatory properties of the solutions are studied too.

The aim of the present paper is to study for any $p, n > 0$ the nonlinear delay equation

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

which is one of the possible generalizations of (1.2), mentioned in [8], where only the case $n = p$ is considered. Existence of global absolutely continuous positive solutions, their boundedness and permanence are proved. Moreover, an example is given which shows that the conditions introduced by us are sharp and can not be weakened even for ordinary differential equations.

2. Preliminaries

Suppose that $\inf_{t \in \mathbb{R}^+} \tau(t) > -\infty$ and consider equation (1.3) with the initial condition

$$(2.1) \quad x(t) = \varphi(t), \quad t \in [-T, 0], \quad -T = \inf_{t \in \mathbb{R}^+} \tau(t) \leq 0,$$

where $\alpha, \beta : \mathbb{R}^+ \rightarrow \mathbb{R}^+, \mathbb{R}^+ = [0, \infty), \tau : \mathbb{R}^+ \rightarrow [-T, \infty), n, p > 0$ and $\varphi : [-T, 0] \rightarrow \mathbb{R}^+$.

We will say that the conditions (S) hold, when the following conditions S1-S3 are fulfilled:

- S1. The functions α, β are Lebesgue measurable and locally essentially bounded.

S2. The function $\tau(t)$ is a Lebesgue measurable, locally bounded and satisfying for $t \geq 0$ the inequalities $\tau(t) \leq t$ and $\sup_{t \in \mathbb{R}^+} (t - \tau(t)) \leq r < \infty$.

S3. The function $\varphi(t)$ is Borel measurable, bounded and $\varphi(0) > 0$.

For every $f : J \rightarrow \mathbb{R}, J \subset \mathbb{R}$ for which $\sup_{t \in J} |f(t)| < \infty$ we set by definition the norm $\|f\| = \sup_{t \in J} |f(t)|$.

Lemma 2.1. *Let the conditions (S) hold.*

Then there exists a unique positive global absolutely continuous solution on \mathbb{R}^+ of the initial value problem (IVP) (1.3), (2.1).

Proof. Let $\varphi(t)$ be an arbitrary fixed initial function and let M_φ denote the set of all functions $y : [-T, \infty) \rightarrow \mathbb{R}$ such that $y(t) = \varphi(t), t \in [-T, 0]$ and $y|_{\mathbb{R}^+}$ is a continuous function.

Let us denote by D_φ the following set $D_\varphi = \{(t, y) | t \in \mathbb{R}^+, y \in M_\varphi\}$. The set D_φ can be equipped with a distance function

$$d((t_1, y_1), (t_2, y_2)) = |t_1 - t_2| + \|y_1^* - y_2^*\|$$

(see [9, Chapter 3, Subs. 2.4]), where $y_i^*(t) = y_i(t), t_i \geq T$ and if $0 \leq t_i < T$. Then $y_i^*(t) = y_i(t), -t_i \leq t \leq 0$ and $y_i^*(t) = y_i(-t_i), -T \leq t \leq -t_i, i = 1, 2$.

Let us define a functional $F : D_\varphi \rightarrow \mathbb{R}$ by

$$(2.2) \quad F(t, y(t)) = \alpha(t) - \beta(t)y(t) \frac{y^p(\tau(t))}{1 + y^n(\tau(t))}.$$

For each $y \in M_\varphi$ the function $F(t, y(t))$ is defined for almost all $t \in \mathbb{R}^+$ and is a Lebesgue integrable function on every closed subinterval $J \subset \mathbb{R}^+$. Moreover, from (2.2) it follows that for almost all $t \in \mathbb{R}^+$ the functional F is continuous in every $y \in M_\varphi$.

Let $\epsilon > 0$ be arbitrary, $(t_0, y_0) \in D_\varphi$ is an arbitrary point and

$$U((t_0, y_0), \epsilon) = \{(t, y) \in D_\varphi | d((t, y), (t_0, y_0)) \leq \epsilon\}$$

is a bounded neighborhood of the point (t_0, y_0) . Since the function $W(u, v) = uv^p(1 + v^n)^{-1}$ has continuous partial derivatives in every bounded subset of the set $\{(u, v) \in \mathbb{R}^2 | v \geq 0\}$, then from conditions (S) it follows that there exists a Lebesgue integrable on J function $\zeta : J \rightarrow \mathbb{R}^+$ (eventually depending on t_0, ϵ and J), such that the inequalities

