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MSC 34K20+92B05CONSTRUCTION OF EXPONENTIALLY DECREASING
ESTIMATES OF SOLUTIONS TO A CAUCHY PROBLEM FOR
SOME NONLINEAR SYSTEMS OF DELAY DIFFERENTIAL
EQUATIONS

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ABSTRACT. The behavior of solutions for several models of living systems, presented as the Cauchy problem for nonlinear systems of delay differential equations, is investigated. A set of conditions providing exponentially decreasing estimates of the components of the solutions of the studied Cauchy problem is established. The parameters of exponential estimates are found as a solution of a nonlinear system of inequalities, based on the right part of the system of differential equations. Results of the studies on mathematical models arising in epidemiology, immunology, and physiology are presented.

Keywords: delay differential equations, initial problem, non-negative solutions, exponentially decreasing estimates of the solutions, M-matrix, mathematical models of living systems.

1. INTRODUCTION

This article is dedicated to studying of the properties of solutions of mathematical models for living systems, presented in the form of a Cauchy problem for delay differential equations that have a particular structure. Taking into account the structure of differential equations, we can study the conditions of global solvability of a Cauchy problem, including non-negativity of solutions provided that the initial data is non-negative, establish the existence of bounded solutions, find the sufficient

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conditions of asymptotic stability of stability positions, and study some other problems.

One of the important questions connected to practical application of some mathematical models is related to finding conditions of exponential decreasing of a part of components of the solution, describing the number of species of some groups or concentration of substances of a particular kind, which belong to one or another living system. Exponential decreasing of a part of components in solutions of mathematical models allows to estimate the speed and time of lowering of these components from the initial level to some favorable or unfavorable one.

Now we move to the description of the object of our study. Suppose that $J = [a, b] \subset R$, $A \subseteq R^m$, $m \geq 2$, $\|v\|_{R^m}$ is the norm of a vector $v \in R^m$, $C(J, A)$ is the set of all continuous functions $z : J \rightarrow A$ with the norm

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

For $u, w \in R^m$, the inequalities $u < 0$, $u > 0$, $u \leq w$, $u \geq w$ are considered componentwise. If $x, y \in C(J, A)$, then for every $t \in J$ the inequality $x(t) \leq y(t)$ is understood as an inequality between the corresponding vectors. We put $I_\omega = [-\omega, 0]$, where $\omega > 0$ is some real constant. We denote by $B_d = \{z \in C(I_\omega, R^m) : \|z\| \leq d\}$ a ball in the space $C(I_\omega, R^m)$.

Consider the Cauchy problem for a system of delay functionally differential equations

$$(1) \quad \frac{dx(t)}{dt} = f(t, x_t) - (\mu + g(t, x_t))x(t), \quad t \geq 0,$$

$$(2) \quad x(t) = \psi(t), \quad t \in I_\omega,$$

where

$$x(t) = (x_1(t), \dots, x_m(t))^T, \quad \psi(t) = (\psi_1(t), \dots, \psi_m(t))^T,$$

$$f(t, x_t) = (f_1(t, x_t), \dots, f_m(t, x_t))^T,$$

$$g(t, x_t) = \text{diag}(g_1(t, x_t), \dots, g_m(t, x_t)), \quad \mu = \text{diag}(\mu_1, \dots, \mu_m), \quad m \geq 2,$$

the delayed variable $x_t : I_\omega \rightarrow R^m$ is defined by the following: for every fixed $t \geq 0$ $x_t(\theta) = x(t + \theta)$, $\theta \in I_\omega$, $\psi(t)$ is the initial function, $f_i(t, x_t)$, $g_i(t, x_t)$ are some mappings, μ_i are constants, $1 \leq i \leq m$, by $dx(t)/dt$ we mean the right-hand derivative (componentwise). We assume that the mappings, functions, and constants, belonging to (1), (2), satisfy for every $1 \leq i \leq m$ the set of conditions listed below:

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

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

3) $f_i(t, z)$, $g_i(t, z)$ are continuous in $(t, z) \in R_+ \times C(I_\omega, A_\xi)$ and locally Lipschitz in z : for every $d \in R$, $d > 0$, there exist constants $L_f^{(i)} = L_f^{(i)}(\xi, d) > 0$, $L_g^{(i)} = L_g^{(i)}(\xi, d) > 0$, such that for all $z_1, z_2 \in B_d \cap C(I_\omega, A_\xi)$ and $t \in [0, \infty)$, the following inequalities hold:

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

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

5) $\mu_i > 0$.

Refer as a solution of the Cauchy problem (1), (2) on the interval $[0, \tau)$, $\tau > 0$ to a continuous function $x = (x_1, \dots, x_m)^T$ on the interval $I_\omega \cup [0, \tau)$, continuously differentiable (componentwise) on the interval $[0, \tau)$, satisfying the initial conditions (2) and the equations (1) for all $t \in [0, \tau)$; with $t = 0$ for $dx_i(t)/dt$ we will use a right-hand derivative, namely,

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

We will say that the Cauchy problem (1), (2) is uniquely solvable on the semi-axis $[0, \infty)$ (globally solvable), whenever it has a unique solution on every finite interval $[0, \tau)$.

In works [1], [2], a number of conditions providing global solvability of the problem (1), (2) and non-negativity of all components $x(t)$ are listed, and an approach to constructing componentwise upper estimates for $x(t)$ is developed.

The goal of this article is to apply and develop this approach to studying of mathematical models of living systems, proposed in papers [1], [2]. In Section 2, we briefly describe the results from [1], [2] that allow to find exponentially decreasing estimates by a part of components of the solution $x(t)$. The mentioned estimates are constructed in the framework of additional assumptions with respect to components of the mapping $f(t, x_t)$. Section 3 provides examples demonstrating application of the approach proposed in [2] in the cases when the additional assumptions with respect to the components of the mapping $f(t, x_t)$ are met fully or partially. Each of the examples represents in detail the way of constructing the parameters of exponential estimates ce^{-rt} of components of the solution $x(t)$, which are found as solutions of nonlinear systems of inequalities with respect to the constant $r > 0$ and the vector $c = (c_1, \dots, c_k)^T$, $c_i > 0$, $1 \leq i \leq k < m$. The emerging nonlinear systems of inequalities for c and r are written out based on majorant estimates of components of the mapping $f(t, x_t)$ in the form of some constants, linear or nonlinear mappings.

2. ADDITIONAL ASSUMPTIONS AND EXPONENTIALLY DECREASING ESTIMATES BY A PART OF COMPONENTS OF THE SOLUTION.

To study the Cauchy problem (1), (2), we turn to studying the solution of the system of integral equations

$$(3) \quad x(t) = e^{-\int_0^t (\mu + g(s, x_s)) ds} \psi(0) + \int_0^t e^{-\int_a^t (\mu + g(s, x_s)) ds} f(a, x_a) da, \quad t \geq 0,$$

complemented with initial data (2). The expression $e^{-\int_a^t (\mu + g(s, x_s)) ds}$, used in (3), is understood as a diagonal matrix constructed based on the matrix $\mu + g(s, x_s)$. The system of equations (3) is obtained from (1) by integrating by the variation of constants formula with (2) taken into account.

We refer as a solution of the problem (3), (2) on the interval $[0, \tau]$, $\tau > 0$, to a function $x = (x_1, \dots, x_m)^T$, continuous on the interval $I_\omega \cup [0, \tau]$, satisfying initial condition (2) and equation (3) for all $t \in [0, \tau]$.

We will say that the problem (3), (2) is uniquely solvable on the semi-axis $[0, \infty)$ (globally solvable), whenever it has a unique solution on every finite interval $[0, \tau]$.

Resting on results of paper [3], we have that the problems (1), (2) and (3), (2) are equivalent.

We fix $\tau > 0$. By C_ψ we will mean the set consisting of all functions $x \in C(I_\omega \cup [0, \tau], R^m)$, such that $x(t) = \psi(t)$, $t \in I_\omega$. We assume that $C_{\psi,0}$ is a set consisting of functions $x \in C_\psi$, such that $x(t) \geq 0$, $t \in I_\omega \cup [0, \tau]$. Let $v = v(t) = (v_1(t), \dots, v_m(t))^T$ be some function with non-negative components, continuous on the interval $I_\omega \cup [0, \tau]$. We put that $C_{\psi,0,v}$ consists of functions $x \in C_\psi$, satisfying the equations $0 \leq x(t) \leq v(t)$, $t \in I_\omega \cup [0, \tau]$.

Based on problem (3), (2), we define an operator F , which matches every function $x \in C_{\psi,0}$ to a function $F(x) \in C_{\psi,0}$ by the formulae

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

$$F(x)(t) = e^{-\int_0^t (\mu + g(s, x_s)) ds} \psi(0) + \int_0^t e^{-\int_a^t (\mu + g(s, x_s)) ds} f(a, x_a) da, \quad t \in [0, \tau].$$

In paper [1], the following results were established.

