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Study of solutions of a continuous-discrete model of HIV infection spread

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Abstract — Equations of a continuous-discrete mathematical model describing the propagation of HIV infection among the population of several regions are presented. The model equations take into account the reproduction and migration of the population, the risk of infection of individuals from different social groups, an impulse change in the number of individuals at discrete time moments under the action of various factors. The results of the study of the model solutions are also presented. We obtain conditions for the model parameters and initial data that provide the existence of solutions interpreted as full eradication of HIV infection in all considered regions or maintenance of sizes of groups of infected individuals at some acceptable level. The solutions analysis uses the monotone operators method and properties of nonsingular M-matrices.

Keywords: Mathematical model, HIV-infection, exponential estimates, asymptotic behaviour of model solution, nonsingular M-matrix.

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1. Introduction

The study of the spread dynamics and control of socially significant infectious diseases widely uses the method of mathematical modelling. Modern approaches to construction of mathematical models of epidemic processes in the form of differential equations were presented in monographs [1, 8], in reviews [3, 5, 10], and other papers. One family of such models has the form

$$\frac{\mathrm{d}z(t)}{\mathrm{d}t} = \eta z(t) + f(t,z(t)) - (\mu+\nu)z(t) - g(t,z(t))z(t), \quad t > 0 \tag{1.1}$$

$$z(0) = z^{(0)}. \tag{1.2}$$

In equations (1.1), (1.2) the function $z(t) = (z_1(t),\dots,z_m(t))^T$ specifies the sizes of different population groups of some regions involved in the process of epidemic spread at some time moment $t \geqslant 0$; $z^{(0)}$ denotes the initial size of groups of individuals, $z_i^{(0)} \geqslant 0$, $i = 1,\dots,m$. In particular, the groups considered in the model may include groups of susceptible, infected, sick individuals, and individuals being in remission or on treatment as well. For example, such groups of individuals are used

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in SIRS models and their various modifications. The model presented in [2] uses groups reflecting of the population of a major city and its small towns-satellites.

Equations of system (1.1) contain nonlinear and linear summands describing the rates of changes in sizes of individual groups.

Nonlinear summands reflect contacts and interaction of individuals and are represented as the vector functions

$$f(t,z(t)) = (f_1(t,z(t)),\dots,f_m(t,z(t)))^T$$
$$g(t,z(t))z(t) = \mathrm{diag}\,(g_1(t,z(t)),\dots,g_m(t,z(t)))z(t)$$

where $\mathrm{diag}\,(g_1(t,z(t)),\dots,g_m(t,z(t)))$ is a diagonal matrix.

For fixed $i = 1,\dots,m$ the component $f_i(t,z(t))$ specifies the growth rate of a certain ith group size, the component $g_i(t,z(t))z_i(t)$ is the rate of decrease of a certain ith group size. The components $f(t,z(t))$ may include separate summands entering $g(t,z(t))z(t)$. In addition, $f(t,z(t))$ is the rate of supplement of groups by the individuals used in an implicit or parametric form of description. We assume that the functions $f_i(t,z)$ and $g_i(t,z)$, $i = 1....,m$, are determined and nonnegative on the set $t \geqslant 0, z_1 \geqslant 0,\dots,z_m \geqslant 0$.

The linear summands have the form $\eta z(t)$ and $(\mu+\nu)z(t)$. The linear vector function $\mu z(t)$ specifies the rate of decrease of the group sizes due to natural mortality of individuals and possible loss of individuals from disease, $\mu = \mathrm{diag}\,(\mu_1,\dots,\mu_m)$ is a diagonal matrix. The elements $\mu_i > 0$, $i = 1,\dots,m$, denote the intensities of the processes of natural mortality and loss from disease for individuals.

The linear vector function $\nu z(t)$ describes the rates of decrease of group sizes due to processes of migration or due to transition of individuals from one group to another under the action of the following factors: a spontaneous development of disease, a change of stage or severity of disease, an acquisition of immunity, a change in socio-economic living conditions, etc. The elements $\nu_i \geqslant 0$ of the diagonal matrix $\nu = \mathrm{diag}\,(\nu_1,\dots,\nu_m)$ mean the intensity of processes of migration and transition of individuals between groups.

The linear vector function $\eta z(t)$ specifies the growth rates of groups due to transition of individuals between groups, $\eta = (\eta_{ij})$ is a square matrix. The elements $\eta_{ij} \geqslant 0$, $i,j = 1,\dots,m$, mean the intensity of arrival of individuals into a particular group from other remaining groups.

We assume that the matrices η and ν have the following structure:

$$\nu_i = \sum_{k=1,k\neq i}^{m} \nu_{ik}, \quad i = 1,\dots,m$$
$$\eta_{jj} = 0, \quad j = 1,\dots,m, \qquad \eta_{jn} = \nu_{nj}, \quad j,n = 1,\dots,m, \quad n \neq j.$$

The parameter $\nu_{ik} \geqslant 0$ describes the intensity of transition of individuals of the ith group to the kth group, $i,k = 1,\dots,m$, $i \neq k$.

