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Global stability for non-monotone delay equations (with application to a model of blood cell production)

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A B S T R A C T

A set of sufficient conditions for the global stability of the positive equilibrium is established for a large class of non-monotone time-delayed differential equations by the method of fluctuations and the exponential ordering approach. Then these analytic results are applied to a mathematical model of white blood cell production. Numerical simulations are also presented to illustrate the global stability regions of parameters and the long-term behavior of solutions.

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1. Introduction

Time delays are known to cause instability and periodic oscillations in dynamical systems. Delay differential equations have attracted a significant interest in recent years due to their frequent appearance in a wide range of applications. They serve as mathematical models describing various phenomena in physics, biology, physiology, and engineering, see, e.g., [3,11,16,28] and references therein.

There has been an extensive theoretical works on delay differential equations in the past three decades. The research topics include global asymptotic stability of equilibria, existence of periodic

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solutions, complicated behavior and chaos, see, e.g., [7,19,27]. The main purpose in the analysis of dynamical systems arising in applications is to determine the (long-term) asymptotic behavior of solutions. From the viewpoint of dynamical systems, one wishes to determine the structure of global attractors. In [18], the authors gave sufficient conditions for the existence of interior global attractors and equilibria for uniformly persistent dynamical systems; using the graph theory, a Lyapunov functions approach was developed in [12] for large-scale coupled systems; the global stability in a time-delayed logistic population model and an SIR epidemic model with time delay was addressed in [15] and [4], respectively.

When a time-delayed system admits the comparison principle, the powerful theory of monotone semi-flows can be applied to study the global stability, see, e.g., [19]. However, if the system is not monotone, the global stability is a challenging research topic. For non-quasi-monotone functional differential equations, Smith and Thieme [20] introduced an exponential ordering and proved that if the delay is small enough, then the time-delayed system generates an eventually strongly monotone semi-flow.

The purpose of this paper is to establish the global attractivity for a class of general functional differential equations with distributed delay by using the method of fluctuations (see, e.g., [10,23,27]) and the exponential ordering approach presented in [20]. We obtain a series of criteria for the global stability and then apply them to a mathematical model of white blood cell production.

Hematological disorders are the diseases affecting blood cells and characterized by significant oscillations in the number of circulating cells, with periods from weeks to months and amplitudes varying from normal to low levels or normal to high levels depending on the cell types (see, e.g., [1,9]). Due to their interesting dynamical characteristics, hematological periodic diseases are good candidates for using mathematical modeling and bifurcation theory to better understand the underlying mechanisms of hematopoiesis and even to potentially understand how clinical treatment affects dynamics [14]. Mackey [13] proposed a pluripotential stem cell model by considering the interactive properties between proliferating-phase cell and resting-phase cells with the distinction that cells travel through proliferation as if in a pipeline to undergo mitosis as a fixed cell cycle time. In a more realistic model, the maturation data may follow a statistical distribution. Starting with an age structured model, one can incorporate with experimental data in the maturation process by introducing a distributed time delay function. For more details, we refer to [1]. The global stability of the trivial equilibrium and the local stability of the positive equilibrium were discussed in [1]. More recently, the local stability and Hopf bifurcation were studied in [26] for this model with distributed time delay and the obtained results show that the occurrence of Hopf bifurcation depends on the system parameters and the choice of distribution of time delays. In the current paper, we further study the global stability of the positive equilibrium for such a non-monotone system in order to rule out the existence of oscillations.

The rest of the paper is organized as follows. In the next section, we will discuss the global stability for a class of functional differential equation under certain assumptions and establish sufficient conditions to ensure the global attractivity. In Section 3, we use the obtained results to analyze a blood cell model and provide some explicit conditions and numerical simulations for the global stability. A brief discussion section completes the paper.

2. Global stability

We consider a class of functional differential equation

$$u'(t) = -\alpha u(t) + f_1\big(u(t)\big) + \int_{\tau_0}^{\tau_1} \hat{k}(s) f_2\big(u(t-s)\big)\,ds \tag{1}$$

where $\alpha > 0$, $\hat{k}(s)$ is a generalized kernel function with respect to probability distribution, $\hat{k}(s) \geqslant 0$ for $s \geqslant 0$ and $\hat{k}(s) = 0$ when $0 \leqslant s < \tau_0$ or $s > \tau_1$, and $0 \leqslant \tau_0 < \tau_1$.

When $f_1(u) \equiv 0$, $\hat{k}(s) = \delta(s - \tau)$ (the Dirac delta function) and $f_2(u) = \frac{\beta_0 \theta^n}{\theta^n + u^n}$ or $f_2(u) = \frac{\beta_0 \theta^n u}{\theta^n + u^n}$, Eq. (1) reduces to the models of hematopoiesis proposed by Mackey and Glass [16] in the study of

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