The local and global dynamics of a general cancer tumor growth model with multiphase structure

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Abstract

We present a phase-space analysis of a mathematical model of tumor growth with an immune responses. We consider mathematical analysis of the model equations with multipoint initial condition regarding to dissipativity, boundedness of solutions, invariance of non-negativity, local and global stability and the basins of attractions. We derive some features of behavior of one of three-dimensional tumor growth models with dynamics described in terms of densities of three cells populations: tumor cells, healthy host cells and effector immune cells. We found sufficient conditions, under which trajectories from the positive domain of feasible multipoint initial conditions tend to one of equilibrium points. Here, cases of the small tumor mass equilibrium points-the healthy equilibrium point, the “death” equilibrium point have been examined. Biological implications of our results are discussed.

Keywords: Cancer tumor model, Mathematical modeling, Immune system, Stability of dynamical systems, Multiphase attractors

1. Introduction

Beginning with this article we intend to attempt to investigate the problems of mathematical and biological approaches to modelings of cancer growth dynamics processes and operations. It is important to take into account “the nonlinear property of cancer growth processes” in construction of mathematical logistic models. This nonlinearity approach appears very convenient to display unexpected dynamics in cancer growth processes expressed in different reactions of the dynamics to different concentrations of immune cells at different stages of cancer growth developments [1 – 21]. Taking into account all the complex processes, nonlinear mathematical models can be estimated capable of compensation and minimization the inconsistencies between different mathematical models related to cancer growth-anticancer factor affections. The elaboration of mathematical non-spatial models of the cancer tumor growth in the broad framework of tumor immune interactions studies is one of intensively developing areas in the modern mathematical biology, see works [1 – 9]. Of course, the development of powerful cancer immunotherapies requires first of all an understanding of the mechanisms governing the dynamics of tumor growth. One
of main reasons for creation of non-spatial dynamical models of this nature is related to the fact that they are described by a system of ordinary differential equations, which can be efficiently investigated by powerful methods of qualitative theory of ordinary differential equations and dynamical systems theory. Mathematical models for tumour growth have been extensively studied in the literature to understand the mechanism of the disease and to predict its future behavior. Interactions of tumour cells with other cells of the body, i.e. healthy host cells and immune system cells are the main components of these models and these interactions may yield different outcomes. Some important phenomena of the tumour progression such as tumour dormancy, creeping through, and escape from immune surveillance have been investigated by using these models. Kuznetsov et al. [1] proposed a model of second order, governed by ordinary differential equations (ODEs), which includes the effector immune cell and the tumour cell populations. They demonstrated that even with two cell populations, these models can provide very rich dynamics depending on the system parameters and explained some very important aspects of the stages of cancer progression. Three equation mathematical models of tumor growth with an immune responses were studied e.g. in [4, 5, 7, 9, 10]. For instance, Kirschner and Panetta [4] examined the tumour cell growth in the presence of the effector immune cells and the cytokine IL-2 which has an essential role in the activation and stimulation of the immune system. de Pillis and Radunskaya [5] included a normal tissue cell population in this model, performed phase space analysis and investigated the effect of chemotherapy treatment by using optimal control theory. In [9], interactions between cancer cells, effector cells, and cytokines (such as IL-2, TGF-β, IFN-γ) studied. In [7] interactions between cancer cells, effector cells, and normal tissue cells are investigated. In [6], a four-dimensional model is discussed which can undergo Hopf bifurcations leading to periodic orbits, a possible route to the development of chaotic attractors (for general review see e.g. [1, 3]). In [10] global behavior of the tumour growth population dynamics was investigated. The local stability, the chaotic behavior properties and some features of global behavior tumour growth model of (1) with the classical initial condition were studied in [12] and [11], respectively. The complex oscillations were studied in [16]. Moreover, the model has been also used to define optimal control problems (see e.g. [16 – 18]). Note that nonlinear dynamic systems studied e.g. in [22 – 24]. In contrast to mentioned works, here mathematical analysis of multipoint IVP for (1.1), local and global stability and the multiphase basins of attractions have been investigated. We prove that all orbits are bounded and must converge to one of several possible equilibrium points. Therefore, the long-term behavior of an orbit is classified according to the basin of multipoint attraction in which it starts. Here, we examine the dynamics of one cancer growth model proposed in [5], but possessing multiphase structure, i.e. we consider the following multipoint initial value problem (IVP) for dynamical system