A typical example of a model of form (1.1), (1.2) is the model of HIV infection spread in the population of some region proposed in [9, 17]. Some properties of solutions of the model mentioned here and its multi-dimensional analogue were presented in [12, 13]. The models presented in [9, 17] were constructed on the base of rather detailed review [10] and the original approach connected with the consideration of a variable risk of HIV infection of individuals depending on their level of social adaptation (disadaptation).

The pandemic of HIV infection is developing since the beginning of the 80s of 20th century and is one of the most disastrous epidemics in the history of mankind. The number of people infected with HIV and the number of people dying from HIV-related causes are millions of individuals per year. In order to reduce the damage caused by HIV infection, it is necessary to control the spread of this infection and to carry out activities aimed at detection and treatment of infected persons and sick individuals. The practical work in this direction involves an integrated approach to the analysis of available statistical data at the level of individual cities, regions, and countries. The analysis and processing of large amounts of statistical data require a certain conception and formalization, which are possible only within the framework of special and justified mathematical models. This determines the importance of construction and study of high-dimensional mathematical models of HIV infection spread.

This paper is focused on the development of mathematical models presented in [9, 17, 12, 13] taking into account previously unconsidered factors, namely, (a) migration of people between several regions; (b) abrupt changes in group population sizes at discrete time moments due to various reasons.

The aim of the paper is the development of a continuous-discrete model taking into account the factors indicated above and the study of properties of its solutions. The aim also includes (1) the construction of equations of the model; (2) the calculation of upper estimates for variables of the model allowing us to study their asymptotic behaviour; (3) the determination of relations between the parameters of the model such that the obtained solution can be interpreted as eradication of HIV infection or maintaining the number of HIV-infected individuals at a certain low level.

2. Equations of the basic model and properties of its solutions

2.1. Notations and equations of the model.

Let us consider the adult population in several regions (individuals older than 14 years). In order to describe the structure of population, we use the groups

$$\begin{aligned} S&:\ S_{11},\ldots,S_{1m},\ \ldots,\ S_{r1},\ldots,S_{rm}\\ I&:\ I_{11},\ldots,I_{1m},\ \ldots,\ I_{r1},\ldots,I_{rm}. \end{aligned}$$

The groups I represent HIV-positive individuals, the groups S are for susceptible to HIV individuals. The number of regions is r, the number of groups in each region is m, the total number of groups is $n = mr$. Particular groups included in S and I assume the classification of individuals according to a set of some common features.

In particular, these groups include so-called groups of ‘risk’, i.e., chronic alcoholics, drug addicts, etc. Below we use a continuous numbering of groups, i.e., $S_1, \ldots, S_n$, $I_1, \ldots, I_n$. By $x_i(t)$, $y_j(t)$ we denote the number of individuals in the groups S_i, I_j at the time moment t, $i, j = 1, \ldots, n$. We write the system of equations of the model in the form

$$\frac{\mathrm{d}x_i(t)}{\mathrm{d}t} = \sum_{k=1,k\neq i}^{n} \gamma_{ki}x_k(t) - \sum_{k=1}^{n} \gamma_{ik}x_i(t) - \sum_{j=1}^{n} \beta_{ij}y_j(t)x_i(t) + f_{S_i}(t)$$

$$\frac{\mathrm{d}y_i(t)}{\mathrm{d}t} = \sum_{k=1,k\neq i}^{n} \alpha_{ki}y_k(t) - \sum_{k=1}^{n} \alpha_{ik}y_i(t) + \sum_{j=1}^{n} \beta_{ij}y_j(t)x_i(t), \quad t > 0$$

$$x_i(0) = x_i^{(0)}, \qquad y_i(0) = y_i^{(0)}, \quad i = 1, \ldots, n.$$

In these equations the functions $f_{S_i}(t)$ specify the rates of arrival of individuals into the groups S_i due to demographic processes (younger generation in the considered regions, migration of individuals from regions not included explicitly in the model structure).

The parameters γ_{ik} denote the intensities of transitions of individuals from the groups S_i to the group S_k including emigration of individuals of the group S_i to other regions. The parameters γ_{ii} specify the intensity of natural mortality of individuals of the group S_i. The parameters α_{ik} have similar sense (for individuals of the groups I_i, I_k) and α_{ii} includes the intensity of loss of individuals of the group I_i from diseases caused by HIV infection.

The parameters β_{ij} reflect of the intensity of contacts of individuals from the groups S_i and I_j causing the appearance of new HIV-infected individuals. We assume that in each particular region the individuals of the group S_i are in contact with individuals of at least one group I_j of this region. Moreover, there are no contacts of individuals of the groups S_i and I_j from different regions.

The values $x_i^{(0)}$ and $y_i^{(0)}$ determine the initial sizes of groups of individuals, $i = 1, \ldots, n$.

We assume that the functions, parameters, and initial data entering the equations of the model satisfy the following conditions:
H1) $f_{S_i}(t)$ are nonnegative, continuous, bounded on $[0, \infty)$ functions, $i = 1, \ldots, n$;
H2) $\gamma_{ik} \geqslant 0$, $\alpha_{ik} \geqslant 0$, $k \neq i$, $\gamma_{ii} > 0$, $\alpha_{ii} > 0$, $i, k = 1, \ldots, n$;
H3) $\beta_{ij} \geqslant 0$, $i, k = 1, \ldots, n$, $\beta_{ij} = 0$ if the indices i, j correspond to different regions and for each fixed $i = 1, \ldots, n$ we have $\beta_{i1} + \cdots + \beta_{in} > 0$;
H4) $x_i^{(0)} \geqslant 0$, $y_i^{(0)} \geqslant 0$, $i = 1, \ldots, n$.

