Siberian Mathematical Journal, Vol. 59, *No.* 1, *pp.* 113–125, 2018

GLOBAL SOLVABILITY AND ESTIMATES OF SOLUTIONS TO THE CAUCHY PROBLEM FOR THE RETARDED FUNCTIONAL DIFFERENTIAL EQUATIONS THAT ARE USED TO MODEL LIVING SYSTEMS

© **N. V. Pertsev**

UDC 517.929

Abstract: We study the Cauchy problem for the retarded functional differential equations that model the dynamics of some living systems. We find certain conditions ensuring the existence, uniqueness, and nonnegativity of solutions on finite and infinite time intervals. We obtain upper bounds for solutions and prove the continuous dependence of solutions on the initial data on finite time intervals.

DOI: 10.1134/S0037446618010135

Keywords: retarded functional differential equation, Cauchy problem, global solvability, nonnegativity of solutions, boundedness of solutions, mathematical biology, living systems

Introduction

Many mathematical models describing the dynamics of living systems can be expressed as

$$\frac{dx_i(t)}{dt} = f_i(t, x_t) - (\mu_i + g_i(t, x_t))x_i(t), \quad t \geq 0, \tag{1}$$

$$x_i(t) = \psi_i(t), \quad t \in I_\omega = [-\omega, 0],\ 1 \leq i \leq m, \tag{2}$$

where $x(t) = (x_1(t), \dots, x_m(t))^T$ is the number of species in the living system at time t, $x_i(t)$ is the number of type i elements, $\psi_i(t)$ is the initial number of type i elements, for $1 \leq i \leq m$, while $\omega \geq 0$ is some constant, $x_t : I_\omega \to R^m$ is a retarded variable defined as $x_t(\theta) = x(t + \theta)$ for $\theta \in I_\omega$ and $t \geq 0$; for $t = 0$, taking (2) into account, we put $x_0(\theta) = \psi(\theta) = (\psi_1(\theta), \dots, \psi_m(\theta))^T$ for $\theta \in I_\omega$. The right-hand side of (1) determines the rate of change of $x_i(t)$, where $f_i(t, x_t)$ is the birth rate of type i elements in the system, $(\mu_i + g_i(t, x_t))x_i(t)$ is the death rate of type i elements, their passage to other systems, or transformation into elements of type $j \neq i$, for $1 \leq i, j \leq m$.

To further formalize (1), (2) and study of the model, we will use the following notation and definitions. Denote the $m \times m$ identity matrix by I and the norm of a vector $v \in R^m$ by $\|v\|_{R^m} = \sum_{i=1}^m |v_i|$. Given $u, w \in R^m$, the inequalities $u < 0$, $u > 0$, $u \leq w$, and $u \geq w$ are understood componentwise. For $J = [a, b] \subset R$ and $A \subseteq R^m$, denote by $C(J, A)$ the set of all continuous functions $z : J \to A$. Given $\gamma \in R_+$, $C(J, R^m)$ is a Banach space with the norm

$$\|z\|_\gamma = \max_{\theta \in J}(e^{-\gamma\theta}\|z(\theta)\|_{R^m}), \quad z \in C(J, R^m).$$

In case $\gamma = 0$ we use the standard notation $\|z\|_0 = \|z\|$. Denote the balls in $C(I_\omega, R^m)$ by $B_d = \{z \in C(I_\omega, R^m) : \|z\| \leq d\}$. If $x, y \in C(J, A)$ then for each $t \in J$ we understand the inequality $x(t) \leq y(t)$ as the inequality between the corresponding vectors.

A functional $h : C(I_\omega, R_+^m) \to R_+^m$ is called *isotonic* whenever $h(z^{(1)}) \leq h(z^{(2)})$ for all $z^{(1)}, z^{(2)} \in C(I_\omega, R_+^m)$ with $z^{(1)}(\theta) \leq z^{(2)}(\theta)$, where $\theta \in I_\omega$.

Say that a functional $K : C(I_\omega, R_+^m) \times C(I_\omega, R_+^m) \to R_+^m$ has the *mixed monotonicity property* if $K(x, y)$ is isotonic in x and antitonic in y; namely, $K(x^{(1)}, y^{(1)}) \leq K(x^{(2)}, y^{(2)})$ for all $(x^{(i)}, y^{(i)}) \in C(I_\omega, R_+^m) \times C(I_\omega, R_+^m)$, for $i = 1, 2$, with $x^{(1)}(\theta) \leq x^{(2)}(\theta)$ and $y^{(1)}(\theta) \geq y^{(2)}(\theta)$, where $\theta \in I_\omega$.

Omsk. Translated from *Sibirskiĭ Matematicheskiĭ Zhurnal*, Vol. 59, No. 1, pp. 143–157, January–February, 2018; DOI: 10.17377/smzh.2018.59.113. Original article submitted December 11, 2016.

Let us introduce a series of assumptions about the mappings, functions, and constants appearing in (1), (2), and denote the collection of them for all $1 \le i \le m$ by (H0):

(1) $f_i, g_i : R_+ \times C(I_\omega, A_\xi) \to R$, where $A_\xi = \{u \in R^m : u \ge \xi\}$, $\xi \in R^m$, with $\xi < 0$ is a fixed vector;

(2) $f_i, g_i : R_+ \times C(I_\omega, R_+^m) \to R_+$;

(3) $f_i(t, z)$ and $g_i(t, z)$ are continuous in $(t, z) \in R_+ \times C(I_\omega, A_\xi)$ and locally Lipschitz in z: for each $d \in R$ with $d > 0$ there exist constants $L_f^{(i)} = L_f^{(i)}(\xi, d) > 0$ and $L_g^{(i)} = L_g^{(i)}(\xi, d) > 0$ such that

$$|f_i(t, z_1) - f_i(t, z_2)| \le L_f^{(i)} \|z_1 - z_2\|, \quad |g_i(t, z_1) - g_i(t, z_2)| \le L_g^{(i)} \|z_1 - z_2\|$$

for all $z_1, z_2 \in B_d \cap C(I_\omega, A_\xi)$ and $t \in [0, \infty)$;

(4) $\psi_i : I_\omega \to R_+$ is a continuous function;

(5) $\mu_i > 0$.

We regard (1), (2) as a Cauchy problem for retarded functional differential equations. Refer as a *solution* of the Cauchy problem (1), (2) on the finite interval $[0, \tau)$ to a continuous function $x = (x_1, \dots, x_m)^T$ on the interval $I_\omega \cup [0, \tau)$ which is continuously (componentwise) differentiable on the interval $[0, \tau)$ and satisfies the initial conditions (2) and equations (1) for all $t \in [0, \tau)$; for $t = 0$ put

$$\frac{dx_i(0)}{dt} = f_i(0, \psi) - (\mu_i + g_i(0, \psi))\psi_i(0), \quad 1 \le i \le m.$$

Say that the Cauchy problem (1), (2) is *uniquely solvable* on the semiaxis $[0, \infty)$, or *globally solvable*, whenever it has a unique solution on every finite interval $[0, \tau)$.