Lemma 1. *If problem (3), (2) has a solution on the interval $[0, \tau]$, $\tau > 0$, then this solution is unique.*

Lemma 2. *Suppose that given some $\tau > 0$ there exists a set of functions $C_{\psi,0,v}$, such that $F : C_{\psi,0,v} \rightarrow C_{\psi,0,v}$. Then problem (3), (2) has a unique solution on the interval $[0, \tau]$, and this solution x is such that $x \in C_{\psi,0,v}$.*

The study of the problem (3), (2) on the interval $[0, \infty)$ is reduced to finding the set of functions $C_{\psi,0,v}$, invariant for the operator F , under the condition that the required function $v = v(t)$ can be chosen to be defined on the whole interval $I_\omega \cup [0, \infty)$. In paper [1], $v(t) = ce^{\gamma t}$, where c is a vector with positive components, γ is a non-negative constant, was taken as such function. The choice of $v(t)$ of the mentioned form allowed to prove the global solvability of problem (3), (2) and non-negativity of the solution, and construct upper estimates of the solution $x(t)$ on the interval $[0, \infty)$.

We will provide the result established in paper [2]. We assume that, given some $1 \leq k < m$, the components of the mapping

$$f(t, x_t) = (f_1(t, x_t), \dots, f_k(t, x_t), f_{k+1}(t, x_t), \dots, f_m(t, x_t))^T$$

satisfy the following assumptions:

(H1) for all $(t, x_t) \in R_+ \times C(I_\omega, R_+^m)$, the inequality

$$(4) \quad (f_{k+1}(t, x_t), \dots, f_m(t, x_t))^T \leq p = (p_{k+1}, \dots, p_m)^T,$$

holds, where $p_{k+1} > 0, \dots, p_m > 0$ are some constants;

(H2) the vector $\eta = (\eta_{k+1}, \dots, \eta_m)^T > 0$ with the components

$$(5) \quad \eta_j = \frac{p_j}{\mu_j}, \quad k + 1 \leq j \leq m,$$

and the set $D_\eta = \{u \in R_+^m : u_j \leq \eta_j, k + 1 \leq j \leq m\}$ are such that for all $(t, x_t) \in R_+ \times C(I_\omega, D_\eta)$, the estimate

$$(6) \quad (f_1(t, x_t), \dots, f_k(t, x_t))^T \leq L(x_t^{(k)}) \\ = \sum_{i=0}^n L_{k,i} x^{(k)}(t - \omega_i) + \int_{-\omega}^0 L_{k,n+1}(\theta) x^{(k)}(t + \theta) d\theta,$$

is true, where $x^{(k)}(t) = (x_1(t), \dots, x_k(t))^T$, the delays $0 < \omega_i \leq \omega < \infty$, $1 \leq i \leq n$, $\omega_0 = 0$, $L_{k,0}, \dots, L_{k,n}, L_{k,n+1}(\theta) - k \times k$ are non-negative matrices, the elements $L_{k,n+1}(\theta)$ are Riemann integrable, and every row of the matrix

$$(7) \quad L_{[k]} = \sum_{i=0}^n L_{k,i} + \int_{-\omega}^0 L_{k,n+1}(\theta) d\theta$$

contains at least one positive element.

Resting on assumptions (H1), (H2), we denote

$$\begin{aligned} \mu_{[k]} &= \text{diag}(\mu_1, \dots, \mu_k), \quad I_{[k]} = \text{diag}(1, \dots, 1), \\ \psi_{[k]}(t) &= (\psi_1(t), \dots, \psi_k(t))^T, \quad t \in I_\omega, \end{aligned}$$

and introduce a system of inequalities with respect to the vector $c \in R^k$ and the constant $r \in R$:

$$(8) \quad c > 0, \quad \left(\mu_{[k]} - rI_{[k]} - \sum_{i=0}^n e^{r\omega_i} L_{k,i} - \int_{-\omega}^0 e^{-r\theta} L_{k,n+1}(\theta) d\theta \right) c \geq 0,$$

$$(9) \quad c \geq \max_{t \in I_\omega} (e^{rt} \psi_{[k]}(t)), \quad 0 < r < \min(\mu_1, \dots, \mu_k).$$

In the following statements and arguments we will use the properties of matrices of a special form. Let $G = (g_{ij}) - m \times m$ be a real matrix such that $g_{ij} \leq 0$, $1 \leq i, j \leq m$, $i \neq j$. We will call the matrix G a non-singular M-matrix if it is non-singular and the matrix G^{-1} is non-negative [4], [5]. The following statements are equivalent to [4], [5]: 1) G is a non-singular M-matrix; 2) all eigenvalues of G have positive real parts; 3) all corner minors of G are positive; 4) there exists $\xi \in R^m$, $\xi > 0$, such that $G\xi > 0$; 5) the matrix $(-G)$ satisfies the criterion of Sevastyanov—Kotelyanskii. The complete list of equivalent statement is provided in [4].

Theorem 1. *Suppose that the assumptions (H1), (H2) are fulfilled, $\mu_{[k]} - L_{[k]}$ is a non-degenerate M-matrix, and the components of the initial function ψ are such that*

$$(10) \quad \max_{t \in I_\omega} \psi_j(t) \leq \eta_j, \quad k+1 \leq j \leq m.$$

Then the Cauchy problem (1), (2) is uniquely solvable on the semi-axis $[0, \infty)$, and for its solution $x = x(t)$ with all $t \in I_\omega \cup [0, \infty)$, the following componentwise estimates hold:

$$(11) \quad 0 \leq x_i(t) \leq c_i e^{-rt}, \quad 1 \leq i \leq k,$$

$$(12) \quad 0 \leq x_j(t) \leq \eta_j, \quad k+1 \leq j \leq m,$$

where $c = (c_1, \dots, c_k)^T$ and r satisfy the inequalities (8), (9), the constants $\eta_{k+1}, \dots, \eta_m$ are defined by the formula (5).

The sketch of the proof of Theorem 1 is as follows. We fix $\tau > 0$ and construct a set of functions $C_{\psi,0,v}$, in which

$$\begin{aligned} v(t) &= (v_1(t), \dots, v_k(t), v_{k+1}(t), \dots, v_m(t))^T, \\ v^{(k)}(t) &= (v_1(t), \dots, v_k(t)) = (c_1 e^{-rt}, \dots, c_k e^{-rt}), \\ (v_{k+1}(t), \dots, v_m(t)) &= (\eta_{k+1}, \dots, \eta_m), \quad t \in R, \end{aligned}$$

where $c = (c_1, \dots, c_k)^T$, r and $\eta_{k+1}, \dots, \eta_m$ are mentioned in the statement of this theorem. Based on relations (4)–(9), we get that for every function $x \in C_{\psi,0,v}$ it is true that $F(x) \in C_{\psi,0,v}$. The parameters $v(t)$ do not depend on τ . Applying Lemmas 1, 2, we establish that problem (3), (2) has on the interval $[0, \infty)$ a unique solution $x(t)$, and inequalities (11), (12) hold.

Note that Theorem 1 does not cover all possible variants of the studied Cauchy problem (1), (2). This is due to the fact that the assumptions (H1), (H2) can be met not for all the components of the mapping $f(t, x_t)$. Moreover, some components of $f(t, x_t)$ can admit estimates which do not effect the construction of exponentially decreasing estimates of a part of the components of the solution $x(t)$. The examples of such Cauchy problems are provided in the next section.

3. EXAMPLES OF STUDYING OF CONCRETE MODELS OF LIVING SYSTEMS.

EXAMPLE 1. Consider a mathematical model describing the spread of tuberculosis among adult population of a separate region (individuals older than 16). Let X_1 be a group of latently infected individuals, X_2 a group of individuals sick with tuberculosis, X_3 a group of individuals susceptible to the disease. We denote the size of the mentioned groups at the moment of time t by $x(t) = (x_1(t), x_2(t), x_3(t))^T$.

