Available online at www.sciencedirect.com
ScienceDirect
Applied Mathematics and Computation 190 (2007) 846–850
APPLIED MATHEMATICS AND COMPUTATION
www.elsevier.com/locate/amc

On the global attractivity controversy for a delay model of hematopoiesis

Gergely Röst *

Analysis and Stochastics Research Group, Hungarian Academy of Sciences, Bolyai Institute, University of Szeged, Aradi vértanúk tere 1, H-6720 Szeged, Hungary
Department of Mathematics and Statistics, York University, 4700 Keele Str., Toronto, Ont., Canada M3J 1P3

Abstract

Recently, particular counterexamples were constructed to some theorems of a previous paper, concerning the global attractivity of the positive equilibrium for the delay equation

$$\dot{p}(t) = \frac{\beta p^m(t-\tau)}{1+p^n(t-\tau)} - \gamma p(t).$$

The purpose of this note is to explore the underlying phenomenon from a more general point of view, and to give an explanation of the situation. A theorem is proved regarding attractivity properties of the equilibrium zero.

Keywords: Delay differential equation; Stability; Global attractivity; Hematopoiesis

1. Introduction

Consider the scalar delay differential equation with constant coefficients

$$\dot{p}(t) = \frac{\beta p^m(t-\tau)}{1+p^n(t-\tau)} - \gamma p(t), \tag{1}$$

where $\tau, \beta, \gamma \in (0, \infty)$ and $m, n \in \mathbb{N}$. This equation was proposed to describe the dynamics of hematopoiesis, the process of blood cell production. When $m = 1$, Eq. (1) reduces to the well-known "classical" Mackey–Glass equation.

Clearly 0 is an equilibrium of Eq. (1), and a positive equilibrium $\bar{p}$, if exists, satisfies

$$\gamma\bar{p} = \frac{\beta\bar{p}^m}{1+\bar{p}^n}. \tag{2}$$

* Address: Department of Mathematics and Statistics, York University, 4700 Keele Str., Toronto, Ont., Canada M3J 1P3.
E-mail address: rost@math.u-szeged.hu

0096-3003/$ - see front matter
doi:10.1016/j.amc.2007.01.103

In the special case where $n > m$ and there is a unique positive equilibrium $\bar{p}$, [1] claimed that

(i) if p is a positive solution of Eq. (1), which does not oscillate about $\bar{p}$, then $\lim_{t\to\infty} p(t) = \bar{p}$, and
(ii) if τ is small enough, then $\lim_{t\to\infty} p(t) = \bar{p}$ for every positive solution p.

Counterexamples were recently constructed in [2] for the above claim for certain values of the parameters, however it was not clear why this claim is invalid in general.

In Section 2, we discuss the relation between the shape of the delayed feedback function and the dynamics of solutions. We show that if $m \geqslant 2$, then the positive equilibrium can not be attractive, simply because of the linear stability of the zero solution. Hence, there is no need to construct specific counterexamples to show that the cited results of [1] are not valid.

In Section 3, applying the theory of monotone dynamical systems (see [3]), we prove that the trivial equilibrium is not only stable, but even attracts a large subset of positive solutions, independently of the delay τ.

2. The delayed feedback function

The differential equation

$$\dot{x}(t) = -\mu x(t) + f(x(t-\tau)) \tag{3}$$

with parameter $\mu \geqslant 0$ was widely discussed in the literature. The global dynamics, structure of the global attractor, existence and properties of periodic orbits were studied in details for the monotone positive and the monotone negative feedback case, see [4–7] and references thereof. The case, where $f(\xi)$ is not a monotone function, is obviously more complicated. It was shown [8] that a unimodal feedback may lead to chaotic behavior.

Many well-known model equations are of the form Eq. (3), when f is a positive "hump-shaped" function. We mention the Nicholson blowflies equation [3], where $f(\xi) = a\xi\exp(-b\xi)$, or the Mackey–Glass equation [9], where $f(\xi) = a\xi/(1+\xi^n)$. The latter is also an example of a scalar delay differential equation that exhibits chaotic behavior. The profile suggested by the Nicholson blowflies equation and the Mackey–Glass equation is sketched in Fig. 1a. Much has done about the global attractivity of the positive equilibrium, however, the equivalence of local and global stability is still an open and interesting problem. For an overview and related results, see [10] and references therein.

Functions with a slightly different profile, as described in Fig. 1b, are also used in various population models, with $f(\xi) = a\xi^2\exp(-b\xi)$, or $f(\xi) = \beta\xi^m/(1+\xi^n)$ with $n > m \geqslant 2$.