It is known [1, Chapter 2, Section 2.1] that finding a solution of the Cauchy problem (1), (2) is equivalent to solving the system of integral equations

$$x_i(t) = \psi_i(0) + \int_0^t (f_i(s, x_s) - (\mu_i + g_i(s, x_s))x_i(s))\, ds, \quad 1 \le i \le m, \ t \ge 0, \tag{3}$$

complemented with the initial data (2). Apart from (3), (2), there are other equivalent formulations of the Cauchy problem (1), (2). Integrating (1), (2) by variation of constants, we arrive at the system of integral equations

$$x_i(t) = e^{-\int_0^t (\mu_i + g_i(s, x_s))\, ds} \psi_i(0) + \int_0^t e^{-\int_a^t (\mu_i + g_i(s, x_s))\, ds} f_i(a, x_a)\, da, \ 1 \le i \le m, \ t \ge 0, \tag{4}$$

complemented with the initial data (2). Moreover, we can also express (4) in another form, useful for estimating the solutions to (1), (2). Namely,

$$x_i(t) = e^{-\int_0^t (\mu_i + g_i(s, x_s))\, ds} \left(\psi_i(0) + \int_0^t \frac{f_i(a, x_a)}{\mu_i + g_i(a, x_a)}\, d\, e^{\int_0^a (\mu_i + g_i(s, x_s))\, ds} \right), \tag{5}$$
$$1 \le i \le m, \ t \ge 0.$$

The goal of this article is to obtain a collection of conditions on the mappings $f_i(t, z)$ and $g_i(t, z)$ for $1 \le i \le m$ which will ensure:

(1) the global solvability of the Cauchy problem (1), (2);

(2) the nonnegativity and boundedness of solutions to this problem on $[0, \infty)$;

(3) continuous dependence of the solutions on the initial data on finite time intervals.

1. Auxiliary Statements

Put

$$f(t,x_t)=(f_1(t,x_t),\dots,f_m(t,x_t))^T,$$
$$g(t,x_t)=\operatorname{diag}(g_1(t,x_t),\dots,g_m(t,x_t)),$$
$$\varphi(t,x_t)=(\varphi_1(t,x_t),\dots,\varphi_m(t,x_t))^T=f(t,x_t)-(\mu+g(t,x_t))x(t),$$
$$\rho(t,x_t)=(\rho_1(t,x_t),\dots,\rho_m(t,x_t))^T,$$
$$\rho_i(t,x_t)=f_i(t,x_t)/(\mu_i+g_i(t,x_t)),\quad 1\le i\le m,\ t\ge 0,$$
$$\mu=\operatorname{diag}(\mu_1,\dots,\mu_m),$$
$$e^{-\int\limits_a^t(\mu+g(s,x_s))\,ds}=\operatorname{diag}\Bigl(e^{-\int\limits_a^t(\mu_1+g_1(s,x_s))\,ds},\dots,e^{-\int\limits_a^t(\mu_m+g_m(s,x_s))\,ds}\Bigr),\quad t\ge a\ge 0.$$

Rearrange the systems (3), (2) and (4), (2) as

$$x(t)=\psi(0)+\int\limits_0^t\varphi(a,x_a)\,da,\quad t\ge 0,\tag{6}$$

$$x(t)=\psi(t),\quad t\in I_\omega,\tag{7}$$

$$x(t)=e^{-\int\limits_0^t(\mu+g(s,x_s))\,ds}\psi(0)+\int\limits_0^t e^{-\int\limits_a^t(\mu+g(s,x_s))\,ds}f(a,x_a)\,da,\quad t\ge 0,\tag{8}$$

$$x(t)=\psi(t),\quad t\in I_\omega.\tag{9}$$

Refer as a *solution* to (6), (7) (or (8), (9)) on the interval $[0,\tau]$, where $\tau>0$, to a continuous function x on $[-\omega,\tau]$ satisfying (7) and (6) for all $t\in[0,\tau]$ (respectively (9) and (8)).

Lemma 1. *On assuming* (H0), *if* (6), (7) *has a solution on* $[0,\tau]$ *then the later is unique.*

Proof. Take two solutions x and y to (6), (7) on some interval $[0,\tau]$, where $\tau>0$. By definition, x and y are continuous functions on $[-\omega,\tau]$,

$$x(t)=y(t)=\psi(t)\ge 0,\quad t\in I_\omega,$$

$$x(t)=\psi(0)+\int\limits_0^t\varphi(a,x_a)\,da,\quad y(t)=\psi(0)+\int\limits_0^t\varphi(a,y_a)\,da,\quad t\in[0,\tau];$$

moreover, $x(t)\ge\xi$ and $y(t)\ge\xi$ componentwise for all $t\in[-\omega,\tau]$, where the vector ξ is specified in (H0). Since x and y are continuous, there exists a constant $d>0$ such that $x(t),y(t)\in B_d\cap C(I_\omega,A_\xi)$ for $t\in[-\omega,\tau]$. Since x and y are bounded, while $f_i(t,z)$ and $g_i(t,z)$ have the local Lipschitz property, introduce Lipschitz constants $L_\varphi^{(i)}>0$ for the components $\varphi_i(t,z)$ of the mapping $\varphi(t,z)$ for $1\le i\le m$. Estimate $|x_i(t)-y_i(t)|$ for $t\in[-\omega,\tau]$. It is clear that $|x_i(t)-y_i(t)|=0$ for $t\in[-\omega,0]$. Consider the case $t\in[0,\tau]$. We have

$$x_i(t)-y_i(t)=\int\limits_0^t(\varphi_i(a,x_a)-\varphi_i(a,y_a))\,da,$$

$$|x_i(t)-y_i(t)|\le\int\limits_0^t|\varphi_i(a,x_a)-\varphi_i(a,y_a)|\,da\le\int\limits_0^t L_\varphi^{(i)}\,\|x_a-y_a\|\,da,\quad 1\le i\le m.$$

This yields $\|x(t)-y(t)\|_{R^m}=0$ for $t\in I_\omega$ and

$$\|x(t)-y(t)\|_{R^m}\le M_\varphi\int\limits_0^t\|x_a-y_a\|\,da,\quad t\in[0,\tau],$$

where $M_\varphi=\sum_{i=1}^m L_\varphi^{(i)}>0$. Observe that the constant M_φ depends on τ, ξ, and d, but is independent of t. Take $t\in[0,\tau]$ and $\theta\in I_\omega$. Then

$$\|x(t+\theta)-y(t+\theta)\|_{R^m}=0,\quad t+\theta\le 0,$$

$$\|x(t+\theta))-y(t+\theta)\|_{R^m}\le M_\varphi\int\limits_0^{t+\theta}\|x_a-y_a\|\,da\le M_\varphi\int\limits_0^t\|x_a-y_a\|\,da,\quad t+\theta\ge 0,$$

$$\|x_t-y_t\|=\max_{\theta\in I_\omega}\|x(t+\theta))-y(t+\theta)\|_{R^m}\le M_\varphi\int\limits_0^t\|x_a-y_a\|\,da.$$