$$|F(t, y(t))| \leq \zeta(t), \quad |F(t, y_1(t)) - F(t, y_2(t))| \leq \zeta(t) \|y_1 - y_2\|$$

hold for all points $(t, y), (t, y_1), (t, y_2) \in U((t_0, y_0), \epsilon)$. Then there exists a point $t_\varphi > 0$ such that IVP (1.3), (2.1) has a unique solution $x : (0, t_\varphi) \rightarrow \mathbb{R}^+$ which is absolutely continuous on every closed interval $J_*, J_* \subset (0, t_\varphi)$ (see [9, Chapter 3, Subs. 2.4]). Moreover, if $\lim_{t \rightarrow t_\varphi - 0} x(t)$ is finite, then $t_\varphi = \infty$.

Since $x(0) = \varphi(0) > 0$ according to condition S3 and because $x(t)$ is continuous on $[0, t_\varphi)$, then there exists $\delta \in (0, t_\varphi)$ such that $x(t) > 0$ as $t \in [0, \delta)$. We shall prove that $x(t) > 0$ for any $t \in [0, t_\varphi)$. Assume, on the contrary, that $x(t) \leq 0$ for some $t \in [0, t_\varphi)$ and denote $\tilde{t} = \inf\{t \in [0, t_\varphi) : x(t) \leq 0\} > 0$.

Thus, we have $x(t) > 0$ for $t \in [0, \tilde{t})$ and $x(\tilde{t}) = 0$. On the other hand, from the conditions (S) it follows that the function $\frac{x^p(\tau(t))}{1+x^n(\tau(t))}$ is bounded and nonnegative on the interval $[-r, \tilde{t}]$. Consequently, there exists a positive constant

$$C_{\tilde{t}} = \sup_{t \in [0, \tilde{t}]} \frac{x^p(\tau(t))}{1+x^n(\tau(t))},$$

which implies $x'(t) \geq -C_{\tilde{t}}\beta(t)x(t)$. Hence

$$x(\tilde{t}) \geq x(0) \exp\left(-C_{\tilde{t}} \int_0^{\tilde{t}} \beta(s) ds\right) > 0.$$

The last inequalities violate our assumption that $x(\tilde{t}) = 0$. Therefore, the solution is positive for each $t \in [0, t_\varphi)$.

Equation (1.3) yields $x'(t) \leq \alpha(t)$, hence $x(t) \leq x(0) + \int_0^t \alpha(s) ds$. It means that $\lim_{t \rightarrow t_\varphi - 0} x(t) < \infty$ and therefore $t_\varphi = \infty$.

Thus we have proved the existence of the unique positive global absolutely continuous solution of the IVP (1.3), (2.1). □

Definition 2.1 ([8]). *All positive solutions of a given equation are said to be permanent if there exist $m > 0$ and $M > 0$ such that for any solution $x(t)$ we have*

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

Definition 2.2. *If at least one of the constants m and M depends on some of the solutions, then we will say that the solutions are weakly permanent.*

Definition 2.3. *We will say that the property P is ultimately fulfilled for some function $f : [-r, \infty) \rightarrow \mathbb{R}$ if there exists a point $t_p \geq 0$ such that for the function f the property P holds for each $t \geq t_p$.*

3. Main results

Theorem 3.1. *Let the following conditions be fulfilled:*

1. *The conditions (S) hold.*
2. *There exist positive numbers a, A, b and B such that*

$$0 < a \leq \alpha(t) \leq A < \infty \text{ and } 0 < b \leq \beta(t) \leq B < \infty.$$

3. $p \geq n$.

Then all positive solutions of (1.3) are weakly permanent.

Proof. Let $x(t)$ be an arbitrary global positive solution of IVP (1.3), (2.1), existing according to Lemma 2.1.

Then from (1.3) it follows that for $t \geq 0$ we have $x'(t) \leq A$ and since $p \geq n$ it is simple to see that the function $H(x) = \frac{x^p}{1+x^n}$ is strictly increasing for $x > 0$.

(a) Let assume that there exists a solution $x(t)$ such that $\lim_{t \rightarrow \infty} x(t) = 0$. Then from (1.3) it follows that there exists a number $\epsilon \in (0, a)$, such that ultimately we have $x'(t) \geq a - \epsilon > 0$. Thus, $x(t)$ is ultimately strictly increasing, which is a contradiction. Hence, for each positive solution is fulfilled $\limsup_{t \rightarrow \infty} x(t) > 0$.