We introduce the notations

$$x(t) = (x_1(t), \ldots, x_n(t))^T, \qquad y(t) = (y_1(t), \ldots, y_n(t))^T$$

$$f_S(t) = (f_{S_1}(t), \ldots, f_{S_n}(t))^T, \qquad D(x(t)) = \mathrm{diag}\,(x_1(t), \ldots, x_n(t))$$

$$A = (a_{ij}), \qquad L = (\ell_{ij}), \qquad B = (\beta_{ij})$$

$$a_{ii} = -\sum_{k=1}^{n} \gamma_{ik} < 0, \qquad \ell_{ii} = -\sum_{k=1}^{n} \alpha_{ik} < 0$$

$$a_{ik} = \gamma_{ki} \geqslant 0, \qquad \ell_{ik} = \alpha_{ki} \geqslant 0, \quad i,k = 1,\dots,n, \quad k \neq i$$

and rewrite the system of model equations in the vector form

$$\frac{\mathrm{d}x(t)}{\mathrm{d}t} = Ax(t) - D(x(t))By(t) + f_S(t) \tag{2.1}$$

$$\frac{\mathrm{d}y(t)}{\mathrm{d}t} = Ly(t) + D(x(t))By(t), \quad t > 0 \tag{2.2}$$

$$x(0) = x^{(0)},\ y(0) = y^{(0)}. \tag{2.3}$$

2.2. Some properties of matrices entering the equations of the basic model

Let us present some facts from the theory of matrices of special form [4, 11]. By E we denote the $n \times n$ identity matrix. Let $S = (s_{ij})$ be an $n \times n$ real matrix whose elements satisfy the condition $s_{ij} \leqslant 0$ for all $i \neq j$. It is called a nonsingular M-matrix if S^{-1} exists and S^{-1} is nonnegative (all its elements are nonnegative). The following assertions are equivalent:

(1) S is a nonsingular M-matrix;

(2) there exists $\xi \in R^n$, $\xi > 0$, such that $S\xi > 0$ (inequalities for vectors mean component-wise inequalities);

(3) all eigenvalues of S have positive real parts;

(4) diagonal elements of the matrix S are positive and the spectral radius $\rho(S_*)$ of the matrix

$$S_* = E - \operatorname{diag}\left(s_{11}^{-1},\dots,s_{nn}^{-1}\right)S$$

satisfies the condition $\rho(S_*) < 1$.

Consider the matrices entering system of equations (2.1), (2.2). The matrices A and L are quasi-nonnegative (their off-diagonal elements are nonnegative). The matrices $(-A)$ and $(-L)$ are such that their off-diagonal elements are nonpositive. Assume $\xi = (1,\dots,1)^T$. It is not too difficult to see that the inequalities $(-A)^T\xi > 0$, $(-L)^T\xi > 0$ hold (component-wise). This means that $(-A)^T$ and $(-L)^T$ are nonsingular M-matrices. Therefore, all eigenvalues of the matrices $(-A)^T$ and $(-L)^T$ have positive real parts. Thus, $(-A)$ and $(-L)$ are nonsingular M-matrices. Moreover, all eigenvalues of the matrix A have negative real parts (the matrix A relates to the family of the so-called stable matrices).

The quasi-nonnegativity of the matrix A implies that the matrix $\exp(At)$ is nonnegative for each fixed $t \geqslant 0$. The matrix B is nonnegative and has block-diagonal structure. Each its block is an $m \times m$ matrix with nonzero rows.

2.3. Properties of solutions to equations of the basic model

Relations (2.1)–(2.3) are a Cauchy problem for a system of nonlinear differential equations. The solution to Cauchy problem (2.1)–(2.3) is said to be the functions $x(t)$, $y(t)$ determined and continuous on a certain interval $[0,\delta)$ and satisfying initial conditions (2.3) and equations (2.1), (2.2) for all $t \in [0,\delta)$.

We use two approaches to analyze properties of solutions to Cauchy problem (2.1)–(2.3). The first approach relates to application of the standard technique of analysis of model equations. The second approach is essentially based on the structure of model equations admitting the construction of a system of majorant equations in an integral form.

2.3.1. Standard analysis. One of easily interpreted solutions to Cauchy problem (2.1)–(2.3) appears for $y_i^{(0)} = 0$, $i = 1,\dots,n$. In this case problem (2.1)–(2.3) admits a solution where $y(t) \equiv 0$ and $x(t)$ is determined as a solution to an auxiliary Cauchy problem for the system of linear differential equations

$$x(0) = x^{(0)}, \qquad \frac{\mathrm{d}x(t)}{\mathrm{d}t} = Ax(t) + f_S(t), \quad t > 0.$$

As the result, we get that Cauchy problem (2.1)–(2.3) has the solution

$$x(t) = x^{(0)}(t) = \mathrm{e^{At}x^{(0)}} + \int_0^{\mathrm{t}} \mathrm{e^{A(t-a)}f_S(a)\,da}$$

$$y(t) \equiv 0, \quad 0 \leqslant t < \infty. \tag{2.4}$$

Note that the matrices $\exp(At)$ and $\exp(A(t-a))$ are nonnegative for $0 \leqslant a \leqslant t$. The components of the vector $x^{(0)}$ are nonnegative. The components of the function $f_S(a)$ are nonnegative and bounded from above, $0 \leqslant a < \infty$. The matrix A is stable. Therefore, the function $x^{(0)}(t)$ is nonnegative and bounded from above for all $t \geqslant 0$. The solution to problem (2.1)–(2.3) of form (2.4) can be interpreted as the absence of HIV infection in the considered regions.