The equations of the model are as follows:

$$(13) \quad \frac{dx_1(t)}{dt} = f_1(t, x_t) - (\lambda_1 + \gamma)x_1(t),$$

$$(14) \quad \frac{dx_2(t)}{dt} = f_2(t, x_t) - (\lambda_2 + \alpha)x_2(t), \quad t \geq 0,$$

$$(15) \quad \frac{dx_3(t)}{dt} = f_3(t, x_t) - (\lambda_3 + \beta x_2(t))x_3(t),$$

$$(16) \quad x_1(0) = x_1^0, \quad x_3(0) = x_3^0, \quad x_2(t) = \psi_2(t), \quad t \in I_\omega = [-\omega, 0].$$

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

$$\begin{aligned} f_1(t, x_t) &= (1 - \delta)\beta x_2(t)x_3(t) + \alpha x_2(t) \\ &+ \rho(t - \omega) \left(1 - \exp\left(-\int_{-\omega}^0 \varphi(\theta)x_2(t + \theta) d\theta\right) \right), \\ f_2(t, x_t) &= \delta\beta x_2(t)x_3(t) + \gamma x_1(t), \\ f_3(t, x_t) &= \rho(t - \omega) \exp\left(-\int_{-\omega}^0 \varphi(\theta)x_2(t + \theta) d\theta\right). \end{aligned}$$

All parameters in equations (13)–(15) are positive, $\delta < 1$. The function $\varphi(\theta)$, $\theta \in I_\omega$ is continuous, non-negative, and is not identically equal to zero. The function $\rho(s)$ is continuous, non-negative, and is not identically equal to zero, $s \in I_\omega \cup [0, \infty)$ and is bounded from above by a positive constant:

$$\sup_{t \geq 0} \rho(t - \omega) \leq \rho^*.$$

The initial data in (16) are such that $x_1^0 \geq 0$, $x_3^0 \geq 0$, the function $\psi_2(t)$ is non-negative and continuous.

The system of equations (13)–(15) with the initial data (16) corresponds to the Cauchy problem (1), (2). Moreover, we can write that

$$\psi_1(t) = x_1^0, \psi_3(t) = x_3^0, t \in I_\omega.$$

We turn to the assumptions (H1), (H2). Let $x_1(t), x_2(t), x_3(t)$ be non-negative continuous functions, $-\omega \leq t < \infty$. Based on the structure of the components $f(t, x_t)$, we obtain that for all $t \geq 0$ it is true that $f_3(t, x_t) \leq p_3 = \rho^*$, and if

$$(17) \quad x_3(t) \leq \eta_3 = \frac{\rho^*}{\lambda_3}, t \geq 0,$$

then the following inequalities hold:

$$f_1(t, x_t) \leq ((1 - \delta)\beta\eta_3 + \alpha)x_2(t) + \rho^* \int_{-\omega}^0 \varphi(\theta)x_2(t + \theta) d\theta,$$

$$f_2(t, x_t) \leq \delta\beta\eta_3x_2(t) + \gamma x_1(t), t \geq 0.$$

Denote $J_\varphi = \int_{-\omega}^0 \varphi(\theta) d\theta$. We will write out the matrices $L_{k,i}, L_{[k]}, \mu_{[k]} - L_{[k]}$ that emerge in the assumptions (H1), (H2) with $m = 3, k = 2, k + 1 = 3, n = 0$:

$$\mu_{[2]} = \begin{pmatrix} \lambda_1 + \gamma & 0 \\ 0 & \lambda_2 + \alpha \end{pmatrix}, \quad L_{2,0} = \begin{pmatrix} 0 & (1 - \delta)\beta\eta_3 + \alpha \\ \gamma & \delta\beta\eta_3 \end{pmatrix},$$

$$L_{2,1}(\theta) = \begin{pmatrix} 0 & \rho^*\varphi(\theta) \\ 0 & 0 \end{pmatrix}, \quad L_{[2]} = \begin{pmatrix} 0 & (1 - \delta)\beta\eta_3 + \alpha + \rho^*J_\varphi \\ \gamma & \delta\beta\eta_3 \end{pmatrix},$$

$$\mu_{[2]} - L_{[2]} = \begin{pmatrix} \lambda_1 + \gamma & -(1 - \delta)\beta\eta_3 - \alpha - \rho^*J_\varphi \\ -\gamma & \lambda_2 + \alpha - \delta\beta\eta_3 \end{pmatrix}.$$

Additionally, we assume that

$$(18) \quad x_3^0 \leq \eta_3.$$

Applying Theorem 1, we require that $\mu_{[2]} - L_{[2]}$ is a non-singular M-matrix. We will use the criterion which requires all main minors M_1, M_2 of the matrix $\mu_{[2]} - L_{[2]}$ to be positive. The mentioned minors are as follows: $M_1 = \lambda_1 + \gamma > 0$,

$$M_2 = \det(\mu_{[2]} - L_{[2]}) = (\lambda_1 + \gamma)(\lambda_2 + \alpha - \delta\beta\eta_3) - \gamma((1 - \delta)\beta\eta_3 + \alpha + \rho^*J_\varphi).$$

Transforming the inequality $M_2 > 0$, we arrive at the relation

$$(19) \quad R_{0,1} = \frac{\delta\beta\eta_3}{\lambda_2 + \alpha} + \frac{\gamma((1 - \delta)\beta\eta_3 + \alpha + \rho^*J_\varphi)}{(\lambda_1 + \gamma)(\lambda_2 + \alpha)} < 1,$$

which means that $\mu_{[2]} - L_{[2]}$ is a non-singular M-matrix. Following the common terminology [6], [7], we will call the constant $R_{0,1}$ the basic reproductive number. The first term in the right-hand side of the formula for $R_{0,1}$ means the coefficient of producing sick individuals due to the transitions $X_3 \rightarrow X_2$, and the second term due to the transitions $X_3 \rightarrow X_1 \rightarrow X_2 \leftrightarrow X_1$.

Hence, if inequalities (18), (19) are fulfilled, then due to Theorem 1, the component $x_3(t)$ of the studied model is non-negative and satisfies the estimate (17), and the components $x_1(t), x_2(t)$ of the solution admit the exponentially decreasing estimates

$$(20) \quad 0 \leq x_i(t) \leq c_i e^{-rt}, i = 1, 2, t \in I_\omega \cup [0, \infty),$$

where the positive constants c_1, c_2, r are obtained from the system of inequalities of the form (8), (9). We turn to finding these constants.

We denote: $c_{[2]} = (c_1, c_2)^T$, $\psi_{[2]}(t) = (x_1^{(0)}, \psi_2(t))^T$, $t \in I_\omega$,

$$H(r) = (h_{ij}(r)) = \mu_{[2]} - rI_{[2]} - L_{2,0} - \int_{-\omega}^0 e^{-r\theta} L_{2,1}(\theta) d\theta, \quad r \in R.$$

We obtain that

$$H(r) = \begin{pmatrix} \lambda_1 + \gamma - r & -(1 - \delta)\beta\eta_3 - \alpha - \rho^* \int_{-\omega}^0 e^{-r\theta} \varphi(\theta) d\theta \\ -\gamma & \lambda_2 + \alpha - \delta\beta\eta_3 - r \end{pmatrix}, \quad r \in R,$$

It is easy to see that $H(0) = \mu_{[2]} - L_{[2]}$ and $\det H(0) > 0$. Inequalities (8), (9) lead to the following relations:

$$(21) \quad c_{[2]} > 0, \quad H(r)c_{[2]} \geq 0,$$

$$(22) \quad c_{[2]} \geq \max_{t \in I_\omega} (e^{rt} \psi_{[2]}(t)), \quad 0 < r < \min(\lambda_1 + \gamma, \lambda_2 + \alpha).$$

We will find the constant r as the root of the equation

$$(23) \quad \det H(r) = 0, \quad 0 < r < \min(\lambda_1 + \gamma, \lambda_2 + \alpha).$$

We have that

$$\det H(r) = (\lambda_1 + \gamma - r)(\lambda_2 + \alpha - \delta\beta\eta_3 - r) - \gamma((1 - \delta)\beta\eta_3 + \alpha + \rho^* \int_{-\omega}^0 e^{-r\theta} \varphi(\theta) d\theta).$$

Relation (19) yields the inequality $\lambda_2 + \alpha > \delta\beta\eta_3$. Taking into account this inequality, we will find the root r of equation (23) based on the following relation:

$$(24) \quad (\lambda_1 + \gamma - r)(\lambda_2 + \alpha - \delta\beta\eta_3 - r) = \gamma((1 - \delta)\beta\eta_3 + \alpha + \rho^* \int_{-\omega}^0 e^{-r\theta} \varphi(\theta) d\theta),$$

$$(25) \quad 0 < r < r_H = \min(\lambda_1 + \gamma, \lambda_2 + \alpha - \delta\beta\eta_3).$$

Putting $r \in R$, $0 \leq r \leq r_H$, we introduce the functions

$$\begin{aligned} \varphi_1(r) &= (\lambda_1 + \gamma - r)(\lambda_2 + \alpha - \delta\beta\eta_3 - r), \\ \varphi_2(r) &= \gamma((1 - \delta)\beta\eta_3 + \alpha + \rho^* \int_{-\omega}^0 e^{-r\theta} \varphi(\theta) d\theta). \end{aligned}$$

We have that $\varphi_1(0) > \varphi_2(0)$, because $\det H(0) > 0$ and $\varphi_1(r_H) = 0 < \varphi_2(r_H)$. The function $\varphi_1(r)$ is strictly monotonously decreasing, and the function $\varphi_2(r)$ is strictly monotonously increasing on the interval $r \in (0, r_H)$. Therefore, equation (24), taking into account (25), has exactly one root $r = r_* \in (0, r_H)$. Putting that $r = r_*$, we confirm that equation (23) has a solution.