The Gronwall–Bellman Lemma yields $\|x_t-y_t\|\equiv 0$ for $t\in[0,\tau]$. Thus, $x(t)=y(t)$ for all $t\in[-\omega,\tau]$, which completes the proof of Lemma 1. $\square$

Fix $\tau>0$. Denote by $C_\psi\subset C([-\omega,\tau],R^m)$ the set $x\in C([-\omega,\tau],R^m)$ such that $x(t)=\psi(t)$ for $t\in I_\omega$ and by $C_{\psi,0}\subset C_\psi$, the set $x\in C_\psi$ with $x(t)\ge 0$ for $t\in[-\omega,\tau]$. Take a function $\upsilon=\upsilon(t)=(\upsilon_1(t),\dots,\upsilon_m(t))^T$ continuous on $[-\omega,\tau]$ with nonnegative components, including the case that $\upsilon=\upsilon(t)=(\upsilon_1,\dots,\upsilon_m)^T$ is a nonnegative vector, and denote by $C_{\psi,0,\upsilon}$ the set of functions $x\in C_\psi$ satisfying $0\le x(t)\le\upsilon(t)$ for $t\in[-\omega,\tau]$. Observe that the sets $C_{\psi,0,\upsilon}$, $C_{\psi,0}$, and C_ψ are closed in $C([-\omega,\tau],R^m)$. Consequently, for every $\gamma\ge 0$ they are complete metric spaces with the norms $\|z\|_\gamma$ for $z\in C([-\omega,\tau],R^m)$.

Define the operator F associating to $F(x)\in C_{\psi,0}$ each $x\in C_{\psi,0}$ as

$$F(x)(t)=\psi(t),\quad t\in I_\omega,$$

$$F(x)(t)=e^{-\int\limits_0^t(\mu+g(a,x_a))\,da}\psi(0)+\int\limits_0^t e^{-\int\limits_a^t(\mu+g(s,x_s))\,ds}f(a,x_a)\,da,\quad t\in[0,\tau].$$

Lemma 2. *On assuming* (H0), *if there exists a set $C_{\psi,0,\upsilon}$ of functions with $F:C_{\psi,0,\upsilon}\to C_{\psi,0,\upsilon}$ then* (8), (9) *has a unique solution $x\in C_\psi$, and furthermore $x\in C_{\psi,0,\upsilon}$.*

Proof. By definition,

$$0\le x(t)\le\upsilon^*=(\upsilon_1^*,\dots,\upsilon_m^*)^T,\quad t\in[-\omega,\tau],$$

for all $x\in C_{\psi,0,\upsilon}$, where $\upsilon_i^*=\max_{t\in[-\omega,\tau]}\upsilon_i(t)\ge 0$ for $1\le i\le m$. To verify that F is a contraction operator on $C_{\psi,0,\upsilon}$ with respect to the norm $\|\cdot\|_\gamma$ for some $\gamma>0$, take $x,y\in C_{\psi,0,\upsilon}$. Since $0\le x(t),y(t)\le\upsilon^*$ for $t\in[-\omega,\tau]$, there is $d>0$ such that $x(t),y(t)\in B_d\cap C(I_\omega,A_\xi)$ for $t\in[-\omega,\tau]$. Put $N_{\upsilon^*}=\{u\in R_+^m:u\le\upsilon^*\}$. The Lipschitz constants $L_f^{(i)}$ and $L_g^{(i)}$ of f_i and g_i depend on ξ and υ^* for $1\le i\le m$. Since f_i is continuous for all $(t,z)\in[0,\tau]\times C(I_\omega,N_{\upsilon^*})$, we have $0\le f_i(t,z)\le M_f^{(i)}$, where $M_f^{(i)}>0$ are constants depending on υ^* for $1\le i\le m$.

Fixing $1\le i\le m$ and some constant $\gamma>0$, estimate

$$e^{-\gamma t}|F_i(x)(t)-F_i(y)(t)|,\quad t\in[-\omega,\tau].$$

The definition implies that $e^{-\gamma t}|F_i(x)(t)-F_i(y)(t)|=0$ for $t\in I_\omega$. For $t\in[0,\tau]$ we have

$$e^{-\gamma t}(F_i(x)(t)-F_i(y)(t))=e^{-\gamma t}B_i(t)+e^{-\gamma t}S_i(t)$$

$$=e^{-\gamma t}\left(e^{-\int\limits_0^t(\mu_i+g_i(a,x_a))\,da}-e^{-\int\limits_0^t(\mu_i+g_i(a,y_a))\,da}\right)\psi_i(0)$$

$$+e^{-\gamma t}\int\limits_0^t\left(e^{-\int\limits_a^t(\mu_i+g_i(s,x_s))\,ds}f_i(a,x_a)-e^{-\int\limits_a^t(\mu_i+g_i(s,y_s))\,ds}f_i(a,y_a)\right)da.$$

The nonnegativity of $g_i(a,x_a)$ and $g_i(a,y_a)$ yields

$$e^{-\gamma t}|B_i(t)|=e^{-\gamma t}\left|e^{-\int\limits_0^t(\mu_i+g_i(a,x_a))\,da}-e^{-\int\limits_0^t(\mu_i+g_i(a,y_a))\,da}\right|\psi_i(0)$$

$$\le\psi_i(0)e^{-\gamma t}\int\limits_0^t|g_i(a,x_a)-g_i(a,y_a)|\,da\le\psi_i(0)e^{-\gamma t}\int\limits_0^t L_g^{(i)}\|x_a-y_a\|\,da$$

$$\le L_g^{(i)}\psi_i(0)e^{-\gamma t}\int\limits_0^t e^{\gamma a}e^{-\gamma a}\max_{\theta\in I_\omega}(\|x(a+\theta)-y(a+\theta)\|_{R^m})\,da$$

$$\le L_g^{(i)}\psi_i(0)e^{-\gamma t}\int\limits_0^t e^{\gamma a}\max_{\theta\in I_\omega}(e^{-\gamma(a+\theta)}\|x(a+\theta)-y(a+\theta)\|_{R^m})\,da$$

$$\le L_g^{(i)}\psi_i(0)e^{-\gamma t}\int\limits_0^t e^{\gamma a}\max_{a\in[0,t]}\max_{\theta\in I_\omega}(e^{-\gamma(a+\theta)}\|x(a+\theta)-y(a+\theta)\|_{R^m})\,da$$

$$\le L_g^{(i)}\psi_i(0)e^{-\gamma t}\int\limits_0^t e^{\gamma a}\max_{a+\theta\in[-\omega,\tau]}(e^{-\gamma(a+\theta)}\|x(a+\theta)-y(a+\theta)\|_{R^m})\,da$$

$$=\frac{L_g^{(i)}\psi_i(0)}{\gamma}\|x-y\|_\gamma(1-e^{-\gamma t}),\quad t\in[0,\tau].$$