For the special case $f(\xi) = \beta\xi^m/(1+\xi^n)$, $\beta > 0$, $n > m \geqslant 2$, studied in [1,2], we have $f'(\xi) = 0$ if $\xi = 0$ or $\xi = \xi_0 := \sqrt[m]{\frac{m}{n-m}}$. Moreover, f is monotonically increasing on $[0, \xi_0]$ and decreasing on $[\xi_0, \infty)$. Remark that $f(0) = f'(0) = 0$, so we are in the case Fig. 1b. Linearizing Eq. (1) at zero, we obtain the variational equation

$$\dot{y}(t) = -\mu y(t). \tag{4}$$

Therefore, the zero equilibrium is locally asymptotically stable, independently of the delay τ. Its such a positive equilibrium (if exists) can not be globally attractive. This explains why the aforementioned claim of [1] is

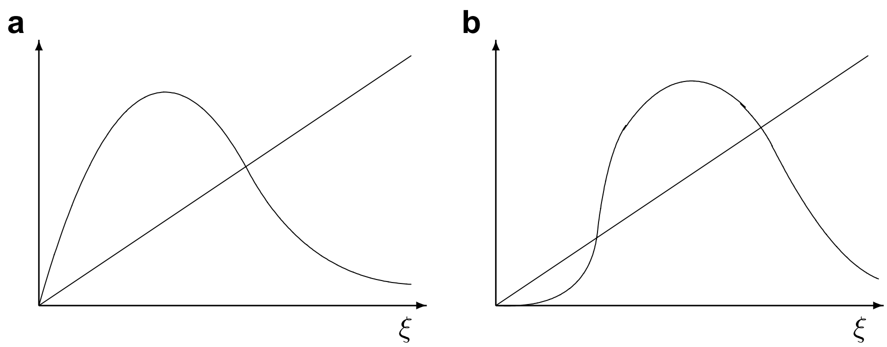

Fig. 1. Different possible profiles of the delayed feedback function $f(\xi)$.

incorrect. We note that in the proof of the claim, the authors first proved that if a solution $p(t) > \bar{p}$ does not oscillate about $\bar{p}$, then $\lim_{t\to\infty} p(t) = \bar{p}$. This argument is correct, the remark "the case $p(t) < \bar{p}$ is similar, hence omitted" is wrong. It is similar only if the shape of the delayed feedback function behaviors like Fig. 1a, not b.

The case $f(\xi) = \beta\xi^m/(1+\xi^n)$ with $m \geqslant 2$ is qualitatively different from the case $m = 1$. If $\beta > 0$, $n > m \geqslant 2$, then there is a certain propriate value μ_0 of μ such that Eq. (3) with $\mu = \mu_0$ possesses a unique positive equilibrium. When $\mu < \mu_0$, then the system has at least two positive equilibria, when $\mu > \mu_0$, than Eq. (3) has no positive equilibrium.

3. Attractivity of the trivial equilibrium

It becomes natural now that we should consider the attractivity of the trivial equilibrium of Eq. (3) with the profile described in Fig. 1b. In this section, we consider Eq. (3), where

$$f(\xi) \geqslant 0 \text{ for all } \xi \geqslant 0, f(0) = 0, f'(0) = 0 \text{ and there is a unique } \xi_0 > 0 \text{ such that } f'(\xi) > 0 \text{ if } 0 < \xi < \xi_0,\ f'(\xi_0) = 0 \text{ and } f'(\xi_0) < 0 \text{ if } \xi > \xi_0. \tag{5}$$

The function $f(\xi) = \beta\xi^m/(1+\xi^n)$, with $\beta > 0$ and $n > m \geqslant 2$, fulfills (5). Remark that (5) allows the existence of several positive equilibria of Eq. (3).

Let us recall some related definitions and terminology from the theory of semiflows (for more details, see [3]). Let $C = C([-\tau, 0], \mathbb{R})$ denote the Banach space of continuous functions $\phi : [-\tau, 0] \to \mathbb{R}$ with the norm given by

$$||\phi|| = \max_{-\tau\leqslant s\leqslant 0} |\phi(s)|.$$

Every $\phi \in C$ determines a unique continuous function $x = x^\phi : [-\tau, \infty) \to \mathbb{R}$, which is differentiable on $(0, \infty)$, satisfies (3) for all $t > 0$, and $x(s) = \phi(s)$ for all $s \in [-\tau, 0]$. The segment $x_t \in C$ of a solution is defined by the relation $x_t(s) = x(t+s)$, where $s \in [-\tau, 0]$ and $t \geqslant 0$. Then, $x_0 = \phi$ and $x_t(0) = x(t)$. The family of maps