Further, let $y^{(0)} \neq 0$. Note that the right-hand sides of equations (2.1), (2.2) have continuous partial derivatives at each point $(x_1,\dots,x_n,y_1,\dots,y_n) \in R^n \times R^n$. Based on the structure of right-hand sides of equations of system (2.1), (2.2) and using the methods of the theory of monotone and positive operators [6, 7], we can show that Cauchy problem (2.1)–(2.3) has a unique, nonnegative, bounded from above solution determined on the interval $t \in [0,\infty)$. The sketch of proof of this assertion was given in [13].

2.3.2. Upper and lower estimates of solutions to the considered Cauchy problem. Let us consider the problem of construction of two-sided estimates for the solution $x(t)$, $y(t)$ to Cauchy problem (2.1)–(2.3). We assume that inequalities between vectors from R^n are understood as inequalities between their components.

The notation $\xi \in R^n$, $\xi > 0$, is equivalent to the fact that all components of the vector ξ are positive. For functions $z^{(1)}(t)$ and $z^{(2)}(t)$ determined on a certain interval $[a,b)$ and taking values in R^n the inequality $z^{(1)}(t) \leqslant z^{(2)}(t)$ means the inequality between the corresponding vectors for each fixed $t \in [a,b)$. The following estimates were obtained in [13]:

$$0 \leqslant x(t) \leqslant u^{(0)}, \quad 0 \leqslant y(t) \leqslant v^{(0)}, \quad 0 \leqslant t < \infty$$

where $u^{(0)}, v^{(0)} \in R^n$, $u^{(0)} > 0$, $v^{(0)} > 0$. The vectors $u^{(0)}$ and $v^{(0)}$ are calculated as solutions to some auxiliary systems of inequalities and equations. Further we seek for two-sided estimates having the form

$$0 \leqslant x(t) \leqslant u^{(0)}, \quad 0 \leqslant y(t) \leqslant \varphi\, \mathrm{e}^{-\rho \mathrm{t}}, \quad 0 \leqslant \mathrm{t} < \infty \tag{2.5}$$

where $\varphi \in R^n$, $\varphi > 0$, $\rho \in R$, $\rho > 0$. Existence conditions for estimates (2.5) can be interpreted as conditions of eradication of HIV infection in all considered regions.

Proceeding to Cauchy problem (2.1)–(2.3) written as an equivalent system of integral equations, we introduce the following notations:

$$A_0 = \operatorname{diag}(|a_{11}|, \ldots, |a_{nn}|),\ L_0 = \operatorname{diag}(|\ell_{11}|, \ldots, |\ell_{nn}|)$$

$$A_1 = A + A_0,\ L_1 = L + L_0$$

$$Q(y(a)) = A_0 + \operatorname{diag}\Big(\sum_{j=1}^{n} \beta_{1j} y_j(a), \ldots, \sum_{j=1}^{n} \beta_{nj} y_j(a)\Big), \quad a \geqslant 0$$

$$G_1(t,s,y) = \mathrm{e}^{-\int_{\mathrm{s}}^{\mathrm{t}} \mathrm{Q}(\mathrm{y}(\mathrm{a}))\,\mathrm{da}} = \operatorname{diag}\Big(\mathrm{e}^{-\int_{\mathrm{s}}^{\mathrm{t}} \mathrm{Q}_1(\mathrm{y}(\mathrm{a}))\,\mathrm{da}}, \ldots, \mathrm{e}^{-\int_{\mathrm{s}}^{\mathrm{t}} \mathrm{Q}_{\mathrm{n}}(\mathrm{y}(\mathrm{a}))\,\mathrm{da}}\Big)$$

$$G_2(t,s) = \mathrm{e}^{-\mathrm{L}_0(\mathrm{t}-\mathrm{s})} = \operatorname{diag}\Big(\mathrm{e}^{-|\ell_{11}|(\mathrm{t}-\mathrm{s})}, \ldots, \mathrm{e}^{-|\ell_{\mathrm{nn}}|(\mathrm{t}-\mathrm{s})}\Big)$$

$$0 \leqslant s \leqslant t$$

$$F_1(x,y)(t) = G_1(t,0,y)x^{(0)} + \int_0^t G_1(t,s,y)\big(A_1 x(s) + f_S(s)\big)\,\mathrm{d}s$$

$$F_2(x,y)(t) = G_2(t,0)y^{(0)} + \int_0^t G_2(t,s)\big(L_1 + D(x(s))B\big)y(s)\,\mathrm{d}s$$

assuming that $x = x(t)$, $y = y(t)$ are determined, nonnegative, and continuous on the interval $[0,\infty)$. Rewrite (2.1), (2.2) in the form

$$\frac{\mathrm{d}x(t)}{\mathrm{d}t} = A_1 x(t) - Q(y(t))x(t) + f_S(t) \tag{2.6}$$

$$\frac{\mathrm{d}y(t)}{\mathrm{d}t} = (L_1 + D(x(t))B)y(t) - L_0 y(t), \quad t > 0. \tag{2.7}$$