To find the vector $c_{[2]}$, we will do the following. Based on (23), consider the equation $H(r_*)u = 0$, where $u = (u_1, u_2)^T \in R^2$:

$$\begin{aligned} h_{11}(r_*)u_1 + h_{12}(r_*)u_2 &= 0, \\ h_{21}(r_*)u_1 + h_{22}(r_*)u_2 &= 0. \end{aligned}$$

Since $\det H(r_*) = 0$ and $h_{11}(r_*) = \lambda_1 + \gamma - r_* \neq 0$, then

$$u = (u_1, u_2)^T = \nu u^* = \nu (u_1^*, 1)^T,$$

where $\nu \in R$ is an arbitrary constant, and the component u_1^* is as follows:

$$u_1^* = \frac{(1 - \delta)\beta\eta_3 + \alpha + \rho^* \int_{-\omega}^0 e^{-r_*\theta} \varphi(\theta) d\theta}{\lambda_1 + \gamma - r_*}.$$

Assuming that $\nu > 0$, we establish that r_* and the vector $c_{[2]} = \nu u^*$ satisfy (21). Now we take that $c_{[2]} = \nu_* u^*$, where the constant $\nu_* > 0$ is chosen to satisfy the first of the inequalities from (22), and depends on the components of the initial function $\psi_{[2]}(t)$.

We turn to formula (19). Note that the value of $R_{0,1}$ depends significantly on $\beta\eta_3, \rho^* J_\varphi$. Indeed, for all parameters $\gamma, \alpha, \lambda_1, \lambda_2$, the following inequality holds:

$$\frac{\gamma\alpha}{(\lambda_1 + \gamma)(\lambda_2 + \alpha)} < 1.$$

Hence, the inequality $R_{0,1} < 1$ will be fulfilled for sufficiently small $\beta\eta_3$ and $\rho^* J_\varphi$. The parameters $\beta\eta_3, \rho^* J_\varphi$ reflect the speeds of emerging of new sick and infected individuals per one existing sick individual as a result of contacts of sick individuals with susceptible adult individuals and growing individuals of the age of around 16. Therefore, in the framework of the considered model, the restriction of the possibility of contacts between the mentioned groups of individuals can lead to eradication of the disease in the area.

EXAMPLE 2. Consider the mathematical model describing production of some substances Y_1, Y_2, Y_3 under the influence of the feedback from the stimulant Y_4 and the inhibitor Y_5 . The variables $y_1(t), y_2(t), y_3(t), y_4(t), y_5(t)$ stand for the number (in conventional units) of Y_1, Y_2, Y_3, Y_4, Y_5 at the moment of time t . We will study the Cauchy problem for the system of differential equations

$$\begin{aligned} \frac{dy_1(t)}{dt} &= \frac{1}{1 + \gamma y_5(t - \omega_1)} - \lambda_1 y_1(t), \\ \frac{dy_2(t)}{dt} &= \frac{\alpha y_4(t - \omega_2) y_1(t)}{1 + \beta y_4(t - \omega_2)} - \lambda_2 y_2(t), \\ \frac{dy_3(t)}{dt} &= y_2(t) - \lambda_3 y_3(t), \quad t \geq 0, \\ \frac{dy_4(t)}{dt} &= y_3(t) - \lambda_4 y_4(t), \\ \frac{dy_5(t)}{dt} &= y_4(t) - \lambda_5 y_5(t), \\ y_1(0) &= y_1^0, \quad y_2(0) = y_2^0, \quad y_3(0) = y_3^0, \\ y_4(t) &= \psi_4(t), \quad y_5(t) = \psi_5(t), \quad t \in I_\omega = [-\max\{\omega_1, \omega_2\}, 0], \end{aligned}$$

where $\lambda_i, 1 \leq i \leq 5, \gamma, \alpha, \beta, \omega_1, \omega_2$ are positive parameters, the initial values y_1^0, y_2^0, y_3^0 are non-negative constants, the initial functions $\psi_4(t), \psi_5(t)$ are non-negative and continuous. Up to notation, the mentioned equations and initial data correspond to the Cauchy problem (1), (2).

For further investigation, we will write these equations and initial data in the form that is more convenient. We re-letter the variables of the studied model:

$$x_1(t) = y_2(t), \quad x_2(t) = y_3(t), \quad x_3(t) = y_4(t), \quad x_4(t) = y_5(t), \quad x_5(t) = y_1(t).$$

We put $x(t) = (x_1(t), x_2(t), x_3(t), x_4(t), x_5(t))^T$ and consider the Cauchy problem for the components of $x(t)$:

$$(26) \quad \frac{dx_1(t)}{dt} = \frac{\alpha x_3(t - \omega_2) x_5(t)}{1 + \beta x_3(t - \omega_2)} - \lambda_2 x_1(t),$$

$$(27) \quad \frac{dx_2(t)}{dt} = x_1(t) - \lambda_3 x_2(t),$$

$$(28) \quad \frac{dx_3(t)}{dt} = x_2(t) - \lambda_4 x_3(t), \quad t \geq 0,$$

$$(29) \quad \frac{dx_4(t)}{dt} = x_3(t) - \lambda_5 x_4(t),$$

$$(30) \quad \frac{dx_5(t)}{dt} = \frac{1}{1 + \gamma x_4(t - \omega_1)} - \lambda_1 x_5(t),$$

$$(31) \quad x_1(0) = y_2^0, \quad x_2(0) = y_3^0, \quad x_5(0) = y_1^0, \quad x_3(t) = \psi_4(t), \quad x_4(t) = \psi_5(t), \quad t \in I_\omega.$$

We assume that $x_i(t)$ are non-negative continuous functions,

$$1 \leq i \leq 5, \quad t \in I_\omega \cup [0, \infty).$$

Based on the structure of the components $f(t, x_t)$ of the system (26)–(30), we obtain that

$$(32) \quad f_5(t, x_t) = \frac{1}{1 + \gamma x_4(t - \omega_1)} \leq p_5 = 1, \quad t \geq 0,$$

and, if the inequality

$$(33) \quad x_5(t) \leq \eta_5 = \frac{p_5}{\lambda_1}, \quad t \geq 0,$$

holds, then for all $t \geq 0$ the following relations are true:

$$(34) \quad f_1(t, x_t) = \frac{\alpha x_3(t - \omega_2) x_5(t)}{1 + \beta x_3(t - \omega_2)} \leq \alpha \eta_5 x_3(t - \omega_2),$$

$$(35) \quad f_2(t, x_t) = x_1(t), \quad f_3(t, x_t) = x_2(t),$$

$$(36) \quad f_4(t, x_t) = x_3(t).$$

From (32)–(36) it is easy to see that the variable $x_4(t)$ is not present in (34)–(36).

Below, two ways to construct exponentially decreasing estimates for a part of the components $x(t)$, based on the assumptions (H1), (H2), Theorem 1, and their modification, are provided.

First way. This way corresponds to the approach presented in Section 2 and described in Example 1. Here, to perform supplementary transformations, we introduce the constant $\varepsilon > 0$ and strengthen the estimate for $f_1(t, x_t)$: instead of (34), we will use the inequality

$$(37) \quad f_1(t, x_t) \leq \alpha \eta_5 x_3(t - \omega_2) + \varepsilon x_4(t), \quad t \geq 0.$$

From here, we can write the vector p and the matrices $L_{k,i}$, $L_{[k]}$, $\mu_{[k]} - L_{[k]}$, emerging in the assumptions (H1), (H2) with $m = 5$, $k = 4$, $k + 1 = 5$, $n = 2$, in particular: $p = p_5 = 1$, $L_{4,1} \equiv 0$, $L_{4,3}(\theta) \equiv 0$, $\theta \in I_\omega$,

$$\mu_{[4]} = \begin{pmatrix} \lambda_2 & 0 & 0 & 0 \\ 0 & \lambda_3 & 0 & 0 \\ 0 & 0 & \lambda_4 & 0 \\ 0 & 0 & 0 & \lambda_5 \end{pmatrix}, \quad L_{4,0} = \begin{pmatrix} 0 & 0 & 0 & \varepsilon \\ 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \end{pmatrix},$$

$$L_{4,2} = \begin{pmatrix} 0 & 0 & \alpha \eta_5 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}, \quad L_{[4]} = \begin{pmatrix} 0 & 0 & \alpha \eta_5 & \varepsilon \\ 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \end{pmatrix},$$

$$\mu_{[4]} - L_{[4]} = \begin{pmatrix} \lambda_2 & 0 & -\alpha\eta_5 & -\varepsilon \\ -1 & \lambda_3 & 0 & 0 \\ 0 & -1 & \lambda_4 & 0 \\ 0 & 0 & -1 & \lambda_5 \end{pmatrix}.$$

In addition, we assume that

$$(38) \quad x_5(0) = y_1^0 \leq \eta_5.$$

Turning to the conditions of Theorem 1, we require that $\mu_{[4]} - L_{[4]}$ was a non-singular M-matrix. We obtain the positivity conditions for all main minors of the matrix $\mu_{[4]} - L_{[4]}$. The mentioned minors are as follows:

$$M_1 = \lambda_2 > 0, \quad M_2 = \lambda_2 \lambda_3 > 0, \quad M_3 = \lambda_2 \lambda_3 \lambda_4 - \alpha\eta_5, \quad M_4 = \lambda_5 M_3 - \varepsilon.$$

Assume that the following inequality holds:

$$(39) \quad \lambda_2 \lambda_3 \lambda_4 - \alpha\eta_5 > 0.$$

Then we can choose $\varepsilon = \varepsilon_* > 0$, such that $\mu_{[4]} - L_{[4]}$ was a non-singular M-matrix.