\[ \dot{x}_1 = B_1(x_1) - D_1(x_1, x_2) - h_1(x_1, x_3), \]
\[ \dot{x}_2 = B_2 (x_2) - D_2 (x_2) - h_2 (x_1, x_2), \quad (1.1) \]
\[ \dot{x}_3 = B_3 (x_1, x_3) - D_3 (x_3) - h_3 (x_1, x_3), \quad t \in [0, T), \]

\[ x_1 (t_0) = x_{10} + \sum_{k=1}^{m} \alpha_{1k} x_1 (t_k), \quad x_2 (t_0) = x_{20} + \sum_{k=1}^{m} \alpha_{2k} x_2 (t_k), \quad (1.2) \]
\[ x_3 (t_0) = x_{30} + \sum_{k=1}^{m} \alpha_{3k} x_3 (t_k), \quad t_0 \in [0, T), \quad t_k \in O_\delta (t_0), \]

where \( x_1 = x_1 (t), \; x_2 = x_2 (t), \; x_3 = x_3 (t) \) denote the densities of tumor cells, healthy host cells and the effector immune cells, respectively at the moment; \( t \), \( \alpha_{jk} \) are real numbers, \( m \) is a natural number and

\[ O_\delta (t_0) = \{ t \in \mathbb{R} : |t - t_0| < \delta \} \text{ for a } \delta > 0; \quad (1.3) \]

\( B_i (x_i), \; i = 1, 2 \) correspond to the logistic growth of tumor and normal health cells in the absence of any effect from immune cells populations; \( D_1, h_1 \) are the death rates of tumor cells respectively, with interaction of normal and immune cells; \( D_2 \) is the natural death rate of normal health cells \( x_2 \) and \( h_2 \) is the death rate of \( x_2 \) with interaction of tumor cells; \( D_3 \) is the natural death rate of immune cells \( x_3 \) and \( h_3 \) is the death rate of \( x_3 \) with interaction of tumor cells; The third equation of the model describes the change in the immune cells population with time \( t \). The first term \( B_3 (x_1, x_3) \) of the third equation illustrates the stimulation of the immune system by the tumor cells with tumor specific antigens. The rate of recognition of the tumor cells by the immune system depends on the antigenicity of the tumor cells. The model of the recognition process is given by the rational type function which depends on the number of tumor cells; \( \alpha_{jk} \) are real numbers and \( m \) is a natural number such that,

\[ x_{j0} + \sum_{k=1}^{m} \alpha_{jk} x_j (t_k) \geq 0, \; j = 1, 2, 3. \quad (1.4) \]

Note that, for \( \alpha_{j1} = \alpha_{j2} = ... \alpha_{jm} = 0 \) and

\[ B_1 (x_1) = r_1 x_1 (1 - k_1 x_1), \quad D_1 (x_1, x_2) = a_{12} x_1 x_2, \quad h_1 (x_1, x_3) = a_{13} x_1 x_3, \]
\[ B_2 (x_2) = r_2 x_2 (1 - k_2 x_2), \quad D_2 (x_2) = 0, \quad h_2 (x_1, x_2) = a_{21} x_1 x_2, \]
\[ B_3 (x_1, x_3) = \frac{r_3 x_1 x_3}{x_1 + k_3}, \quad D_3 (x_1, x_3) = d_3 x_3, \quad h_3 (x_1, x_3) = a_{31} x_1 x_3 \]

the problem (1.3) – (1.4) becomes the following IVP

\[ \dot{x}_1 = r_1 x_1 (1 - k_1 x_1) - a_{12} x_1 x_2 - a_{13} x_1 x_3, \]
\[
\dot{x}_2 = r_2 x_2 \left(1 - k_2^{-1} x_2 \right) + a_{21} x_1 x_2 \\
\dot{x}_3 = \frac{r_3 x_1 x_3}{x_1 + k_3} - a_{31} x_1 x_3 - d_3 x_3, \quad t \in [0, T],
\]
considered in [5], where \(a_{ij}, r_i, d_3\) are positive numbers, \(\alpha_{jk}\) are real numbers and \(m\) is a natural number such that
\[
x_1(t_0) > 0, \ x_2(t_0) > 0, \ x_3(t_0) > 0,
\]
where the first term of the first equation corresponds to the logistic growth of tumor cells in the absence of any effect from other cells populations with the growth rate of \(r_1\) and maximum carrying capacity \(k_1\). The competition between host cells and tumor cells \(x_1(t)\) which results in the loss of the tumor cells population is given by the term \(a_{12} x_1 x_2\). Next, the parameter \(a_{13}\) refers to the tumor cell killing rate by the immune cells \(x_3(t)\). In the second equation, the healthy tissue cells also grow logistically with the growth rate of \(r_2\) and maximum carrying capacity \(k_2\). We assume that the cancer cells proliferate faster than the healthy cells which gives \(r_1 > r_2\). The tumor cells also inactivate the healthy cells at the rate of \(a_{21}\). The third equation of the model describes the change in the immune cells population with time \(t\). The first term of the third equation illustrates the stimulation of the immune system by the tumor cells with tumor specific antigens. The model of the recognition process depends on the number of tumor cells with positive constants \(r_3\) and \(k_3\). The immune cells are inactivated by the tumor cells at the rate of \(a_{31}\) as well as they die naturally at the rate \(d_3\).