Integrating (2.6), (2.7) by the method of variation of constants and taking (2.3) into account, we get the system

$$x(t) = F_1(x,y)(t), \qquad y(t) = F_2(x,y)(t), \quad t \geqslant 0. \tag{2.8}$$

The solution to system (2.8) is said to be the functions $x(t)$, $y(t)$ determined and continuous on a certain segment $[0,\tau]$, $\tau > 0$, and satisfying (2.8) for all $t \in [0,\tau]$.

By $f_S^{(*)} \in R^n$ we denote a vector such that

$$f_S^{(*)} > 0, \quad 0 \leqslant f_S(t) \leqslant f_S^{(*)}, \quad t \in [0,\infty).$$

Let $x = x(t)$, $y = y(t)$ be determined, nonnegative, and continuous on the interval $[0,\infty)$. For all $0 \leqslant t < \infty$ we have the relations

$$F_1(x,y)(t) \geqslant 0, \qquad F_2(x,y)(t) \geqslant 0$$

$$F_1(x,y)(t) \leqslant H_1(x)(t) = \mathrm{e}^{-\mathrm{A_0 t}}\Big(\mathrm{x}^{(0)} + \int_0^{\mathrm{t}} \mathrm{e}^{\mathrm{A_0 s}}\big(\mathrm{A_1 x(s)} + \mathrm{f_S^{(*)}}\big)\,\mathrm{ds}\Big).$$

Assume that $x^{(i)} = x^{(i)}(t)$, $y^{(i)} = y^{(i)}(t)$, $i = 1,2$, are determined, nonnegative, and continuous on the interval $[0,\infty)$ and, in addition,

$$x^{(1)}(t) \leqslant x^{(2)}(t), \qquad y^{(1)}(t) \leqslant y^{(2)}(t), \quad 0 \leqslant t < \infty.$$

In this case for each $t \in [0,\infty)$ we have

$$H_1(x^{(1)})(t) \leqslant H_1(x^{(2)})(t), \qquad F_2(x^{(1)},y^{(1)})(t) \leqslant F_2(x^{(2)},y^{(2)})(t).$$

In order to obtain estimates (2.5), we introduce the functions

$$u^{(0)}(t) = u^{(*)} = \text{const}, \qquad v^{(0)}(t) = \varphi\,\mathrm{e}^{-\rho \mathrm{t}}, \quad 0 \leqslant \mathrm{t} < \infty \tag{2.9}$$

containing the parameters

$$u^{(*)} \in R^n, \quad u^{(*)} > 0, \qquad \varphi \in R^n, \quad \varphi > 0, \qquad \rho \in R, \quad \rho > 0 \tag{2.10}$$

and calculate the solution to the system of inequalities

$$H_1(u^{(0)})(t) \leqslant u^{(0)}(t), \qquad F_2(u^{(0)},v^{(0)})(t) \leqslant v^{(0)}(t), \quad 0 \leqslant t < \infty.$$

Taking into account the equality $u^{(0)}(t) = u^{(*)}$, we obtain the inequalities

$$\mathrm{e}^{-\mathrm{A_0 t}}\Big(\mathrm{x}^{(0)} + \int_0^{\mathrm{t}} \mathrm{e}^{\mathrm{A_0 s}}\big(\mathrm{A_1 u}^{(*)} + \mathrm{f_S^{(*)}}\big)\,\mathrm{ds}\Big) \leqslant \mathrm{u}^{(*)} \tag{2.11}$$

$$\mathrm{e}^{-\mathrm{L_0 t}}\Big(\mathrm{y}^{(0)} + \int_0^{\mathrm{t}} \mathrm{e}^{\mathrm{L_0 s}}\big(\mathrm{L_1} + \mathrm{D(u^{(*)})B}\big)\,\varphi\,\mathrm{e}^{-\rho \mathrm{s}}\,\mathrm{ds}\Big) \leqslant \varphi\,\mathrm{e}^{-\rho \mathrm{t}} \tag{2.12}$$

and each of these inequalities is considered for $0 \leqslant t < \infty$ along with (2.10). Let us consider (2.11) and recall that $(-A)$ is a nonsingular M-matrix. Therefore, the inverse matrix $(-A)^{-1}$ exists, is nonnegative, and each its row contains at least one positive element. Assume

$$u^{(*)} = (-A)^{-1} f_S^{(*)}. \tag{2.13}$$

Since $f_S^{(*)} > 0$, we have $u^{(*)} > 0$. We assume $x^{(0)} \leqslant u^{(*)}$. In this case the vector $u^{(*)} \in R^n$ defined by (2.13) has positive components and satisfies (2.11). Let us proceed to (2.12) and introduce the matrix