Furthermore, for $t\in[0,\tau]$ we have

$$|S_i(t)|=\left|\int\limits_0^t\left(e^{-\int\limits_a^t(\mu_i+g_i(s,x_s))\,ds}f_i(a,x_a)-e^{-\int\limits_a^t(\mu_i+g_i(s,y_s))\,ds}f_i(a,y_a)\right)da\right|$$

$$=\left|\int\limits_0^t e^{-\mu_i(t-a)}\left(e^{-\int\limits_a^t g_i(s,x_s)\,ds}f_i(a,x_a)-e^{-\int\limits_a^t g_i(s,y_s)\,ds}f_i(a,y_a)\right)da\right|$$

$$\le\int\limits_0^t e^{-\mu_i(t-a)}\left|e^{-\int\limits_a^t g_i(s,x_s)\,ds}f_i(a,x_a)-e^{-\int\limits_a^t g_i(s,y_s)\,ds}f_i(a,y_a)\right|da$$

$$\le\int\limits_0^t e^{-\mu_i(t-a)}\left(L_f^{(i)}\|x_a-y_a\|+M_f^{(i)}\int\limits_a^t L_g^{(i)}\|x_s-y_s\|\,ds\right)da$$

$$\le L_f^{(i)}\int\limits_0^t e^{\gamma a}e^{-\gamma a}\|x_a-y_a\|\,da+M_f^{(i)}L_g^{(i)}\int\limits_0^t e^{-\mu_i(t-a)}\left(\int\limits_a^t e^{\gamma s}e^{-\gamma s}\|x_s-y_s\|\,ds\right)da.$$

This implies that

$$e^{-\gamma t}|S_i(t)| \le \frac{L_f^{(i)}}{\gamma}\|x-y\|_\gamma(1-e^{-\gamma t}) + e^{-\gamma t}M_f^{(i)}L_g^{(i)}\|x-y\|_\gamma \int\limits_0^t e^{-\mu_i(t-a)}\left(\int\limits_a^t e^{\gamma s}\,ds\right)da$$

$$\le \frac{L_f^{(i)}}{\gamma}\|x-y\|_\gamma(1-e^{-\gamma t}) + \frac{M_f^{(i)}L_g^{(i)}}{\gamma}\|x-y\|_\gamma\frac{1-e^{-\mu_i t}}{\mu_i}, \quad t\in[0,\tau].$$

Combining the estimates, we infer that

$$e^{-\gamma t}|F_i(x)(t)-F_i(y)(t)| \le \frac{1}{\gamma}\big(L_g^{(i)}\psi_i(0)+L_f^{(i)}+M_f^{(i)}L_g^{(i)}\mu_i^{-1}\big)\|x-y\|_\gamma$$

for all $t\in[0,\tau]$.

Choose a constant $\gamma>0$ such that

$$q=\frac{1}{\gamma}\sum_{i=1}^m\big(L_g^{(i)}\psi_i(0)+L_f^{(i)}+M_f^{(i)}L_g^{(i)}\mu_i^{-1}\big)<1.$$

We arrive at the estimate

$$\|F(x)-F(y)\|_\gamma = \max_{t\in[-\omega,\tau]}(e^{-\gamma t}\|F(x)(t)-F(y)(t)\|_{R^m})$$

$$= \max_{t\in[-\omega,\tau]}\left(e^{-\gamma t}\sum_{i=1}^m|F_i(x)(t)-F_i(y)(t)|\right)\le q\|x-y\|_\gamma.$$

Consequently, F is a contraction on $C_{\psi,0,\upsilon}$ with respect to the norm $\|\cdot\|_\gamma$.

By assumption, $C_{\psi,0,\upsilon}$ is invariant under F. By the contraction mapping principle, the equation $x=F(x)$ has a unique solution $x^*\in C_{\psi,0,\upsilon}$. Observe that x^* is a solution to (8), (9) on the interval $[0,\tau]$ and simultaneously a solution to the equivalent problem (6), (7) on this interval. Resting on Lemma 1, we conclude that (8), (9) has a unique solution $x^*\in C_\psi$, and furthermore $x^*\in C_{\psi,0,\upsilon}$. The proof of Lemma 2 is complete. □

2. Additional Assumptions and Invariant Sets of Functions for the Operator *F*

Let us introduce a series of assumptions on the mappings f and ρ. Each of the assumptions below serves as a base for constructing an invariant set $C_{\psi,0,\upsilon}$ for F:

(H1) for all $(t,z)\in R_+\times C(I_\omega,R_+^m)$ we have the estimate $f(t,z)\le h(z)$, where $h: C(I_\omega,R_+^m)\to R_+^m$ is a continuous isotonic functional;

(H2) there exists $p\in R_+^m$ such that $f(t,z)\le p$ for all $(t,z)\in R_+\times C(I_\omega,R_+^m)$;

(H3) for all $(t,z)\in R_+\times C(I_\omega,R_+^m)$ we have the estimate

$$f(t,z)\le p+\int\limits_{-\omega}^0 d\nu(\theta)z(\theta),$$

where $p\in R_+^m$, while ν is an $m\times m$ matrix with entries defined and nondecreasing on I_ω, and the matrix $\Delta\nu=\nu(0)-\nu(-\omega)$ has at least one positive entry;

(H4) for all $(t,z)\in R_+\times C(I_\omega,R_+^m)$ we have the estimate $\rho(t,z)\le\beta(z)$, where $\beta: C(I_\omega,R_+^m)\to R_+^m$ is a continuous isotonic functional;

(H5) there exists $r\in R_+^m$ such that $\rho(t,z)\le r$ for all $(t,z)\in R_+\times C(I_\omega,R_+^m)$;

(H6) for all $(t,z)\in R_+\times C(I_\omega,R_+^m)$ we have the estimates

$$L(z,z)\le\rho(t,z)\le K(z,z),$$

where $L,K: C(I_\omega,R_+^m)\times C(I_\omega,R_+^m)\to R_+^m$ are continuous functionals with the mixed monotonicity property.

Lemma 3. *On assuming* (H0) *and* (H1), *if there exists* $q \in R_+^m$ *with*

$$h(q) \le \mu q \tag{10}$$

and the initial function ψ *satisfies*

$$\max_{t \in I_\omega} \psi(t) \le q \tag{11}$$

then for each $\tau > 0$ *the set* $C_{\psi,0,q}$ *is invariant under* F.