(b) Let assume that there exists a solution $x(t)$ such that $\lim_{t \rightarrow \infty} x(t) = \infty$. Since $H(x)$ is strictly increasing for $x > 0$, then from (1.3) it follows that ultimately $x'(t) < 0$ and therefore $x(t)$ is ultimately strictly decreasing, which is impossible. Hence, for each positive solution is fulfilled $\liminf_{t \rightarrow \infty} x(t) < \infty$.

(c) Let $\limsup_{t \rightarrow \infty} x(t) = \infty$. From case (b) it follows that $\liminf_{t \rightarrow \infty} x(t) = q \geq 0$ and therefore there exists a sequence $\{t_k\}$, where $\lim_{k \rightarrow \infty} t_k = \infty$, such that $\lim_{k \rightarrow \infty} x(t_k) = \infty$ and $x'(t_k) \geq 0$ for each $k \in \mathbb{N}$, where by \mathbb{N} we denote the set of all natural numbers. For all $t \geq r$ we have $0 < x(t) \leq x(\tau(t)) + rA$ and therefore $\lim_{k \rightarrow \infty} x(\tau(t_k)) = \infty$. Then from (1.3) we obtain

$$(3.1) \quad 0 \leq x'(t_k) = \alpha(t_k) - \beta(t_k)x(t_k) \frac{x^p(\tau(t_k))}{1+x^n(\tau(t_k))}.$$

From (3.1) it follows that $\lim_{k \rightarrow \infty} \alpha(t_k) = \infty$, which contradicts condition 2 of Theorem 3.1. Thus for each positive solution $\limsup_{t \rightarrow \infty} x(t) < \infty$.

(d) Let us suppose that $\liminf_{t \rightarrow \infty} x(t) = 0$. Then from (a) and (c) it follows that $0 < \limsup_{t \rightarrow \infty} x(t) = q^* < \infty$ and there exists a sequence $\{t_k^*\}$, $\lim_{k \rightarrow \infty} t_k^* = \infty$, such that $\lim_{k \rightarrow \infty} x(t_k^*) = 0$ and $x'(t_k^*) \leq 0$ for each $k \in \mathbb{N}$. Then from (1.3) it follows

$$(3.2) \quad 0 \geq x'(t_k^*) = \alpha(t_k^*) - \beta(t_k^*)x(t_k^*) \frac{x^p(\tau(t_k^*))}{1 + x^n(\tau(t_k^*))}.$$

Since $0 < \limsup_{t \rightarrow \infty} x(t) = q^* < \infty$ then (3.2) implies that $\liminf_{k \rightarrow \infty} \alpha(t_k^*) \leq 0$ which contradicts condition 2 of Theorem 3.1.

The proof is complete. □

Theorem 3.2. *Let the following conditions be fulfilled:*

1. *The conditions (S) hold.*
2. *There exist positive numbers a, A, b and B such that*

$$0 < a \leq \alpha(t) \leq A < \infty \text{ and } 0 < b \leq \beta(t) \leq B < \infty.$$

3. *$p < n < p + 1$.*

Then all positive solutions of (1.3) are weakly permanent.

Proof. Let $x(t)$ be an arbitrary positive solution of the IVP (1.3), (2.1) and let us suppose that $\lim_{t \rightarrow \infty} x(t) = 0$. Then the solution $x(t)$ is bounded and the function

$$H(x(\tau(t))) = \frac{x(\tau(t))^p}{1 + x(\tau(t))^n}$$

is bounded too. Then similarly to case (a) in Theorem 3.1 we can conclude that $x(t)$ is ultimately strictly increasing, which is impossible.

If for some solution we suppose that $\liminf_{t \rightarrow \infty} x(t) = 0$, then from the case considered above it follows that $\limsup_{t \rightarrow \infty} x(t) = q^* > 0$. Then there exists a sequence $\{t_k^*\}$, $\lim_{k \rightarrow \infty} t_k^* = \infty$, such that $\lim_{k \rightarrow \infty} x(t_k^*) = 0$ and $x'(t_k^*) \leq 0$ for each $k \in \mathbb{N}$ and for all $t \geq r$ we have $0 < x(\tau(t)) \leq x(t) + rA$. Since $\sup_k x(\tau(t_k^*)) < \infty$, then from (1.3) and (3.2) it follows that $\liminf_{t \rightarrow \infty} \alpha(t_k^*) \leq 0$, which is impossible.