$$L^{(*)} = -(L + D(u^{(*)})B) = L_0 - (L_1 + D(u^{(*)})B). \tag{2.14}$$

The properties of elements of the matrices L_1, B and the inequality $u^{(*)} > 0$ imply that the matrix $L_1 + D(u^{(*)})B$ is nonnegative and has no zero rows. Suppose $L^{(*)}$ is a nonsingular M-matrix. Using the results of [14, 15], we get that inequality (2.12) (taking into account (2.10)) has a solution and the parameters φ and ρ included into the function $v^{(0)}(t)$ satisfy the relations

$$\rho \in R,\ 0 < \rho < \min\{|\ell_{11}|, \dots, |\ell_{nn}|\} \tag{2.15}$$

$$\varphi \in R^n,\ \varphi > 0,\ \ \varphi \geqslant y^{(0)},\ \left(L^{(*)} - \rho E\right)\varphi \geqslant 0. \tag{2.16}$$

The ways to calculate solutions to system of inequalities (2.15), (2.16) were described in [14, 15]. In particular, let $L^{(*)}$ be an irreducible matrix. In this case we can take

$$\rho = \rho_* = -\lambda_*,\ \varphi = \varphi^{(*)} = \alpha_0\, \xi^{(*)}$$

as solutions to (2.15), (2.16), where $\lambda_* < 0$ is the Perron root of the quasi-nonnegative matrix $(-L^{(*)})$, $\xi^{(*)} > 0$ is the normalized right eigenvector of this matrix corresponding to λ_*, the number $\alpha_0 > 0$ is taken from the condition $\alpha_0\, \xi^{(*)} \geqslant y^{(0)}$.

2.3.3. Main result.

Based on above assumptions and applying results of the theory of monotone operators and the principle of contracting mappings [6, 7] to system (2.8), we get the following result.

Assertion 2.1 *Let assumptions H1)–H4) hold for the functions, parameters and initial data of Cauchy problem (2.1)–(2.3). Assume that the vector $u^{(*)}$ and the matrix $L^{(*)}$ given by (2.13), (2.14) are such that $L^{(*)}$ is a nonsingular M-matrix and the inequality $x^{(0)} \leqslant u^{(*)}$ is valid. In this case the solution to Cauchy problem (2.1)–(2.3) exists, is unique on any finite segment $[0, \tau]$, $\tau > 0$, and the following estimates are valid:*

$$0 \leqslant x(t) \leqslant u^{(*)},\ 0 \leqslant y(t) \leqslant \varphi^{(*)} \mathrm{e}^{-\rho_* \mathrm{t}},\ 0 \leqslant \mathrm{t} < \infty$$

where ρ_* and $\varphi^{(*)}$ satisfy (2.15) and (2.16), respectively.

3. Equations of the continuous-discrete model and two-sided estimates of its solutions

System (2.1)–(2.3) of basic model equations admits a modification that can take explicitly into account an impulse (abrupt) variation of population of individuals. Assume that such variation occurs at some discrete time moments and is caused by the following factors:

- a seasonal migration of individuals of the groups S, I;
- transition or migration of individuals between the groups S_i, S_k and the groups I_j, I_i due to abrupt changes in social and economic conditions, treatment of chronic alcoholics and drug addicts, detection and registration of HIV-infected individuals;
- emergence of individuals reaching the age of 14 who were HIV-infected at birth;
- infection of individuals of the groups S living in a particular region due to the mechanisms not related to their direct contacts with the individuals of the groups I of this region;
- infection of individuals of the groups S in their short-term stay in other regions and contacts with HIV-infected or sick individuals.

Define the sequence $\{t_k, \delta(t_k), \varepsilon(t_k)\}$ describing the impulse (abrupt) variation of the population size of the groups S, I at some time moments t_k, where

$$0 < t_1 < t_2 < \ldots < t_k < \ldots,\ k = 1, 2, \ldots$$
$$\delta(t_k) = (\delta_1(t_k), \ldots, \delta_n(t_k))^T,\ \varepsilon(t_k) = (\varepsilon_1(t_k), \ldots, \varepsilon_n(t_k))^T.$$

For fixed t_k each component of the vectors $\delta(t_k)$, $\varepsilon(t_k)$ can take both nonnegative and negative values, but these two vectors are not zero at the same time. For example, the inequality $\delta_1(t_k) > 0$ means that the variable $x_1(t)$ increases abruptly at the time moment $t = t_k$ due to an impulse arrival of individuals from regions not considered explicitly in the model. The relations $\delta_n(t_k) < 0$, $\varepsilon_n(t_k) = -\delta_n(t_k) > 0$ are interpreted as an abrupt change in the size of the groups S_n and I_n due to infection of several individuals from the group S_n in their short-term stay in one of the regions and contact with HIV-infected individuals there. The relations $\varepsilon_j(t_k) < 0$, $\varepsilon_i(t_k) = -\varepsilon_j(t_k) > 0$ describe the situation of abrupt variation of population size in the groups I_j and I_i due to the fact that some individuals of the group I_j pass examination and are detected as HIV-infected (fall into the group I_i of detected HIV-infected individuals). We assume that each fixed time interval contains a finite number of elements $\{t_k\}$ and $\lim_{k\to\infty} t_k = +\infty$. In addition, we assume that negative values of the components of the vectors $\delta(t_k)$, $\varepsilon(t_k)$ do not lead to negative values of sizes of the groups S_j, I_j, $j = 1, \ldots, n$.