We suppose that the constant influx \(s\) of the activated effector cells into the tumor microenvironment is zero. Therein, note that, the references and nonlinear dynamic systems studied e.g. in [14 − 15]. One of main aims is derivation of sufficient conditions under which the possible biologically feasible dynamics is local and globally stable, and a converges to one of equilibrium points. Since these equilibrium points have a biological sense, we notice that understanding limit properties of dynamics of cells populations based on solving problems (1.1) − (1.2) may be of an essential interest for the prediction of health conditions of a patient without a treatment, when the data (e.g. the status of blood cells shown above) that determines the condition of the patient are compared at various times \(t_0, t_1, ..., t_m\) and correlated. Note that the local and global stability properties of (1.1) with the classical initial condition were studied in [8] and [9], respectively. We prove that all orbits are bounded and must converge to one of several possible equilibrium points.

2. Notations and background.

Consider the multipoint IVP for nonlinear equation
\[
\frac{du}{dt} = f(u), \quad t \in [0, T],
\]
\[ u(t_0) = u_0 + \sum_{k=1}^{m} \alpha_k u(t_k), \quad t_0 \in [0, T), \quad t_k \in (0, T), \quad t_k > t_0 \]

in a Banach space \( X \), where \( \alpha_k \) are complex numbers, \( m \) is a natural number and \( u = u(t) \) is a \( X \)-valued function. Note that, for \( \alpha_1 = \alpha_2 = \ldots = \alpha_m = 0 \) the problem (2.1) becomes the following local Cauchy problem

\[ \frac{du}{dt} = f(u), \quad u(t_0) = u_0, \quad t \in [0, T], \quad t_0 \in [0, T). \]  

(2.2)

For \( u_0 \in X \) let \( \bar{B}_r(u_0) \) denotes a closed ball in \( X \) with radius \( r \) centered at \( u_0 \), i.e.,

\[ \bar{B}_r(u_0) = \{ u \in X : \| u - u_0 \|_X \leq r \}. \]

We can generalized classical Picard existence theorem for nonlinear multi-point IVP (2.1).

By reasoning as a classical case we obtain

**Theorem 2.1.** Let \( X \) be a Banach space. Suppose \( f : X \rightarrow X \) satisfies local Lipschitz condition on \( \bar{B}_r(v_0) \subset X \), i.e.

\[ \| f(u) - f(v) \|_X \leq L \| u - v \|_X \]

for each \( u, v \in \bar{B}_r(v_0) \) and there exists \( \delta > 0 \) such that

\[ t_k \in O_\delta(t_0) = \{ t \in \mathbb{R} : |t - t_0| < \delta \}, \]

where

\[ v_0 = u_0 + \sum_{k=1}^{m} \alpha_k u(t_k). \]

Moreover, let

\[ M = \sup_{u \in \bar{B}_r(v_0)} \| f(u) \|_X < \infty. \]

Then, problem (2.1) has a unique continuously differentiable local solution \( u(t) \) for \( t \in O_\delta(t_0) \), where \( \delta \leq \frac{\delta_0}{M} \).