Let assume that there exists a solution $x(t)$ such that $\lim_{t \rightarrow \infty} x(t) = \infty$. Then the inequalities

$$(3.3) \quad 0 < x(\tau(t)) - rA \leq x(t) \leq x(\tau(t)) + rA$$

are ultimately fulfilled.

From (1.3) and (3.3) it follows that there exists a number $C > 0$ such that the inequality

$$(3.4) \quad 0 < C < \frac{(x(\tau(t)) - rA)^{n-p} x^p(\tau(t))}{1 + x^n(\tau(t))} \leq \frac{x^{n-p}(t) x^p(\tau(t))}{1 + x^n(\tau(t))}$$

ultimately holds.

Since $1 + p - n > 0$, then from (1.3) and (3.4) it follows that ultimately $x'(t) < 0$ and therefore $x(t)$ is ultimately strictly decreasing, which is impossible.

Let us consider the last case: $\limsup_{t \rightarrow \infty} x(t) = \infty$ and $\liminf_{t \rightarrow \infty} x(t) = q > 0$.

Then similarly as in case (c) from the proof of Theorem 3.1 we can conclude that $\limsup_{t \rightarrow \infty} \alpha(t) = \infty$, which contradicts condition 2 of Theorem 3.2. □

Example 1. Let consider IVP (1.3), (2.1) in the case when

$$\tau(t) = t, \quad t \geq -1, \quad p = 1, \quad n = 2, \quad \alpha(t) \equiv \beta(t) \equiv 1, \quad t \in [0, \infty),$$

$$\phi(t) \equiv x(0) = \sqrt[3]{2\sqrt{2} + 3} + \sqrt[3]{2\sqrt{2} - 3}, \quad t \in [-1, 0].$$

Then (1.3) obtains the form

$$x' = \frac{1}{1 + x^2}.$$

This IVP satisfies conditions 1 and 2 of Theorems 3.1 and 3.2, but not conditions 3 of these theorems because $p + 1 = n$.

The unique solution of IVP satisfies the equality $x^3 + 3x - (3t + 4\sqrt{2}) = 0$ and since $1 + \frac{(3t+4\sqrt{2})^2}{4} > 0$ (the cubic function has a unique real positive root for each $t \in \mathbb{R}^+$), then

$$x(t) = \sqrt[3]{\frac{3t + 4\sqrt{2}}{2} + \sqrt{\left(1 + \left(\frac{3t + 4\sqrt{2}}{2}\right)^2\right)}} + \sqrt[3]{\frac{3t + 4\sqrt{2}}{2} - \sqrt{\left(1 + \left(\frac{3t + 4\sqrt{2}}{2}\right)^2\right)}}$$

It is simple to see that this solution is unbounded above when $t \in [0, \infty)$.

This example illustrates that if $p + 1 \leq n$, then IVP (1.3), (2.1) can have an unbounded solution even for ordinary differential equations, and therefore the conditions 3 of Theorem 3.1 and 3.2 are necessary for its validity.

Theorem 3.3. *Let the following conditions be fulfilled:*

1. *The conditions (S) hold.*
2. *There exist positive numbers a, A, b and B such that*

$$0 < a \leq \alpha(t) \leq A < \infty \text{ and } 0 < b \leq \beta(t) \leq B < \infty.$$

3. *Either $p \geq n$ or $p < n < p + 1$.*

Then all positive solutions of (1.3) are permanent.

Proof. From Theorems 3.1 and 3.2 it follows that every positive solution of (1.3) is weakly permanent. This means that the constants m and M depend on the solution $x(t)$, i.e. $m = m(x), M = M(x)$. Let us assume that there does not exist a constant $m > 0$, such that $m \leq m(x)$ for each positive solution $x(t)$ of (1.3).

Then there exists a sequence of positive solutions of (1.3) and sequence $\{t_k\} \subset \mathbb{R}^+$, $\lim_{k \rightarrow \infty} t_k = \infty$, such that $x'_k(t_k) \leq 0$ and $x_k(t_k) < \frac{1}{k}$, $k \in \mathbb{N}$. Then from (2.2) for each $k \in \mathbb{N}$ follows the relation

$$(3.5) \quad 0 \geq x'_k(t_k) = \alpha(t_k) - \beta(t_k)x_k(t_k) \frac{x_k^p(\tau(t_k))}{1 + x_k^n(\tau(t_k))}.$$

Since $|x(t) - x(\tau(t))| \leq \int_{\tau(t)}^t |x'(s)| ds \leq rA$ for $t \geq r$ and $x_k(t_k) < \frac{1}{k}$, therefore $x_k(\tau(t_k)) \leq 1 + rA$ for each $k \in \mathbb{N}$. Thus, from (3.5) it follows that $\liminf_{k \rightarrow \infty} \alpha(t_k) \leq 0$, which is impossible.