Denote $t_0 = 0$ and consider system (2.1), (2.2) in time intervals $t \in [t_{k-1}, t_k)$, $k = 1, 2, \ldots$, supplementing it with initial data for $t = t_{k-1}$. Take into account that on each interval $t \in (t_{k-1}, t_k)$ we have no abrupt variations of the variables of the model. The notations $\mathrm{d}x(t)/\,\mathrm{d}t$, $\mathrm{d}y(t)/\,\mathrm{d}t$ mean right-hand derivatives. Assume that the hypothesis of Assertion 2.1 is valid.

Let $t \in [t_0, t_1]$ and the equations of the model have the form

$$\frac{\mathrm{d}x(t)}{\mathrm{d}t} = Ax(t) - D(x(t))By(t) + f_S(t) \tag{3.1}$$

$$\frac{\mathrm{d}y(t)}{\mathrm{d}t} = Ly(t) + D(x(t))By(t), \quad t_0 \leqslant t < t_1 \tag{3.2}$$

$$x(t_0) = x^{(0)}, \qquad y(t_0) = y^{(0)}. \tag{3.3}$$

We study relations (3.1)–(3.3) as a Cauchy problem for a system of nonlinear differential equations on a finite time interval. The properties of solutions to this problem are obtained from an equivalent system of integral equations considered on the segment $t \in [t_0, t_1]$. If we consider system (3.1)–(3.3) on the interval $t \in [t_0, \infty)$ without impulse variation of the model variables, then the estimates presented in Assertion 2.1 are valid for it. The same estimates are valid for the solution $x^{(1)}(t)$, $y^{(1)}(t)$ to problem (3.1)–(3.3).

Let $t \in [t_1, t_2]$. We suppose the following inequalities hold:

$$0 \leqslant x^{(1)}(t_1) + \delta(t_1) \leqslant u^{(*)}, \qquad y^{(1)}(t_1) + \varepsilon(t_1) \geqslant 0. \tag{3.4}$$

Rewrite the system of equations of the model in the form

$$\frac{\mathrm{d}x(t)}{\mathrm{d}t} = Ax(t) - D(x(t))By(t) + f_S(t) \tag{3.5}$$

$$\frac{\mathrm{d}y(t)}{\mathrm{d}t} = Ly(t) + D(x(t))By(t), \quad t_1 \leqslant t < t_2 \tag{3.6}$$

$$x(t_1) = x^{(1)}(t_1) + \delta(t_1), \qquad y(t_1) = y^{(1)}(t_1) + \varepsilon(t_1). \tag{3.7}$$

We study relations (3.5)–(3.7) as a Cauchy problem for a system of nonlinear differential equations on a finite time interval. The properties of solutions to this problem are obtained from an equivalent system of integral equations considered on the segment $t \in [t_1, t_2]$. Move the initial integration point to the point t_1 by introducing the new independent variable $t' = t - t_1$. If we study problem (3.5)–(3.7) on the interval $t' \in [0, \infty)$ not taking into account the impulse variation of the model variables, then the estimates from Assertion 2.1 are valid from it due to (3.4). The same estimates are valid for the solution $x^{(2)}(t)$, $y^{(2)}(t)$ to problem (3.5)–(3.7).

Applying the approach described above for $k = 2, 3, \ldots$ and assuming that the following inequalities hold:

$$0 \leqslant x^{(k)}(t_k) + \delta(t_k) \leqslant u^{(*)}, \qquad y^{(k)}(t_k) + \varepsilon(t_k) \geqslant 0 \tag{3.8}$$

we come to the Cauchy problem

$$\frac{\mathrm{d}x(t)}{\mathrm{d}t} = Ax(t) - D(x(t))By(t) + f_S(t) \tag{3.9}$$

$$\frac{\mathrm{d}y(t)}{\mathrm{d}t} = Ly(t) + D(x(t))By(t), \quad t_k \leqslant t < t_{k+1} \tag{3.10}$$

$$x(t_k) = x^{(k)}(t_k) + \delta(t_k), \qquad y(t_k) = y^{(k)}(t_k) + \varepsilon(t_k). \tag{3.11}$$

Based on (3.1)–(3.8) and using the method of mathematical induction, we can prove that the solution $x^{(k+1)}(t)$, $y^{(k+1)}(t)$ to the Cauchy problem (3.9)–(3.11) exists, is unique, and satisfies the estimates presented in Assertion 1. As the result, we have got the following statement.