PROOF. Fix $\tau > 0$ and take $x \in C_{\psi,0,q}$. Since h is isotonic, we see that $0 \le h(x_t) \le h(q)$ for $t \in [0,\tau]$. Resting on (11), we obtain $0 \le F(x)(t) = \psi(t) \le q$. Using (10) and (11), we establish for $t \in [0,\tau]$ the estimates

$$0 \le F(x)(t) \le e^{-\mu t}\psi(0) + \int_0^t e^{-\mu(t-a)} f(a, x_a)\, da$$

$$\le e^{-\mu t}\psi(0) + \int_0^t e^{-\mu(t-a)} h(x_a)\, da \le e^{-\mu t}\psi(0) + \int_0^t e^{-\mu(t-a)} h(q)\, da$$

$$= e^{-\mu t}\psi(0) + (I - e^{-\mu t})\mu^{-1} h(q) \le q.$$

Consequently, $F(x) \in C_{\psi,0,q}$ for all $x \in C_{\psi,0,q}$. The vector q is independent of τ. Since τ is arbitrary, the proof of Lemma 3 is complete. □

Lemma 4. *On assuming* (H0) *and* (H2), *put*

$$v = \max\{\max_{t \in I_\omega} \psi(t); \mu^{-1} p\} \in R_+^m. \tag{12}$$

Then for each $\tau > 0$ *the set* $C_{\psi,0,v}$ *is invariant under* F.

PROOF. Using (H2) and (12), turn to Lemma 3 with $h(z) = p$ for $z \in C(I_\omega, R_+^m)$ and $q = v$. The chosen $h(z)$ and q satisfy the hypotheses of Lemma 3, which completes the proof. □

Lemma 5. *On assuming* (H0) *and* (H3), *there exist* $c \in R^m$ *with* $c > 0$ *and* $\eta \in R$ *with* $\eta > 0$ *such that for*

$$\upsilon(t) = ce^{\eta t}, \quad t \in R, \tag{13}$$

and $\tau > 0$ *the set* $C_{\psi,0,\upsilon}$ *is invariant under* F.

PROOF. Resting on (H3), turn to the matrix $\Delta\nu$. By assumption, all its entries are nonnegative and at least one of them is positive. Choose $\eta > 0$ so that $\|\Delta\nu\| < \eta$. Following [2, Chapter 2, Section 2.4], we infer that the matrix $Q(\eta) = I - \eta^{-1}\Delta\nu$ is invertible and all entries of $Q^{-1}(\eta)$ are nonnegative. Each row of $Q^{-1}(\eta)$ obviously contains at least one positive entry. Fix some vector $\varepsilon \in R^m$ with $\varepsilon > 0$. Put

$$b = \max\{\varepsilon + \psi(0) + \mu^{-1} p; \max_{t \in I_\omega}(e^{-\eta t}\psi(t))\} \in R^m,$$

$$c = Q^{-1}(\eta) b \in R^m, \quad \upsilon(t) = ce^{\eta t}, \quad t \in R.$$

It is not difficult to observe that $b > 0$ and $c > 0$. The choice of η and c yields $F(x)(t) = \psi(t) \le \upsilon(t)$

for $t \in I_\omega$. For $0 \le t < \infty$ we obtain the following chain of relations:

$$\begin{aligned}
&\psi(0) + \int_0^t e^{-\mu(t-a)} \Big(p + \int_{-\omega}^0 d\nu(\theta) \upsilon(a+\theta) \Big)\, da \\
&= \psi(0) + \int_0^t e^{-\mu(t-a)} \Big(p + \int_{-\omega}^0 d\nu(\theta) c e^{\eta(a+\theta)} \Big)\, da \\
&\le \psi(0) + \mu^{-1} p + \int_0^t e^{-\mu(t-a)} e^{\eta a}\, da \Delta\nu c \\
&\le \psi(0) + \mu^{-1} p + \int_0^t e^{\eta a}\, da \Delta\nu c \le \psi(0) + \mu^{-1} p + \eta^{-1} e^{\eta t} \Delta\nu c \\
&\le b e^{\eta t} + \eta^{-1} \Delta\nu Q^{-1}(\eta) b e^{\eta t} = (Q(\eta) + \eta^{-1}\Delta\nu) Q^{-1}(\eta) b e^{\eta t} \\
&= (I - \eta^{-1}\Delta\nu + \eta^{-1}\Delta\nu) Q^{-1}(\eta) b e^{\eta t} = c e^{\eta t}.
\end{aligned}$$

Fix $\tau > 0$. Putting $x \in C_{\psi,0,\upsilon}$, we have

$$0 \le F(x)(t) = \psi(t) \le \upsilon(t), \quad t \in I_\omega,$$

$$\begin{aligned}
0 \le F(x)(t) &\le \psi(0) + \int_0^t e^{-\mu(t-a)} f(a, x_a)\, da \\
&\le \psi(0) + \int_0^t e^{-\mu(t-a)} \Big(p + \int_{-\omega}^0 d\nu(\theta) x(a+\theta) \Big)\, da \\
&\le \psi(0) + \int_0^t e^{-\mu(t-a)} \Big(p + \int_{-\omega}^0 d\nu(\theta) \upsilon(a+\theta) \Big)\, da \le \upsilon(t), \quad t \in [0,\tau].
\end{aligned}$$

Consequently, $F(x) \in C_{\psi,0,\upsilon}$ for every $x \in C_{\psi,0,\upsilon}$. The parameters $\upsilon(t)$ are independent of τ. Since τ is arbitrary, the proof of Lemma 5 is complete. $\square$

Lemma 6. *On assuming* (H0) *and* (H4), *if there exists* $c \in R_+^m$ *with*

$$\beta(c) \le c \tag{14}$$

and the initial function ψ *satisfies*

$$\max_{t \in I_\omega} \psi(t) \le c \tag{15}$$

then for each $\tau > 0$ *the set* $C_{\psi,0,c}$ *is invariant under* F.

Proof. Fix $\tau > 0$ and take $x \in C_{\psi,0,c}$. Since β is isotonic, we arrive at the inequalities $0 \le \beta(x_t) \le \beta(c)$ for $t \in [0,\tau]$. Resting on (15), we obtain $0 \le F(x)(t) = \psi(t) \le c$. Using (14), (15), and the expression

$$F_i(x)(t) = e^{-\int_0^t (\mu_i + g_i(s,x_s))\, ds} \Big(\psi_i(0) + \int_0^t \rho_i(a, x_a)\, d\, e^{\int_0^a (\mu_i + g_i(s,x_s))\, ds} \Big), \quad 1 \le i \le m,\ t \ge 0,$$

for the components of F, we establish for $t \in [0, \tau]$ the estimates

$$0 \le F(x)(t) \le e^{-\int\limits_0^t (\mu+g(s,x_s))\,ds}(\psi(0) + (e^{\int\limits_0^t (\mu+g(s,x_s))\,ds} - I)\beta(c))$$
$$= e^{-\int\limits_0^t (\mu+g(s,x_s))\,ds}\psi(0) + (I - e^{-\int\limits_0^t (\mu+g(s,x_s))\,ds})\beta(c) \le c.$$

Consequently, $F(x) \in C_{\psi,0,c}$ for every $x \in C_{\psi,0,c}$. The vector c is independent of τ. Since τ is arbitrary, the proof of Lemma 6 is complete. $\square$

Lemma 7. *On assuming* (H0) *and* (H5), *put*

$$d = \max\{\max_{t\in I_\omega} \psi(t); r\} \in R_+^m. \tag{16}$$

Then for each $\tau > 0$ the set $C_{\psi,0,d}$ is invariant under F.