Therefore, if the inequalities (38) and (39) are fulfilled, then for the variables $x_1(t), x_2(t), x_3(t), x_4(t)$, the estimates

$$(40) \quad 0 \leq x_i(t) \leq c_i e^{-rt}, \quad 1 \leq i \leq 4, \quad t \in I_\omega \cup [0, \infty),$$

are true, where the positive constants c_1, c_2, c_3, c_4, r are found from the system of inequalities of the form (8), (9). We move on to finding these constants.

We denote:

$$\begin{aligned} c_{[4]} &= (c_1, c_2, c_3, c_4)^T, \\ \psi_{[4]}(t) &= (y_2^0, y_3^0, \psi_4(t), \psi_5(t))^T, \quad t \in I_\omega, \\ H_{[4]}(r) &= \mu_{[4]} - rI_{[4]} - L_{4,0} - e^{r\omega_2} L_{4,2}, \quad r \in R. \end{aligned}$$

We obtain that

$$H_{[4]}(r) = \begin{pmatrix} \lambda_2 - r & 0 & -e^{r\omega_2}\alpha\eta_5 & -\varepsilon_* \\ -1 & \lambda_3 - r & 0 & 0 \\ 0 & -1 & \lambda_4 - r & 0 \\ 0 & 0 & -1 & \lambda_5 - r \end{pmatrix},$$

$$H_{[4]}(0) = \mu_{[4]} - L_{[4]}, \quad \det H_{[4]}(0) > 0.$$

Turning to inequalities (8), (9), we arrive at the following relations:

$$(41) \quad c_{[4]} > 0, \quad H_{[4]}(r)c_{[4]} \geq 0,$$

$$(42) \quad c_{[4]} \geq \max_{t \in I_\omega} (e^{rt} \psi_{[4]}(t)), \quad 0 < r < \min(\lambda_2, \lambda_3, \lambda_4, \lambda_5).$$

We will find the constant r as a root of the equation

$$(43) \quad \det H_{[4]}(r) = 0, \quad 0 < r < r_\lambda = \min(\lambda_2, \lambda_3, \lambda_4, \lambda_5).$$

We have that

$$\det H_{[4]}(r) = (\lambda_5 - r)((\lambda_2 - r)(\lambda_3 - r)(\lambda_4 - r) - e^{r\omega_2}\alpha\eta_5) - \varepsilon_*,$$

and equation (43) can be written in the form

$$(44) \quad (\lambda_2 - r)(\lambda_3 - r)(\lambda_4 - r) = \frac{\varepsilon_*}{\lambda_5 - r} + e^{r\omega_2}\alpha\eta_5, \quad 0 < r < r_\lambda.$$

Introduce the functions

$$\varphi_1(r) = (\lambda_2 - r)(\lambda_3 - r)(\lambda_4 - r), \quad \varphi_2(r) = \frac{\varepsilon_*}{\lambda_5 - r} + e^{r\omega_2} \alpha \eta_5, \quad r \in R, \quad 0 \leq r < r_\lambda.$$

We have that $\varphi_1(0) > \varphi_2(0)$ due to (39). The function $\varphi_1(r)$ is strictly monotonously decreasing, and the function $\varphi_2(r)$ is strictly monotonously increasing on the interval $r \in (0, r_\lambda)$, and, moreover, $\varphi_2(r) \rightarrow +\infty$ given $r \rightarrow \lambda_5$, $r < \lambda_5$. Therefore, equation (44) along with equation (43) have on the interval $r \in (0, r_\lambda)$ exactly one root $r = r_*$.

Now, we will find the vector $c_{[4]}$. Based on (41), consider the equation $H_{[4]}(r_*)u = 0$, where $u = (u_1, u_2, u_3, u_4)^T \in R^4$. From (44) it follows that the rank of $H_{[4]}(r_*)$ equals 3. We will write the required solution $u = u^* = (u_1^*, u_2^*, u_3^*, u_4^*)^T$ in the form

$$u_1^* = (\lambda_3 - r_*)(\lambda_4 - r_*)(\lambda_5 - r_*) u_4^*,$$

$$u_2^* = (\lambda_4 - r_*)(\lambda_5 - r_*) u_4^*, \quad u_3^* = (\lambda_5 - r_*) u_4^*.$$

where u_4^* is an arbitrary constant. The constant u_4^* is chosen in a way that the vector $c_{[4]} = c_{[4]}^* = u^* > 0$ satisfies the inequality

$$(45) \quad c_{[4]}^* \geq \max_{t \in I_\omega} (e^{r_* t} \psi_{[4]}(t)).$$

It is obvious that for every initial function $\psi_{[4]}(t)$ there is a positive constant u_4^* that guarantees the fulfillment of inequality (45).

Note that the vector $c_{[4]}^*$ and the constant r_* depend on the constant ε_* . If we do not use in (37) the term $\varepsilon x_4(t)$, that is, if we put $\varepsilon = 0$, then finding the solutions of system (41), (42) will become significantly more complicated.

Second way. This way is based on a modification of the approach proposed in Section 2. The modification is based on another variant of constructing of the set of functions $C_{\psi,0,v}$, invariant for the operator F with every fixed $\tau > 0$. Here, it is significantly important that for the studied Cauchy problem, the variable $x_4(t)$ does not belong to relations (34)–(36).

Assume that inequality (38) is fulfilled. Following the sketch of a proof of Theorem 1, we consider the function

$$v(t) = (c_1 e^{-rt}, c_2 e^{-rt}, c_3 e^{-rt}, x_4^0(t), \eta_5)^T, \quad t \in I_\omega \cup [0, \infty),$$

where the constant η_5 is mentioned in (33), c_1, c_2, c_3, r are the required positive constants, the function $x_4^0(t)$ is found via $c_3 e^{-rt}$ and the integral relation

$$x_4(t) = e^{-\lambda_5 t} \left(\psi_5(0) + \int_0^t e^{\lambda_5 s} x_3(s) ds \right), \quad t \geq 0,$$

for the variable $x_4(t)$, which follows from (29) and is complemented with the initial data $x_4(t) = \psi_5(t)$, $t \in I_\omega$. We denote

$$(46) \quad \psi_5^0 = \max_{t \in I_\omega} \psi_5(t).$$

Assume that given some $c_3 > 0$, $r > 0$, the following relations are true:

$$0 \leq x_3(t) \leq c_3 e^{-rt}, \quad t \in [0, \infty).$$

Then for the variable $x_4(t)$, the a priori estimates

$$0 \leq x_4(t) \leq \psi_5^0, \quad t \in I_\omega,$$

$$0 \leq x_4(t) \leq e^{-\lambda_5 t} \psi_5^0 + h_4(t), \quad t \in [0, \infty),$$

hold, where $h_4(t) = c_3(e^{-\lambda_5 t} - e^{-rt})/(r - \lambda_5)$, if $r \neq \lambda_5$, and $h_4(t) = c_3 t e^{-rt}$, if $r = \lambda_5$. Further, we put that

$$(47) \quad x_4^0(t) = \psi_5^0, \quad t \in I_\omega, \quad x_4^0(t) = e^{-\lambda_5 t} \psi_5^0 + h_4(t), \quad t \in [0, \infty).$$