$$\Phi_t(\phi) : [0, \infty) \times C \ni (t, \phi) \to x_t(\phi) \in C$$

defines a continuous semiflow on C. For any $\xi \in \mathbb{R}$, we write ξ_* for the element of C satisfying $\xi_*(s) = \xi$ for all $s \in [-\tau, 0]$. The set of equilibria of the semiflow generated by (3) is given by

$$E = \{\xi_* \in C : \xi \in \mathbb{R} \text{ and } \mu\xi = f(\xi)\}.$$

Obviously $0_* \in E$. The Banach space C contains the cone

$$C_+ = \{\phi \in C : \phi(s) \geqslant 0, -\tau \leqslant s \leqslant 0\},$$

which generates various order relations on the space C, denoted by usual notations such as $<, \leqslant, \ll$. In particular, $\phi \leqslant \psi$ holds in C if and only if $\phi(s) \leqslant \psi(s)$ for all $s \in [-\tau, 0]$; $\phi < \psi$ if and only if $\phi \leqslant \psi$ and $\phi \neq \psi$; $\phi \ll \psi$ if and only if $\phi(s) < \psi(s)$ for all $s \in [-\tau, 0]$. Thus we can define the order intervals $[\phi, \psi] := \{\zeta \in C : \phi \leqslant \zeta \leqslant \psi\}$ if $\phi \leqslant \psi$ and $(\phi, \psi) := \{\zeta \in C : \phi \ll \zeta \ll \psi\}$ if $\phi \ll \psi$.

A semiflow Φ is said to be monotone provided

$$\Phi_t(\phi) \leqslant \Phi_t(\psi), \quad \text{whenever } \phi \leqslant \psi \text{ and } t \geqslant 0.$$

It is easy to see that if $f'(\xi) \geqslant 0$ for all $\xi \in \mathbb{R}$, then (3) defines a monotone semiflow. Furthermore, if (5) is satisfied, then the cone C_+ is positively invariant.

Lemma 1. *If $[q_*, r_*]$ is a positively invariant order interval for some $q < r$ and $f'(\xi) \geqslant 0$ for all $\xi \in [q, r]$, then the solution $x^{r_*}(t)$ with initial value r_* converges to an equilibrium.*

Proof. The positive invariance of the order interval $[q_*, r_*]$ implies $x_t^{r_*} \leqslant r_*$ for all $t \geqslant 0$. In this interval, the semiflow is monotone, hence we have $x_{t+u}^{r_*} \leqslant x_u^{r_*}$, for $t, u > 0$. Equivalently, $q_* \leqslant x_t^{r_*} \leqslant x_u^{r_*} \leqslant r_*$ whenever $0 \leqslant u \leqslant t$. Evaluating each functions in the previous inequality at $s = 0$, yields $q \leqslant x^{r_*}(t) \leqslant x^{r_*}(u) \leqslant r$, that is $x^{r_*}(t)$ is monotone decreasing. We obtain that $\lim_{t\to\infty} x^{r_*}(t) \to w$ for some $w \in [q, r]$, hence the ω-limit set of $x_t^{r_*}$ is the singleton $\{w_*\}$, that must be an equilibrium. □

Lemma 2. *If there is no positive equilibrium, then the order interval* $[0_*, \xi_{0*}]$ *is positively invariant and all positive solutions eventually enter this interval.*

Proof. If 0 is the unique nonnegative equilibrium, then $\mu\xi_0 > f(\xi_0) \geqslant f(\xi)$ for any $\xi \geqslant 0$. First notice that if $x(t)$ is a solution and $x(t_0) \leqslant \xi_0$ for some $t_0 > 0$, then $x(t) \leqslant \xi_0$ for all $t > t_0$. Otherwise there exists a $t_1 \geqslant t_0$ such that $x(t_1) = \xi_0$ and $x'(t_1) \geqslant 0$. But $x'(t_1) = -\mu\xi_0 + f(x(t_1 - \tau)) < 0$, a contradiction. This implies the positive invariance of $[0_*, \xi_{0*}]$.

Now we show that all positive solutions eventually enter this interval. Suppose the contrary, i.e. that there exist a $t_2 > 0$ and a solution $x(t)$ with $x(t) > \xi_0$ for all $t > t_2$. Let $\delta := \mu\xi_0 - f(\xi_0) > 0$. If follows that $x'(t) < -\delta$ for all $t > t_2 + \tau$ and hence $x(t) \to -\infty$ as $t \to \infty$, contradicting to $x(t) > \xi_0$ for all $t > t_2$. □

Lemma 3. *If* $\bar{p}$ *is the unique or the smallest positive equilibrium, then the order interval* $[0_*, \xi_*]$ *is positively invariant for each* $\xi \in (0, \bar{p}]$.