Proof. Using (H5) and (16), turn to Lemma 6 with $\beta(z) = r$ for $z \in C(I_\omega, R_+^m)$ and $c = d$. The chosen $\beta(z)$ and c satisfy the hypotheses of Lemma 6, which completes the proof. $\square$

Lemma 8. *On assuming* (H0) *and* (H6), *if there exist $u, w \in R_+^m$ with*

$$u \le w, \quad u \le L(u,w), \quad w \ge K(w,u), \tag{17}$$

and the initial function ψ satisfies

$$u \le \psi(t) \le w, \quad t \in I_\omega, \tag{18}$$

then for each $\tau > 0$ the set

$$C_{\psi,u,w} = \{x \in C_\psi : u \le x(t) \le w \text{ for } t \in [-\omega, \tau]\}$$

is invariant under F.

Proof. Fix $\tau > 0$ and take $x \in C_{\psi,u,w}$. Using (H6) and the mixed monotonicity of L and K, we arrive at the inequalities

$$L(u,w) \le L(x_t,x_t) \le \rho(t,x_t) \le K(x_t,x_t) \le K(w,u), \quad t \in [0,\tau]. \tag{19}$$

This yields $u \le F(x)(t) = \psi(t) \le w$ for $t \in I_\omega$. Using (17)–(19) and the expression for the components of F in Lemma 6, we establish the following estimates:

$$F(x)(t) \le e^{-\int\limits_0^t (\mu+g(s,x_s))\,ds}(\psi(0) + (e^{\int\limits_0^t (\mu+g(s,x_s))\,ds} - I)K(w,u))$$
$$= e^{-\int\limits_0^t (\mu+g(s,x_s))\,ds}\psi(0) + (I - e^{-\int\limits_0^t (\mu+g(s,x_s))\,ds})K(w,u) \le w,$$

$$F(x)(t) \ge e^{-\int\limits_0^t (\mu+g(s,x_s))\,ds}(\psi(0) + (e^{\int\limits_0^t (\mu+g(s,x_s))\,ds} - I)L(u,w))$$
$$= e^{-\int\limits_0^t (\mu+g(s,x_s))\,ds}\psi(0) + (I - e^{-\int\limits_0^t (\mu+g(s,x_s))\,ds})L(u,w) \ge u, \quad t \in [0,\tau].$$

Consequently, $F(x) \in C_{\psi,u,w}$ for every $x \in C_{\psi,u,w}$. The vectors u and w are independent of τ. Since τ is arbitrary, the proof of Lemma 8 is complete. $\square$

3. The Main Results

Proceed to study (8), (9) on using Lemmas 2–8.

Theorem 1. *Assuming* (H0) *as well as one of* (H2), (H3), *and* (H5), *we have*

(1) *Problem* (8), (9) *is uniquely solvable on* $[0, \infty)$ *and its solution* x *on each interval* $[0, \tau]$ *depends continuously on* ψ.

(2) *The solution* x *to* (8), (9) *satisfies the estimates*

$$0 \leq x(t) \leq v, \quad 0 \leq x(t) \leq ce^{\eta t}, \quad 0 \leq x(t) \leq d, \quad t \in [0, \infty),$$

corresponding to assumptions (H2), (H3), *and* (H5), *where* v *is specified in* (12), *the parameters* c *and* η *are given in Lemma* 5, *while* d *is specified in* (16).

Proof. Assume (H0) and (H2). Using Lemmas 2 and 4, we infer that for every fixed $\tau > 0$ (8), (9) has a unique solution $x \in C_\psi$ and, furthermore, $x \in C_{\psi,0,v}$, where v is specified in (12). Consequently, (8), (9) is uniquely solvable on $[0, \infty)$ and its solution satisfies $0 \leq x(t) \leq v$ for $t \in [0, \infty)$. Assuming (H3) and then (H5), we apply Lemma 2 together with Lemma 5 (respectively Lemma 7) and justify the first two claims of the theorem.

Fix the interval $[0, \tau]$. Take two functions $\psi^{(1)}$ and $\psi^{(2)}$ satisfying the requirement on ψ in (H0). These functions correspond to the two operators $F^{(1)}$ and $F^{(2)}$ coinciding with the operator F for $\psi = \psi^{(1)}$ and $\psi = \psi^{(2)}$, as well as the solutions $x^{(1)}$ and $x^{(2)}$ to (8), (9) with $F = F^{(1)}$ and $F = F^{(2)}$ respectively. Fixing $\psi^{(1)}$, let $\psi^{(2)}$ vary. It is not difficult to observe that, on assuming (H2) and (H5), we can replace the vectors v and d specified in (12) and (16) by

$$v = \max\{\max_{t \in I_\omega} \psi^{(1)}(t); \max_{t \in I_\omega} \psi^{(2)}(t); \mu^{-1}p\}, \quad d = \max\{\max_{t \in I_\omega} \psi^{(1)}(t); \max_{t \in I_\omega} \psi^{(2)}(t); r\}.$$

Assuming (H3), we can choose the parameters of the function $v(t)$ defined in (13) so that $v(t) \geq \psi^{(1)}(t)$ and $v(t) \geq \psi^{(2)}(t)$ for $t \in I_\omega$. Then under each of (H2), (H3), and (H5) there exists $v^* \in R^m$ with $v^* \geq 0$ such that $0 \leq x^{(1)}(t), x^{(2)}(t) \leq v^*$ for all $t \in [-\omega, \tau]$.

Verify that for every $\varepsilon > 0$ there exists $\delta > 0$ such that $\|\psi^{(2)} - \psi^{(1)}\| < \delta$ implies $\|x^{(2)} - x^{(1)}\| < \varepsilon$. Take some constant $\gamma > 0$. Fix $1 \leq i \leq m$. We have

$$e^{-\gamma t}\big|x_i^{(2)}(t) - x_i^{(1)}(t)\big| = e^{-\gamma t}\big|\psi_i^{(2)}(t) - \psi_i^{(1)}(t)\big| < e^{\gamma\omega}\delta$$

for all $t \in [-\omega, 0]$. Repeating the argument of Lemma 2, for $t \in [0, \tau]$ we obtain

$$e^{-\gamma t}\big|x_i^{(2)}(t) - x_i^{(1)}(t)\big| = e^{-\gamma t}\big|F_i^{(2)}(x^{(2)})(t) - F_i^{(1)}(x^{(1)})(t)\big|$$

$$\leq e^{-\gamma t}\big|\psi_i^{(2)}(0) - \psi_i^{(1)}(0)\big| + \frac{L_g^{(i)}\psi_i^{(1)}(0)}{\gamma}\|x^{(2)} - x^{(1)}\|_\gamma + \frac{1}{\gamma}\big(L_f^{(i)} + M_f^{(i)}L_g^{(i)}\mu_i^{-1}\big)\|x^{(2)} - x^{(1)}\|_\gamma.$$

Here the constants $L_g^{(i)}$, $L_f^{(i)}$, and $M_f^{(i)}$, for $1 \leq i \leq m$, depend on ξ and v^*.