Similarly, let us assume that there does not exist a constant $M > 0$, such that $M(x) \leq M$ for each positive solution $x(t)$ of (1.3).

Then we can find a sequence of positive solutions $\{x_k(t)\}$ of (1.3) and a sequence $\{t_k\} \subset \mathbb{R}^+$, $\lim_{k \rightarrow \infty} t_k = \infty$, such that $x'_k(t_k) \geq 0$ and $k \leq x_k(t_k)$, $k \in \mathbb{N}$.

Therefore from (1.3) for each $k \in \mathbb{N}$ we have

$$(3.6) \quad 0 \leq x'_k(t_k) = \alpha(t_k) - \beta(t_k)x_k(t_k) \frac{x_k^p(\tau(t_k))}{1 + x_k^n(\tau(t_k))}.$$

Inequality (3.6) implies that $\limsup_{k \rightarrow \infty} \alpha(t_k) = \infty$, which contradicts condition 2 of Theorem 3.3.

□

Acknowledgements

The authors want to thank the anonymous referees for their critical review of the original manuscript and for the changes suggested.

References

- [1] MACKEY M., AND L. GLASS, Oscillation and chaos in physiological control systems, *Science*, **197**, 1977, 287–289.
- [2] THIEME, H., *Mathematics in population biology*, Princeton University Press, Princeton NJ, 2003.
- [3] KUANG, Y., Delay differential equations with applications in population dynamics, *in: Mathematics in science and engineering*, Vol. 191, Academic press, Boston, MA, 1993.
- [4] CHEN, Y., AND L. HUANG, Existence and global attractivity of a positive periodic respiration model, *Comput. Math. Appl.*, **49**, 2005, 677–687.
- [5] SAKER, S., AND R. AGARWAL, Oscillation and global attractivity in a nonlinear delay periodic model of respiratory dynamics, *Comput. Math. Appl.*, **44**, 2002, 623–632.
- [6] BEREZANSKY, L., AND E. BRAVERMAN, On non-oscillation of a scalar delay differential equation, *Dynam. Systems Appl.*, **6**, 1997, 567–580.
- [7] BEREZANSKY, L., AND E. BRAVERMAN, New stability conditions for linear differential equations with several delays, *Abstr. Appl. Anal.*, 2011, 19 p., Article ID 178568.
- [8] BEREZANSKY, L., E. BRAVERMAN, AND L. IDELS, The Mackey-Glass model of respiratory dynamics: Review and new results, *Nonlinear analysis*, **75**, 2012, 6034–6052.
- [9] KOLMANOVSKII, V., AND A. MYSHKIS, Introduction to the theory and applications of functional differential equations, *In series: Mathematics and its applications*, Vol. 463, Kluwer Academic publishers, Dordrecht, 1999, p. 648.

Faculty of Mathematics and Informatics
University of Plovdiv
236 Bulgaria Blvd.,
4003 Plovdiv, Bulgaria
e-mail: kiskinov@uni-plovdiv.bg,
zandrey@uni-plovdiv.bg,
szlatev@uni-plovdiv.bg

Received 24 October 2012

**ВЪРХУ ПЕРМАНЕНТНОСТТА НА ПОЛОЖИТЕЛНИТЕ
АБСОЛЮТНО НЕПРЕКЪСНАТИ РЕШЕНИЯ НА
ОБОБЩЕН МОДЕЛ НА MASKEY-GLASS**

Христо Кискинов, Андрей Захариев, Стоян Златев

Резюме. В представената работа е изследвано едно от възможните обобщения на уравнението на Maskey-Glass, моделиращо респираторната динамика. Доказано е съществуването на единствено глобално, положително абсолютно непрекъснато решение на задачата на Коши, неговата ограниченост и перманентност. Приведен е пример, който показва че въведените в статията условия не могат да бъдат отслабени даже и в случая на обикновени диференциални уравнения от този тип.