Assertion 3.1 *Let the conditions of Assertion 2.1 hold. In this case Cauchy problem (3.1)–(3.3) has the unique solution* $x^{(1)}(t)$, $y^{(1)}(t)$ *satisfying the estimates*

$$0 \leqslant x^{(1)}(t) \leqslant u^{(*)}, \quad 0 \leqslant y^{(1)}(t) \leqslant \varphi^{(*)} \mathrm{e}^{-\rho_*(\mathrm{t}-\mathrm{t}_0)}, \quad \mathrm{t} \in [\mathrm{t}_0, \mathrm{t}_1],$$

where ρ_* *and* $\varphi^{(*)}$ *satisfy (2.15) and (2.16), respectively. Moreover, for each* $k = 1, 2, \dots$ *we have*

$$0 \leqslant x^{(k+1)}(t_k) = x^{(k)}(t_k) + \delta(t_k) \leqslant u^{(*)}$$
$$y^{(k+1)}(t_k) = y^{(k)}(t_k) + \varepsilon(t_k) \geqslant 0.$$

In this case we have the estimates

$$0 \leqslant x^{(k+1)}(t) \leqslant u^{(*)}, \quad 0 \leqslant y^{(k+1)}(t) \leqslant \varphi^{(k+1)} \mathrm{e}^{-\rho_{\mathrm{k}+1}(\mathrm{t}-\mathrm{t}_\mathrm{k})}$$
$$t \in [t_k, t_{k+1}], \quad k = 1, 2, \dots$$

where the parameters $\rho_{k+1} \in R$ and $\varphi^{(k+1)} \in R^n$ satisfy the relations

$$0 < \rho_{k+1} < \min\{|\ell_{11}|, \dots, |\ell_{nn}|\}$$
$$\varphi^{(k+1)} > 0, \quad \varphi^{(k+1)} \geqslant y^{(k+1)}(t_k), \quad \big(L^{(*)} - \rho_{k+1} E\big)\varphi^{(k+1)} \geqslant 0.$$

4. Conclusions

In this paper we present a new variant of a mathematical model of HIV infection spread. The novelty of the model is in the structure of its equations taking into account the migration of people between regions and the impulse (abrupt) change in the sizes of different population groups. From the mathematical point of view, the model is a Cauchy problem for a high-dimensional system of nonlinear differential equations having special structure. The model admits solution (2.4) interpreted as the absence of HIV infection in all considered regions. Upper estimates of the number of susceptible and infected individuals are obtained for all population groups (Assertions 2.1 and 3.1). Exponential estimates determine the dynamics and rate of decrease of the number of HIV-infected individuals. The existence of such exponential estimates is expressed in terms of the matrix $L^{(*)} = (\ell_{ij}^{(*)})$ given by formula (2.14). Note that the approach proposed in the paper to the study of properties of solutions to the model of HIV infection spread can be extended to the family of models of form (1.1), (1.2).

One of the basic conditions of containment or complete eradication of HIV infection within the framework of the model is the condition that $L^{(*)}$ should be a nonsingular M-matrix. This condition is provided if, for example, the following requirements hold true: a) diagonal elements of the matrix $L^{(*)}$ are positive; b) the spectral radius $\rho(L_*)$ of the matrix

$$L_* = E - \left(\operatorname{diag}(\ell_{11}^{(*)}, \dots, \ell_{nn}^{(*)})\right)^{-1} L^{(*)}$$

is such that $\rho(L_*) < 1$. The number $R_0 = \rho(L_*)$ may be considered as a standard indicator used in the study of models of epidemic processes. Note that the result obtained here is in accordance with the results of study of the stochastic model of HIV infection spread from [16].

Considering $L^{(*)}$, recall that the matrix $(-L)$ is a nonsingular M-matrix. The matrix $D(u^{(*)})B$ continuously depends on $u^{(*)}$, on elements of the matrix B and, in addition, $D(0)B = 0$. Therefore, in order to get a nonsingular M-matrix $L^{(*)}$, we may require a certain 'smallness' of components of the vector $u^{(*)}$ specifying the potential number of individuals of the groups S, or some 'smallness' of elements of the matrix B describing the intensities of contacts of individuals from the groups S and I.

From the practical viewpoint the main result obtained from the study of the model is the following. In order to suppress the spread of HIV in the considered regions we have to carry out activities to reduce the potential sizes $u_1^{(*)}, \dots, u_n^{(*)}$ of some groups of individuals from $S_1, \dots, S_n$. Such groups may be

$$S_k^{(*)} = \{S_{i_1}, \dots, S_{i_k}\}$$

which potential sizes $u_k^{(*)} = \{u_{i_1}^{(*)}, \dots, u_{i_k}^{(*)}\}$ lead to a violation of the condition that L^* is a nonsingular M-matrix.

Therefore, one of the areas of struggle against HIV infection involves the work related to search of groups entering $S_k^{(*)}$. It is necessary to evaluate as the potential sizes $u_k^{(*)}$, so the elements of the matrix B determining the intensity of contacts of individuals from these 'adverse' groups. In order to reduce the sizes of 'adverse' groups, we need an implementation of a set of measures to change (improve) socio-economic conditions of individuals.

It should be noted that in the conditions of uncertainty of the composition of the groups in $S_k^{(*)}$ these measures would be actually aimed at all individuals of the studied regions. Obviously, the measures for treatment and support of detected HIV-infected and sick individuals look more visual and relatively effective. Since the number of such individuals is known, we can estimate total financial costs for their treatment and support. Using the methods of statistical data processing, we can construct short-term forecasts for the dynamics of detected HIV-infected and sick individuals and plan the corresponding financial costs. However, in the long term perspective, the indicated financial costs may significantly increase and exceed permissible values. Therefore, we will inevitably face the challenge of suppression of HIV infection spread and search for conditions ensuring a steady decrease of the number of HIV-infected individuals. One of the variants for determination of the indicated conditions has been obtained in this paper.

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