**Proof.** We rewrite the initial value problem (2.1) as an integral equation

\[ u = v_0 + \int_{t_0}^{t} f(u(s)) \, ds. \]

For \( 0 < \eta < \frac{\delta_0}{M} \) we define the space

\[ Y = C ([\eta, \eta]; \bar{B}_r(v_0)). \]

Let

\[ Q u = v_0 + \int_{t_0}^{t} f(u(s)) \, ds. \]
First, note that if \( u \in Y \) then
\[
\|Qu - v_0\|_X \leq \left\| \int_{t_0}^{t} f(u(s)) \, ds \right\|_X \leq M \eta < r.
\]

Hence, \( Qu \in Y \) so that \( Q : Y \to Y \). Moreover, for all \( u, v \in Y \) we have
\[
\|Qu - Qv\|_X \leq \left\| \int_{t_0}^{t} [f(u(s)) - f(v(s))] \, ds \right\|_X \leq L_f \eta \|u - v\|_X,
\]
where \( L_f \) is a Lipschitz constant for \( f \) on \( \bar{B}_r(v_0) \). Hence, if we choose
\[
\eta < \min \left\{ \frac{r}{M}, \frac{1}{L_f} \right\}
\]
then \( Q \) is a contraction on \( Y \) and it has a unique fixed point. Since \( \eta \) depends only on the Lipschitz constant of \( f \) and on the distance \( r \) of the initial data from the boundary of \( \bar{B}_r(v_0) \). Then repeated application of this result gives a unique local solution defined for \( |t - t_0| < \frac{r}{M} \).

**Theorem 2.2.** Let \( X \) be a Banach space. Suppose that \( f : X \to X \) satisfies global Lipschitz condition, i.e.
\[
\|f(u) - f(v)\|_X \leq L \|u - v\|_X
\]
for each \( u, v \in X \). Moreover, let
\[
M = \sup_{u \in X} \|f(u)\|_X < \infty.
\]

Then problem (2.1) has a unique continuously differentiable global solution \( u(t) \) for all \( t \in [t_0, T] \).

**Proof.** The key point of proof is to show that the constant \( \delta \) of Theorem 2.1 can be made independent of the \( v_0 \). It is not hard to see that the independence of \( v_0 \) comes through the constant \( M \) in therm \( \frac{r}{M} \) in (2.4). Since in the current case the Lipschitz condition holds globally, one can choose \( r \) arbitrary large. Therefore, for any finite \( M \), we can choose \( r \) large enough and by using (2.3), (2.4) we obtain the assertion.

Let \( X \) be a Banach space. \( w \in X \) is called a critical point (or equilibria point) for the equation (2.1) if \( f(w) = 0 \).

We denote the solution of the problem (2.1) by
\[
\phi(t, u_0) = \phi(t, u(t_0), u(t_1), \ldots, u(t_n)).
\]

**Definition 2.1.** Let \( u_0 \in X, u(t) = \phi(t, u_0) \) be a solution of (2.1) and \( w \in X \) be a critical point of (2.1). If there exists a neighbourhood \( O(w) \subset X \) of
Consider the problem \( (1.1) \). Trajectories in this octant are recurrent. Let the next two results show that the positive octant is invariant and that all negative divergence, positively invariant with respect to a region in \( \mathbb{R}^3 \) where \( \delta > 0 \) such that \( \lim_{t \to \infty} u(t) = w \) for \( u_0 + \sum_{k=1}^{m} \alpha_k u(t_k) \subset O(w), t_0 \in [0, T], t_k \in O_\delta(t_0) \) and \( \delta > 0 \), then \( w \) is called a positive multiphase attractor.

**Definition 2.2.** Assume \( w \in X \) is a multiphase attractor point of \( (2.1) \) and \( u(t) = \phi(t, u_0) \) is a solution of \( (2.1) \). A set \( \{ u: u = u_0 + \sum_{k=1}^{m} \alpha_k u(t_k) \} \subset X \) is called a domain of multiphase basin (multiphase attractor or domain of multiphase asymptotic stability) of \( w \) if \( \lim_{t \to \infty} u(t) = w \).

### 3. Boundedness, invariance of non-negativity, and dissipativity

In this section, we shall show that the model equation are bounded with negative divergence, positively invariant with respect to a region in \( \mathbb{R}^3 \) and dissipative. As we are interested in biologically relevant solutions of the system, the next two results show that the positive octant is invariant and that all trajectories in this octant are recurrent. Let

\[
O_K = \{ x = (x_1, x_2, x_3) \in R_+^3 : 0 \leq x_i \leq K_i, i = 1, 2, 3 \}, \tag{3.1}
\]

where

\[
K_i = \max \left\{ 1, x_{i0} + \sum_{k=1}^{m} \alpha_{ik} x_1(t_k) \right\}, t_k \in O_\delta(t_0), i = 1, 2, 3.
\]

Consider the problem \((1.3) - (1.4)\) with \( t_0 = 0 \).

