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The 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.

1. Preliminaries

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

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

was introduced by Mackey and Glass in 1977 [1]. 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 [1], 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 [1–3], mathematical results for (1.1) were presented in [2,4–9].

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

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

with the initial function $x(t) = \varphi(t)$ for $-\tau \le t \le 0, \varphi \in C[[-\tau, 0], \mathbb{R}^+]$ 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

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

and the initial condition

$$x(t) = \varphi(t), \quad t \le 0. \tag{1.4}$$

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

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

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

$$h(t) \le t \quad \text{and} \quad \lim_{t\to\infty} h(t) = \infty. \tag{1.6}$$

Also assume that $\varphi(t)$ 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 Eq. (1.3) into

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

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

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

For example, Eq. (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 the 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 the 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 [6], 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, Eq. (1.2) has a unique positive equilibrium K determined by the equation

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

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

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

where $a = \frac{\alpha}{K}$ and $b = \frac{\alpha n}{K(1+K^n)}$. Based on a classical result [10], any solution of Eq. (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).*