Based on inequalities (32)–(35), we denote:

$$\begin{aligned} c_{[3]} &= (c_1, c_2, c_3)^T, \\ \psi_{[3]}(t) &= (y_2^0, y_3^0, \psi_4(t))^T, \quad t \in I_\omega, \\ H_{[3]}(r) &= \mu_{[3]} - rI_{[3]} - L_{3,0} - e^{r\omega_2} L_{3,2}, \quad r \in R, \end{aligned}$$

where

$$\begin{aligned} \mu_{[3]} &= \begin{pmatrix} \lambda_2 & 0 & 0 \\ 0 & \lambda_3 & 0 \\ 0 & 0 & \lambda_4 \end{pmatrix}, \quad L_{3,0} = \begin{pmatrix} 0 & 0 & 0 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \end{pmatrix}, \\ L_{3,2} &= \begin{pmatrix} 0 & 0 & \alpha\eta_5 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}, \quad L_{[3]} = \begin{pmatrix} 0 & 0 & \alpha\eta_5 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \end{pmatrix}, \\ \mu_{[3]} - L_{[3]} &= \begin{pmatrix} \lambda_2 & 0 & -\alpha\eta_5 \\ -1 & \lambda_3 & 0 \\ 0 & -1 & \lambda_4 \end{pmatrix}. \end{aligned}$$

Assume that inequality (39) is fulfilled and find a solution of the inequalities

$$(48) \quad c_{[3]} > 0, \quad H_{[3]}(r)c_{[3]} \geq 0,$$

$$(49) \quad c_{[3]} \geq \max_{t \in I_\omega} (e^{rt} \psi_{[3]}(t)), \quad 0 < r < \min(\lambda_2, \lambda_3, \lambda_4).$$

We will find the constant r as the root of the equation

$$(50) \quad \det H_{[3]}(r) = (\lambda_2 - r)(\lambda_3 - r)(\lambda_4 - r) - e^{r\omega_2} \alpha\eta_5 = 0, \quad 0 < r < \min(\lambda_2, \lambda_3, \lambda_4).$$

Omitting the details, we establish that equation (50) has a unique root $r = r_0$ on the mentioned interval. Turning to (48), (49), we put that the required

$$c_{[3]} = c_{[3]}^0 = u^0 = (u_1^0, u_2^0, u_3^0)^T,$$

where

$$u_1^0 = (\lambda_3 - r_0)(\lambda_4 - r_0) u_3^0, \quad u_2^0 = (\lambda_4 - r_0) u_3^0,$$

u_3^0 is a positive constant such that $c_{[3]}^0$ satisfies the inequality

$$(51) \quad c_{[3]}^0 \geq \max_{t \in I_\omega} (e^{r_0 t} \psi_{[3]}(t)).$$

It is clear that for every initial function $\psi_{[3]}(t)$ there exists a constant $u_3^0 > 0$ that provides the fulfillment of inequality (51).

Assume that inequalities (38) and (39) are fulfilled. We fix the function

$$v = v(t) = (c_1^0 e^{-r_0 t}, c_2^0 e^{-r_0 t}, c_3^0 e^{-r_0 t}, x_4^0(t), \eta_5)^T, \quad t \in I_\omega \cup [0, \infty).$$

Based on works [1], [2] and following the lines of the sketch of a proof of Theorem 1, we establish that for every fixed $\tau > 0$ the set of functions $C_{\psi,0,v}$ is invariant for the operator F . Then for the solution $x(t)$ of the Cauchy problem (26)–(31), the following estimates are true:

$$\begin{aligned} 0 &\leq x_i(t) \leq c_i^0 e^{-r_0 t}, \quad i = 1, 2, 3, \\ 0 &\leq x_4(t) \leq x_4^0(t), \quad 0 \leq x_5(t) \leq \eta_5, \quad t \in I_\omega \cup [0, \infty). \end{aligned}$$

Note that the constants c_1^0, c_2^0, c_3^0, r_0 do not depend on λ_5 , and the form of the upper estimate $x_4^0(t)$ of the variable $x_4(t)$ is more complicated than the one of the estimate $c_4^* e^{-r_* t}$ that was established within the framework of the first way.

We return to the initial notation. We will rewrite the differential equation for $y_1(t)$, taking into account the initial data, in the form of the Cauchy problem

$$(52) \quad y_1(0) = y_1^0, \quad \frac{dy_1(t)}{dt} = 1 + \left(\frac{1}{1 + \gamma y_5(t - \omega_1)} - 1 \right) - \lambda_1 y_1(t), \quad t \geq 0,$$

assuming that the function $y_5(t)$ is known. Based on the obtained estimates, we have that $y_5(t) \equiv x_4(t) \rightarrow 0$ given $t \rightarrow +\infty$. Using the standard approaches to solving the Cauchy problem for non-uniform linear differential equation and applying to (52) the results of work [8], we obtain that $y_1(t) \rightarrow 1/\lambda_1$ given $t \rightarrow +\infty$.

We express the inequality (39) in the following form:

$$R_{0,2} = \frac{\alpha}{\lambda_1 \lambda_2 \lambda_3 \lambda_4} < 1.$$

The constant $R_{0,2}$ will be called a basic reproductive number. This number shows the relation of intensity of production of the substance Y_2 (the constant α) to the product of intensities of decomposition of the substances Y_1, Y_2, Y_3, Y_4 (the constant $\lambda_1 \lambda_2 \lambda_3 \lambda_4$). From the mentioned results, it follows that in the case when the inequalities $R_{0,2} < 1$ and $y_1^0 \leq 1/\lambda_1$ are fulfilled, the amount of the substances Y_2, Y_3, Y_4, Y_5 decreases to zero over time, while the amount of the substance Y_1 gets to the level $1/\lambda_1$.

EXAMPLE 3. Consider a mathematical model, describing development of HIV-1 infection in a human organism. We will study the dynamics of HIV-1 infection in terms of the following populations of viral particles and cells:

V – virions (viral particles leading to contamination with HIV-1 infection);

I – productively infected cells that produce the virions V ;

T – target cells for the virions V ;

E – lymphocytes-effectors that destroy the cells I ;

Q – precursor cells of the lymphocytes-effectors E .

Let $x_1(t), x_2(t), x_3(t), x_4(t), x_5(t)$ be the sizes of populations of the virions V and the cells I, T, E, Q at the moment of time t ,

$$x(t) = (x_1(t), x_2(t), x_3(t), x_4(t), x_5(t))^T.$$

The equations of the model have the following form:

$$(53) \quad \frac{dx_1(t)}{dt} = \nu x_2(t) - (\mu_1 + \gamma_{1,3} x_3(t)) x_1(t),$$

$$(54) \quad \frac{dx_2(t)}{dt} = \delta_2 \gamma_{1,3} x_1(t - \omega_1) x_3(t - \omega_1) + \delta_2 \gamma_{2,3} x_2(t - \omega_1) x_3(t - \omega_1) - (\mu_2 + \gamma_{2,4} x_4(t)) x_2(t),$$

$$(55) \quad \frac{dx_3(t)}{dt} = \rho_3(t) - (\mu_3 + \gamma_{1,3} x_1(t) + \gamma_{2,3} x_2(t)) x_3(t), \quad t \geq 0,$$

$$(56) \quad \frac{dx_4(t)}{dt} = n_4 \beta x_5(t - \omega_2) x_3(t - \omega_2) x_1(t - \omega_2) - (\mu_4 + \delta_4 \gamma_{2,4} x_2(t)) x_4(t),$$

$$(57) \quad \frac{dx_5(t)}{dt} = \rho_5(t) + n_5 \beta x_5(t - \omega_2) x_3(t - \omega_2) x_1(t - \omega_2) - (\mu_5 + \beta x_3(t) x_1(t)) x_5(t),$$

$$(58) \quad x_i(t) = \psi_i(t), \quad i = 1, 2, 3, 5, \quad t \in I_\omega = [-\max\{\omega_1, \omega_2\}, 0], \quad x_4(0) = x_4^0.$$

All the parameters in equations (53)–(57) are positive and, moreover, $\delta_2 < 1$, $\delta_4 < 1$. The functions $\rho_3(t)$, $\rho_5(t)$ are continuous, non-negative, not identically zero, $t \in [0, \infty)$, and bounded from above by the positive constants:

$$\sup_{t \geq 0} \rho_3(t) \leq \rho_3^*, \quad \sup_{t \geq 0} \rho_5(t) \leq \rho_5^*.$$

The initial data in (58) is such that $x_4^0 \geq 0$, the functions $\psi_i(t)$ are non-negative and continuous, $i = 1, 2, 3, 5$, $t \in I_\omega$. We denote $\psi_4(t) = x_4^0$, $t \in I_\omega$. The system (53)–(58) corresponds to the Cauchy problem (1), (2).