Proof. For each $\xi \in [0_*, \bar{p}_*]$, $f(\xi) < \mu\xi$. The function $f(\xi)$ is increasing on $[0_*, \bar{p}_*] \subset [0_*, \xi_{0*}]$, hence if $x(t_0) = \xi$ and $x(t) \leqslant \xi$ for $t < t_0$, then $x'(t_0) = -\mu\xi + f(x(t_0 - \tau)) < -\mu\xi + f(\xi) < 0$. □

Theorem 1.

(*i*) *If* 0 *is the unique nonnegative equilibrium, then all solutions of* (3) *with initial values* $\phi(s) \geqslant 0$ *for* $s \in [-\tau, 0]$ *converge to the zero solution.*

(*ii*) *If* $\bar{p}$ *is the unique or the smallest positive equilibrium, then all solutions with initial values contained in the order interval* $[0_*, \bar{p}_*)$ *converge to* 0.

Proof. When 0 is the unique equilibrium, then by Lemma 2 all solutions enter the positively invariant order interval $[0_*, \xi_{0*}]$ where the semiflow is monotone and we can apply Lemma 1.

When $\bar{p}$ is the unique or the smallest positive equilibrium, then we restrict our attention to the order interval $[0_*, \bar{p}_*]$, which is positively invariant by Lemma 3. Since $\bar{p} \leqslant \xi_0$, the semiflow restricted to the order interval $[0_*, \bar{p}_*]$ is monotone and $E = \{0_*, \bar{p}_*\}$. Due to Lemma 1, all solutions converge to 0 or $\bar{p}$. To prove the theorem, it is enough to show that a point of $[0_*, \bar{p}_*)$ can not converge to $\bar{p}$. By Lemma 3, if $c < \bar{p}$, then $[0_*, c_*]$ is positively invariant. For any $\phi \in [0_*, \bar{p}_*)$, we can choose a $c < \bar{p}$ such that $\phi < c_*$, then $\phi \in [0_*, c_*]$. Hence by the invariance of the order interval $[0_*, c_*]$, we find that x^ϕ can not converge to $\bar{p}$ and Lemma 1 guarantees that x^ϕ converges to 0. □

Acknowledgement

Supported in part by the Hungarian Foundation for Scientific Research, Grant T 049516 and National Sciences and Engineering Research Council of Canada.

References

[1] S.H. Saker, Oscillation and global attractivity in hematopoiesis model with delay time, Appl. Math. Comput. 136 (2003) 241–250.
[2] S.J. Yang, B. Shi, D.C. Zhang, M.J. Gai, Counterexamples to the article Oscillation and global attractivity in hematopoiesis model with delay time, Appl. Math. Comput. 168 (2005) 973–980.
[3] H.L. Smith, Monotone dynamical systems: an introduction to the theory of competitive and cooperative systems, Mathematical Surveys and Monographs, vol. 41, American Mathematical Society (AMS), Providence, RI, 1995.
[4] H.-O. Walther, The two-dimensional attractor of $x'(t) = -\mu x(t) + f(x(t-1))$, Mem. Am. Math. Soc. 113 (544) (1995) 1–76.
[5] T. Krisztin, H.-O. Walther, J. Wu, Shape, smoothness and invariant stratification of an attracting set for delayed monotone positive feedback, Fields Institute Monographs, 11, American Mathematical Society (AMS), Providence, RI, 1999.
[6] T. Krisztin, Periodic orbits and the global attractor for delayed monotone negative feedback, Proc. Colloq. Qual. Theory Differ. Equat. (Szeged 1999), Electron. J. Qual. Theory Differ. Equat. 15 (2000) 1–12.

[7] T. Krisztin, H.-O. Walther, Unique periodic orbits for delayed positive feedback and the global attractor, J. Dynam. Differ. Equat. 13 (1) (2001) 1–57.
[8] B. Lani-Wayda, Erratic solutions of simple delay equations, Trans. Am. Math. Soc. 351 (3) (1999) 901–945.
[9] M.C. Mackey, L. Glass, Oscillation and chaos in physiological control systems, Science 197 (1977) 287–289.
[10] E. Liz, E. Trofimchuk, S. Trofimchuk, Mackey–Glass type delay differential equations near the boundary of absolute stability, J. Math. Anal. Appl. 275 (2) (2002) 747–760.