Choose $\gamma > 0$ so that

$$q = \frac{1}{\gamma}\sum_{i=1}^{m}\big(L_g^{(i)}\psi_i^{(1)}(0) + L_f^{(i)} + M_f^{(i)}L_g^{(i)}\mu_i^{-1}\big) < 1.$$

Combining the estimates on $[-\omega, 0]$ and $[0, \tau]$, we see that

$$\|x^{(2)} - x^{(1)}\|_\gamma < e^{\gamma\omega}m\delta + \delta + q\|x^{(2)} - x^{(1)}\|_\gamma.$$

In consequence, $\|x^{(2)} - x^{(1)}\| < \delta(e^{\gamma(\omega+\tau)}m + e^{\gamma\tau})/(1 - q)$. Choosing $\delta = \varepsilon(1 - q)/(e^{\gamma(\omega+\tau)}m + e^{\gamma\tau})$, we arrive at the required inequality $\|x^{(2)} - x^{(1)}\| < \varepsilon$. The proof of Theorem 1 is complete. $\square$

Theorem 2 is given without proof. Its validity is established on using Lemmas 2, 3, 6, and 8 by analogy with the proof of Theorem 1.

Theorem 2. *Under the hypotheses of one of Lemmas* 3, 6, *and* 8, *we have the following claims.*

(1) *Problem* (8), (9) *is uniquely solvable on the semiaxis* $[0, \infty)$, *and its solution* x *on each interval* $[0, \tau]$ *depends continuously on* ψ.

(2) *The solution* x *to* (8), (9) *satisfies the estimates*

$$0 \le x(t) \le q, \quad 0 \le x(t) \le c, \quad u \le x(t) \le w, \quad t \in [0, \infty),$$

corresponding to (H1), (H4), *and* (H6), *where* q, c, *and* (u, w) *satisfy* (10), (14), *and* (17) *respectively.*

4. Examples

Below we present some models satisfying (H0) and some of the assumptions (H1)–(H6).

Example 1. Denote by $x(t)$ the population size of one species at time t. Suppose that the dynamics of $x(t)$ is described as

$$\frac{dx(t)}{dt} = \frac{ax^2(t)}{1 + bx(t)} - \left(\mu + \gamma x(t) + \int_{-\omega}^{0} \lambda(\theta) x(t + \theta)\, d\theta\right) x(t), \quad t \ge 0, \tag{20}$$

$$x(t) = \psi(t), \quad t \in I_\omega = [-\omega, 0], \tag{21}$$

where $a > 0$, $b > 0$, $\mu > 0$, $\gamma \ge 0$, and $\omega > 0$ are some constants, $\lambda(\theta)$ and $\psi(\theta)$ are nonnegative continuous functions, and $\theta \in I_\omega$. We can write

$$f(t, x_t) = ax^2(t)/(1 + bx(t)), \quad g(t, x_t) = \gamma x(t) + \int_{-\omega}^{0} \lambda(\theta) x(t + \theta)\, d\theta.$$

It is not difficult to observe that (20), (21) satisfies (H0). Suppose that $t \ge 0$ and $x(t) \ge 0$. Then $f(t, x_t) \le (a/b)x(t)$, which guarantees the fulfillment of (H3). Moreover, in the cases $\gamma = 0$ and $\gamma > 0$ assumptions (H4) and (H5) are satisfied respectively since

$$f(t, x_t)/(\mu + g(t, x_t)) \le \beta(x_t) = (a/\mu)x^2(t)/(1 + bx(t)),$$

$$f(t, x_t)/(\mu + g(t, x_t)) \le r = a/(b\gamma) = \text{const}\,.$$

Example 2. Consider the mathematical model describing protein synthesis regulation [3]:

$$\frac{dx_1(t)}{dt} = \frac{1}{1 + x_5^\gamma(t - \omega_1)} - \mu_1 x_1(t), \tag{22}$$

$$\frac{dx_2(t)}{dt} = \frac{1 + k_2 x_4^\sigma(t - \omega_2)}{1 + k_4 x_4^\sigma(t - \omega_2)} x_1(t) - \mu_2 x_2(t), \quad t \ge 0, \tag{23}$$

$$\frac{dx_i(t)}{dt} = x_{i-1}(t) - \mu_i x_i(t), \quad i = 3, 4, 5, \tag{24}$$

$$x_1(0) = x_1^{(0)}, \quad x_2(0) = x_2^{(0)}, \quad x_3(0) = x_3^{(0)}, \tag{25}$$

$$x_4(t) = \psi_4(t), \quad x_5(t) = \psi_5(t), \quad t \in I_\omega = [-\max\{\omega_1, \omega_2\}, 0]. \tag{26}$$

In (22)–(26) the variables $x_1(t), \dots, x_5(t)$ stand for the quantities of substances produced in the protein synthesis under the influence of negative and positive feedback. All parameters in (22)–(24) are positive and, moreover, $k_2 > k_4$. The delays ω_1 and ω_2 are positive. In the initial conditions (25) and (26) we have $x_i^{(0)} \geq 0$ for $1 \leq i \leq 3$, while $\psi_4(t)$ and $\psi_5(t)$ are nonnegative continuous functions for $t \in I_\omega$. The model (22)–(26) satisfies (H0) and

$$f_1(t, x_t) = \frac{1}{1 + x_5^\gamma(t - \omega_1)} \leq p_1 = 1,$$

$$f_2(t, x_t) = \frac{1 + k_2 x_4^\sigma(t - \omega_2)}{1 + k_4 x_4^\sigma(t - \omega_2)} x_1(t) \leq (k_2/k_4) x_1(t),$$

$$f_3(t, x_t) = x_2(t), \quad f_4(t, x_t) = x_3(t), \quad f_5(t, x_t) = x_4(t)$$

for all $t \geq 0$ and $x(t) \geq 0$. Consequently, the model under consideration satisfies (H3). It is not difficult to show that (H6) is satisfied together with (H3). Sufficient conditions for the asymptotic stability of equilibrium in (22)–(26) were obtained in [4] on using (H6).