Assume that $x_i(t)$ are non-negative continuous functions, $1 \leq i \leq 5$, $t \in I_\omega \cup [0, \infty)$. Based on the structure of the components $f(t, x_t)$ of the system (53)–(57), we obtain that

$$(59) \quad f_3(t, x_t) = \rho_3(t) \leq p_3 = \rho_3^*, \quad t \geq 0,$$

and, if the inequality

$$(60) \quad x_3(t) \leq \eta_3 = \frac{p_3}{\mu_3}, \quad t \in I_\omega \cup [0, \infty),$$

is fulfilled, then for every $t \geq 0$ the following relations are true:

$$(61) \quad f_1(t, x_t) = \nu x_2(t),$$

$$(62) \quad f_2(t, x_t) = \delta_2 \gamma_{1,3} x_1(t - \omega_1) x_3(t - \omega_1) + \delta_2 \gamma_{2,3} x_2(t - \omega_1) x_3(t - \omega_1) \\ \leq \delta_2 \gamma_{1,3} \eta_3 x_1(t - \omega_1) + \delta_2 \gamma_{2,3} \eta_3 x_2(t - \omega_1),$$

$$(63) \quad f_4(t, x_t) = n_4 \beta x_5(t - \omega_2) x_3(t - \omega_2) x_1(t - \omega_2) \leq n_4 \beta \eta_3 x_5(t - \omega_2) x_1(t - \omega_2),$$

$$(64) \quad f_5(t, x_t) = \rho_5(t) + n_5 \beta x_5(t - \omega_2) x_3(t - \omega_2) x_1(t - \omega_2) \\ \leq \rho_5^* + n_5 \beta \eta_3 x_5(t - \omega_2) x_1(t - \omega_2).$$

From (59)–(64), it is clear that for the Cauchy problem (53)–(58), the assumptions (H1) and (H2) are partially met. Thus, if we only consider the equations for $x_1(t)$, $x_2(t)$, $x_3(t)$, then they meet the mentioned assumptions, since $x_4(t)$ and $x_5(t)$ are not present in relations (59)–(62). Therefore, along with the estimate $0 \leq x_3(t) \leq \eta_3$, $t \in I_\omega \cup [0, \infty)$, we can formally construct the estimates

$$(65) \quad 0 \leq x_1(t) \leq c_1 e^{-rt}, \quad 0 \leq x_2(t) \leq c_2 e^{-rt}, \quad t \in I_\omega \cup [0, \infty),$$

where the positive constants c_1 , c_2 , r are found from the system of inequalities of the form (8), (9) given $m = 3$, $k = 2$, $k + 1 = 3$, $n = 1$. The values of the mentioned constants do not depend on the values of the variables $x_4(t)$, $x_5(t)$, $t \in I_\omega \cup [0, \infty)$.

We turn to finding c_1 , c_2 , r . Keeping the lettering of the variables and using (59)–(62), we consider the auxiliary Cauchy problem

$$(66) \quad \frac{dx_1(t)}{dt} = \nu x_2(t) - \mu_1 x_1(t), \quad t \geq 0,$$

$$(67) \quad \frac{dx_2(t)}{dt} = \delta_2 \gamma_{1,3} \eta_3 x_1(t - \omega_1) + \delta_2 \gamma_{2,3} \eta_3 x_2(t - \omega_1) - \mu_2 x_2(t),$$

$$(68) \quad x_1(t) = \psi_1(t), \quad x_2(t) = \psi_2(t), \quad t \in I_\omega.$$

Based on (66)–(68), we denote:

$$c_{[2]} = (c_1, c_2)^T, \quad \psi_{[2]}(t) = (\psi_1(t), \psi_2(t))^T, \quad t \in I_\omega,$$

$$\begin{aligned}\mu_{[2]} &= \begin{pmatrix} \mu_1 & 0 \\ 0 & \mu_2 \end{pmatrix}, \quad L_{2,0} = \begin{pmatrix} 0 & \nu \\ 0 & 0 \end{pmatrix}, \\ L_{2,1} &= \begin{pmatrix} 0 & 0 \\ \delta_2\gamma_{1,3}\eta_3 & \delta_2\gamma_{2,3}\eta_3 \end{pmatrix}, \quad L_{[2]} = \begin{pmatrix} 0 & \nu \\ \delta_2\gamma_{1,3}\eta_3 & \delta_2\gamma_{2,3}\eta_3 \end{pmatrix}, \\ \mu_{[2]} - L_{[2]} &= \begin{pmatrix} \mu_1 & -\nu \\ -\delta_2\gamma_{1,3}\eta_3 & \mu_2 - \delta_2\gamma_{2,3}\eta_3 \end{pmatrix}, \\ H_{[2]}(r) &= \mu_{[2]} - rL_{[2]} - L_{2,0} - e^{r\omega_1}L_{2,1}, \quad r \in R.\end{aligned}$$

Performing elementary transformations, we find that

$$H_{[2]}(r) = \begin{pmatrix} \mu_1 - r & -\nu \\ -e^{r\omega_1}\delta_2\gamma_{1,3}\eta_3 & \mu_2 - r - e^{r\omega_1}\delta_2\gamma_{2,3}\eta_3 \end{pmatrix}, \quad r \in R.$$

Assume that the following inequality holds:

$$(69) \quad \mu_1(\mu_2 - \delta_2\gamma_{2,3}\eta_3) > \nu\delta_2\gamma_{1,3}\eta_3.$$

Then $\mu_{[2]} - L_{[2]}$ is a non-singular M-matrix and there exists a solution of the system

$$(70) \quad c_{[2]} > 0, \quad H_{[2]}(r)c_{[2]} \geq 0,$$

$$(71) \quad c_{[2]} \geq \max_{t \in I_\omega} (e^{rt}\psi_{[2]}(t)), \quad 0 < r < \min(\mu_1, \mu_2).$$

The solution of the system of inequalities (70), (71) is constructed the following way. We put that $r = r_*$, where r_* is the unique root of the equation

$$\mu_2 - r - e^{r\omega_1}\delta_2\gamma_{2,3}\eta_3 = \frac{e^{r\omega_1}\nu\delta_2\gamma_{1,3}\eta_3}{\mu_1 - r}$$

on the interval $0 < r < \min(\mu_1, \mu_2)$, $c_1 = c_1^* = \nu c_2^*/(\mu_1 - r_*)$, where the constant $c_2^* > 0$ is chosen in a way that the vector $c_{[2]}^* = (c_1^*, c_2^*)^T$ satisfies the inequality

$$c_{[2]}^* \geq \max_{t \in I_\omega} (e^{r_*t}\psi_{[2]}(t)).$$

We return to relations (63), (64) and the variables $x_4(t)$, $x_5(t)$. Turning to (60) and (65), we set that

$$(72) \quad 0 \leq x_3(t) \leq \eta_3, \quad 0 \leq x_1(t) \leq x_1^* = c_1^*e^{r_*\omega}, \quad t \in I_\omega \cup [0, \infty),$$

where $\omega = \max\{\omega_1, \omega_2\}$. Keeping the lettering of the variables and using (63), (64), we consider the auxiliary Cauchy problem

$$(73) \quad \frac{dx_4(t)}{dt} = n_4\beta\eta_3x_1^*x_5(t - \omega_2) - \mu_4x_4(t),$$

$$(74) \quad \frac{dx_5(t)}{dt} = \rho_5^* + n_5\beta\eta_3x_1^*x_5(t - \omega_2) - \mu_5x_5(t), \quad t \geq 0,$$

$$(75) \quad x_4(t) = \psi_4(t), \quad x_5(t) = \psi_5(t), \quad t \in I_\omega.$$

We reformulate the problem (73)–(75) as an equivalent problem in the form of the system of linear integral equations

$$(76) \quad x_4(t) = e^{-\mu_4t} \left(\psi_4(0) + \int_0^t e^{\mu_4s} n_4\beta\eta_3x_1^*x_5(s - \omega_2) ds \right),$$

$$(77) \quad x_5(t) = e^{-\mu_5t} \left(\psi_5(0) + \int_0^t e^{\mu_5s} (\rho_5^* + n_5\beta\eta_3x_1^*x_5(s - \omega_2)) ds \right), \quad t \geq 0,$$

complemented with the initial data (75). Using the sketch of a proof of Lemma 5 and Theorem 1 from work [1], we get that there exists a function

$$w(t) = (w_4(t), w_5(t))^T = (q_4 e^{\gamma t}, q_5 e^{\gamma t})^T, \quad t \in I_\omega \cup [0, \infty),$$

containing positive constants q_4, q_5, γ and satisfying the inequalities

$$(78) \quad e^{-\mu_4 t} \left(\psi_4(0) + \int_0^t e^{\mu_4 s} n_4 \beta \eta_3 x_1^* w_5(s - \omega_2) ds \right) \leq w_4(t),$$

$$(79) \quad e^{-\mu_5 t} \left(\psi_5(0) + \int_0^t e^{\mu_5 s} (\rho_5^* + n_5 \beta \eta_3 x_1^* w_5(s - \omega_2)) ds \right) \leq w_5(t), \quad t \in [0, \infty),$$

$$(80) \quad \psi_4(t) \leq w_4(t), \quad \psi_5(t) \leq w_5(t), \quad t \in I_\omega.$$

Putting together the estimates and inequalities that follow from (59)–(80), we introduce the function

$$v(t) = (c_1^* e^{-r_* t}, c_2^* e^{-r_* t}, \eta_3, q_4 e^{\gamma t}, q_5 e^{\gamma t})^T, \quad t \in I_\omega \cup [0, \infty).$$