Example 3. Consider the mathematical model describing the spread of tuberculosis in the adult population of an isolated domain [5]. Denote by $x_1(t)$, $x_2(t)$, and $x_3(t)$ the numbers of susceptible species, those infected with tuberculosis mycobacteria, and those sick with tuberculosis respectively. The model equations are

$$\frac{dx_1(t)}{dt} = f_1(t, x_t) - (\mu_1 + \lambda x_3(t)) x_1(t), \tag{27}$$

$$\frac{dx_2(t)}{dt} = f_2(t, x_t) - (\mu_2 + \gamma + \alpha x_3(t)) x_2(t), \quad t \geq 0, \tag{28}$$

$$\frac{dx_3(t)}{dt} = f_3(t, x_t) - (\eta + \mu_3) x_3(t), \tag{29}$$

$$x_1(0) = x_1^0, \quad x_2(0) = x_2^0, \quad x_3(t) = \psi_3(t), \quad t \in I_\omega = [-\omega, 0]. \tag{30}$$

The components of $f(t, x_t) = (f_1(t, x_t), f_2(t, x_t), f_3(t, x_t))^T$ are of the form

$$f_1(t, x_t) = r(t - \omega) \exp\Bigg(-\int_0^\omega \varphi(s) x_3(t + s - \omega)\, ds\Bigg),$$

$$f_2(t, x_t) = (1 - \delta)\lambda x_1(t) x_3(t) + \eta x_3(t) + r(t - \omega) - f_1(t, x_t),$$

$$f_3(t, x_t) = \delta\lambda x_1(t) x_3(t) + (\gamma + \alpha x_3(t)) x_2(t).$$

All parameters in (27)–(29) are positive, $\delta < 1$, the delay ω is greater than zero, while $x_1^0 \geq 0$ and $x_2^0 \geq 0$. The functions $\varphi(s)$ of $s \in [0, \omega]$ and $\psi_3(t)$ of $t \in I_\omega$ are continuous and nonnegative. The function $r(s)$ is continuous, nonnegative, and bounded above for $s \in [-\omega, \infty)$. The model (27)–(30) satisfies (H0). Supposing that $t \geq 0$ and $x(t) \geq 0$, we see that

$$f_1(t, x_t) \leq h_1(x_t) = r^* = \sup_{t \geq 0} r(t - \omega) < \infty,$$

$$f_2(t, x_t) \leq h_2(x_t) = (1 - \delta)\lambda x_1(t) x_3(t) + \eta x_3(t) + r^* \int_0^\omega \varphi(s) x_3(t + s - \omega)\, ds,$$

$$f_3(t, x_t) \leq h_3(x_t) = \delta\lambda x_1(t) x_3(t) + (\gamma + \alpha x_3(t)) x_2(t),$$

meaning that (H1) is satisfied. Note that in [5] there are obtained, using (H1), the conditions under which the limits

$$\lim_{t \to +\infty} x_2(t) = 0, \quad \lim_{t \to +\infty} x_3(t) = 0$$

exist for the solution to (27)–(30). $\square$

Example 4. Consider the mathematical model used in [6, Chapter 2, Section 2.1] for studying the dynamics of infectious diseases:

$$\frac{dx_1(t)}{dt} = b_1 x_1(t) - (\mu_1 + \gamma_{13} x_3(t)) x_1(t), \tag{31}$$

$$\frac{dx_2(t)}{dt} = b_2 + \varphi(x_4(t)) x_1(t-\omega) x_3(t-\omega) - \mu_2 x_2(t), \tag{32}$$

$$\frac{dx_3(t)}{dt} = b_3 x_2(t) - (\mu_3 + \gamma_{31} x_1(t)) x_3(t), \quad t \geq 0, \tag{33}$$

$$\frac{dx_4(t)}{dt} = b_4 x_1(t) - \mu_4 x_4(t), \tag{34}$$

$$x_1(t) = \psi_1(t), \quad x_3(t) = \psi_3(t), \quad t \in I_\omega = [-\omega, 0], \quad x_2(0) = x_2^{(0)}, \quad x_4(0) = x_4^{(0)}. \tag{35}$$

This model uses the following notation: $x_1(t)$, $x_2(t)$, and $x_3(t)$ stand for the concentrations of antigens, plasma cells, and antibodies respectively, while $x_4(t)$ is a relative characteristic of the target organ attacked by the antigens. All parameters appearing in (31)–(34) are positive, while $b_1 > \mu_1$ and $\omega > 0$. In the initial conditions (35) we have $x_2^{(0)} \geq 0$ and $x_4^{(0)} \geq 0$, while the functions $\psi_1(t)$ and $\psi_3(t)$ are nonnegative and continuous for $t \in I_\omega$. The function $\varphi(u)$ is given as

$$\varphi(u) = 1, \ u \in [0, u_*], \quad \varphi(u) = \max\{(1-u)/(1-u_*); 0\}, \ u \in [u_*, \infty),$$

where $0 < u_* < 1$ is a parameter. Model (31)–(35) satisfies (H0). At the same time, the structure of its equations complicates the use of (H1)–(H6). In order to obviate this problem, apply to (31)–(35) the method of steps. Consider (31)–(35) on the intervals of time $t \in [n\omega, (n+1)\omega)$ for $n = 0, 1, 2, \dots$. In (32) we have $0 \leq \varphi(x_4(t)) \leq 1$, while the factor $x_1(t-\omega)x_3(t-\omega)$ amounts to a nonnegative continuous function. Consequently, on each of these intervals it suffices to use (H3), and the strategy of proof of Theorem 1 works. Moving along the intervals $[0, \omega)$, $[\omega, 2\omega)$, $\dots$ and redefining the initial data, we establish the global solvability of the model (31)–(35), the nonnegativity of its solution, and the continuous dependence of solutions on the initial data of (35) on each finite interval. $\square$

References

1. Hale J. K., *Theory of Functional Differential Equations*, Springer-Verlag, New York, Heidelberg, and Berlin (1977).
2. Ortega J. M. and Rheinboldt W. C., *Iterative Solution of Nonlinear Equations in Several Variables*, Academic Press, New York and London (1970).
3. Mahaffy J. M., "Cellular control models with linked positive and negative feedback and delays. Linear analysis and local stability," J. Theor. Biol., vol. 106, 103–118 (1984).
4. Karelina R. O. and Pertsev N. V., "Construction of two-sided estimates for solutions of some systems of differential equations with aftereffect," Sib. Zh. Ind. Mat., vol. 8, no. 4, 60–72 (2005).
5. Pertsev N. V., "Analysis of solutions to mathematical models of epidemic processes with common structural properties," Sib. Zh. Ind. Mat., vol. 18, no. 2, 85–98 (2015).
6. Marchuk G. I., *Mathematical Models in Immunology. Numerical Methods and Experiments* [Russian], Nauka, Moscow (1991).

N. V. Pertsev
Sobolev Institute of Mathematics, Omsk Branch, Omsk, Russia
E-mail address: homlab@ya.ru