Using works [1], [2] and following the lines of the sketch of a proof of Theorem 1, we establish that for every fixed $\tau > 0$, the set of functions $C_{\psi,0,v}$ is invariant for the operator F . Then for the solution $x(t)$ of the Cauchy problem (53)–(58), the following estimates are true:

$$0 \leq x_1(t) \leq c_1^* e^{-r_* t}, \quad 0 \leq x_2(t) \leq c_2^* e^{-r_* t}, \quad 0 \leq x_3(t) \leq \eta_3, \\ 0 \leq x_4(t) \leq q_4 e^{\gamma t}, \quad 0 \leq x_5(t) \leq q_5 e^{\gamma t}, \quad t \in I_\omega \cup [0, \infty).$$

More functional upper estimates for $x_4(t), x_5(t)$ can be constructed based on the Cauchy problem for the auxiliary variables $y_4(t), y_5(t)$:

$$(81) \quad \frac{dy_4(t)}{dt} = n_4 \beta \eta_3 c_1^* e^{-r_*(t-\omega_2)} y_5(t - \omega_2) - \mu_4 y_4(t),$$

$$(82) \quad \frac{dy_5(t)}{dt} = \rho_5^* + n_5 \beta \eta_3 c_1^* e^{-r_*(t-\omega_2)} y_5(t - \omega_2) - \mu_5 y_5(t), \quad t \geq 0,$$

$$(83) \quad y_4(t) = \psi_4(t), \quad y_5(t) = \psi_5(t), \quad t \in I_\omega.$$

Due to linearity of differential equations, the Cauchy problem (81)–(83) is globally solvable, and its solution $y_4(t), y_5(t)$ can be found with the help of the so-called method of steps. Applying this method, we assume that the variable t takes values on the intervals $[0, \omega_2], [\omega_2, 2\omega_2]$ and so on. Each of the equations of the Cauchy problem (81)–(83) is solved as a linear non-uniform differential equation with a given initial condition. Non-negativity of $y_4(t), y_5(t)$ follows from the form of the right-hand sides of equations (81), (82) and the non-negativity of the initial data (83). From the structure of the initial equations for $x_4(t), x_5(t)$, written in integral form, and the estimates (63), (64), it follows that $x_4(t) \leq y_4(t), x_5(t) \leq y_5(t)$ for all $t \in I_\omega \cup [0, \infty)$.

To study the asymptotics of $y_4(t), y_5(t)$ given $t \rightarrow +\infty$, we turn to the Cauchy problem for equation (82). We put $y_5(t) = \rho_5^*/\mu_5 + e^{-\mu_5 t} w(t)$. The variable $w(t)$ represents the solution of the Cauchy problem

$$(84) \quad \frac{dw(t)}{dt} - b_1 e^{-r_* t} w(t - \omega_2) = b_2 e^{(\mu_5 - r_*)t}, \quad t \geq 0,$$

$$(85) \quad w(t) = w_0(t) = e^{\mu_5 t} (\psi_5(t) - \rho_5^*/\mu_5), \quad t \in [-\omega_2, 0],$$

where

$$b_1 = n_5 \beta \eta_3 c_1^* e^{(r_* + \mu_5)\omega_2} > 0, \quad b_2 = \rho_5^* n_5 \beta \eta_3 c_1^* e^{r_* \omega_2} / \mu_5 > 0.$$

We use the Cauchy representation formula for solutions of linear differential equation and systems of delay equations [9] (Ch. 2, pp. 64–69), [10] (P. 2, pp. 29; appendix B, pp. 465, 466, 480).

We denote: $\tilde{w}_0(s) = w_0(s - \omega_2)$, $0 \leq s \leq \omega_2$, $\tilde{w}_0(s) = 0$, $s > \omega_2$. Applying the mentioned Cauchy formula to problem (84), (85), we obtain that

$$w(t) = C(t, 0)w(0) + b_2 \int_0^t C(t, s)e^{(\mu_5 - r_*)s} ds + b_1 \int_0^t C(t, s)e^{-r_*s} \tilde{w}_0(s) ds, \quad t \geq 0,$$

where $C(t, s)$ is the Cauchy function. Given fixed $0 \leq s \leq t < \infty$, for the Cauchy function, the estimate

$$|C(t, s)| \leq \exp\left(\int_s^t b_1 e^{-r_*a} da\right) \leq \exp\left(\int_0^\infty b_1 e^{-r_*a} da\right) = \exp(b_1/r_*) = \hat{C} < \infty$$

is true, hence, the function $C(t, s)$ is bounded. Then for the solution $w(t)$ of problem (84), (85), the following estimate is true:

$$|w(t)| \leq \hat{C}|w(0)| + \hat{C} b_2 \int_0^t e^{(\mu_5 - r_*)s} ds + \hat{C} b_1 \int_0^{\omega_2} |w_0(s - \omega_2)| ds, \quad t \geq 0.$$

Estimating separate terms in the formula for the solution $w(t)$ and omitting the details, we establish the following relations: if $\mu_5 < r_*$, then $|w(t)| \leq N_1$, if $\mu_5 = r_*$, then $|w(t)| \leq N_2 + N_3 t$, if $\mu_5 > r_*$, then $|w(t)| \leq N_4 + N_5 e^{(\mu_5 - r_*)t}$, $t \in [0, \infty)$, where N_1, \dots, N_5 are positive constants. For each of the three listed cases, $e^{-\mu_5 t} w(t) \rightarrow 0$ given $t \rightarrow +\infty$. Then $y_5(t) \rightarrow \rho_5^*/\mu_5$, and from (81) it directly follows that $y_4(t) \rightarrow 0$ given $t \rightarrow +\infty$.

Based on the mentioned estimate $|w(t)|$, it is easy to write out the upper estimates for $y_5(t)$, $y_4(t)$ and, therefore, the upper estimates for the variables $x_4(t)$, $x_5(t)$ of the studied model. Moreover, we directly obtain that $x_4(t) \rightarrow 0$ given $t \rightarrow +\infty$ and $\limsup_{t \rightarrow +\infty} x_5(t) \leq \rho_5^*/\mu_5$.

Concluding the study of the model, we represent the inequality (69) in the form

$$R_{0,3} = \frac{\delta_2 \eta_3 (\mu_1 \gamma_{2,3} + \nu \gamma_{1,3})}{\mu_1 \mu_2} < 1.$$

We will call the constant $R_{0,3}$ a basic reproductive number, which reflects the reproduction of viral particles and productively infected cells. Note that the expression for $R_{0,3}$ does not contain any constants, taking into account the effect of a specific immune response (of cells E and Q) on HIV-1 infection. The inequality $R_{0,3} < 1$ is fulfilled due to particular relations between the constants, reflecting the dynamics of a non-specific immune response and other protective factors.

In the framework of the considered model, we establish that in the case when the inequalities $R_{0,3} < 1$, $\psi_3(t) \leq \eta_3$, $t \in I_\omega$, hold, the size of the populations of the virions V and productively infected cells I decrease to zero levels over time. We will say that the eradication of HIV-1 infection happens at the moment of time t_* , if $x_1(t) < 1$, $x_2(t) < 1$ for all $t > t_*$. Based on the exponentially decreasing estimates of the variables $x_1(t)$, $x_2(t)$, we obtain that

$$(86) \quad t_* = \frac{1}{r_*} \max\{\ln c_1^*, \ln c_2^*\}.$$

We assume, in particular, that $\psi_2(t) \equiv 0$, $t \in I_\omega$, and $\psi_1(t)$ is nonzero and strictly monotonously increasing up to the value $\psi_1(0) = V_0 \geq 1$ in some small left neighbourhood of $t = 0$. We can interpret the constant V_0 as the initial number of virions, which get into the organism of a healthy person. Omitting the intermediate layouts, we find that for the mentioned initial functions, we can define the constants c_1^* , c_2^* in the following way:

$$(87) \quad c_1^* = V_0 > 0, \quad c_2^* = \frac{\mu_1 - r_*}{\nu} V_0 > 0.$$

The formulas (86), (87) show the dependence of t_* of the initial number of virions V_0 , which infect the organism of a healthy person.

An important practical result of studying the examples 1, 2, 3 is that we obtain the formula for the basic reproductive number R_0 . The values of $R_0 < 1$, $R_0 > 1$ significantly effect the dynamics of number of components of solutions in one studied model or another. The case $R_0 < 1$ provides exponential decreasing of a part of components of solution of the models and allows to evaluate the time interval until the decreasing of these components from the initial level to some favorable or unfavorable one. The ways to study the considered systems of differential equations are transferred to equations that are close in structure to the former ones, that emerge in models of epidemiology and immunology, see, for example, [11], [12].

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