**Condition 3.1.** Assume:

1. \( B_1(x_i) > 0, D_1(x_1, 2) > 0, D_2(x_2) > 0, B_1(0) = D_1(0, x_2) = 0, \frac{\partial}{\partial x_1} B_1(x_1) > 0, \frac{\partial}{\partial x_2} D_1(x_1, 2) > 0, \frac{\partial}{\partial x_2} D_2(x_2) > 0 \) for \( x_i > 0, i = 1, 2 \); moreover,\( \frac{\partial}{\partial x_1} B_1(0) > \frac{\partial}{\partial x_2} D_1(0, x_2) \) and \( \frac{\partial}{\partial x_2} D_2(0) > \frac{\partial}{\partial x_2} D_2(0) \);
2. \( h_k(x_1, x_3) > 0, h_k(0, x_3) = 0, h_k(x_1, 0) = 0, h_j \in C^1(R_+^2), \frac{\partial h_k}{\partial x_k} \geq 0, \)
   \( \frac{\partial h_k}{\partial x_k} > 0 \) for \( k = 1, 3 \) and \( x \in R_+^3 \);
3. \( h_2(x_1, x_2) > 0, h_2(x_1, 0) = 0, h_2(0, x_2) = 0, \)
   \( \frac{\partial}{\partial x_1} h_2(0, x_2) \neq 0, \frac{\partial}{\partial x_2} h_2(0, x_2) = 0, \frac{\partial}{\partial x_1} h_k(0, x_3) \neq 0, \)
   \( \frac{\partial}{\partial x_3} h_k(0, x_3) = 0, k = 1, 3 \) for \( x \in R_+^3 \);
4. \( 0 < B_3(x_1, x_3) \in C^1(R_+^2), \frac{\partial}{\partial x_1} B_3(x_1, x_3) > 0, \frac{\partial}{\partial x_3} B_3(x_1, x_3) > 0, B_3(x_1, 0) = 0, B_3(0, x_3) = 0 \) and \( \frac{\partial}{\partial x_3} B_3(x_1, x_3) < \frac{d}{dx_3} [D_3(x_3) - h_3(x_3, x_3)] \) for \( x_1, x_3 > 0 \);
5. \( D_3(x_3) > 0, D_4(0) = 0, D_4(0) \in C^1(R_+^2) \) and \( \frac{\partial}{\partial x_3} D_4(x_3) > 0 \) for \( x_3 > 0 \);
(6) there exist constants $K_i > 0$ such that $B_1 (K_1) = D_1 (K_1, x_2)$, $B_2 (K_2) = D_2 (K_2)$ and
\[
\frac{d}{dx_1} B_1 (K_1) < \frac{d}{dx_2} D_1 (K_1, x_2), \quad \frac{\partial}{\partial x_1} B_1 (x_1) < \frac{\partial}{\partial x_1} D_1 (x_1, x_2) - h_1 (x_1, x_3),
\]
\[
\frac{d}{dx_2} B_2 (x_2) < \frac{d}{dx_2} D_2 (x_2) - h_2 (x_1, x_2)
\]
for $x_2 > 0$ by hypothesis (2). Then $\dot{x}_1 < 0$ in around of $K_1$. Thus
\[
x_1 (t) \leq \max \left\{ K_1, x_{10} + \sum_{k=1}^{m} \alpha_{1k} x_1 (t_k) \right\}, \quad \dot{x}_1 < 0 \text{ for } x_1 > 1.
\]
Hence,
\[
\limsup_{t \to \infty} x_1 (t) \leq K_1.
\]
(3.2)

Theorem 3.1. Let the Condition 3.1 hold. Then: (1) $O_K$ is positively invariant with respect to $(1.1) - (1.2)$; (2) all solutions of the problem $(1.1) - (1.2)$ are uniformly bounded and are attracted into the region $O_K$; (3) the system $(1.1)$ is dissipative.

Proof. By Theorem 2.1 there exists a unique solution of multipoint problem $(1.1) - (1.2)$.

(1) Consider the first equation of the system $(1.3)$:
\[
\dot{x}_1 = B_1 (x_1) - D_1 (x_1, x_2) - h_1 (x_1, x_3)
\]
By assumption $h_1 (x_1, x_3) > 0$ we get
\[
\dot{x}_1 < B_1 (x_1) - D_1 (x_1, x_2).
\]
But there exists $K_1$ such that $B_1 (K_1) = D_1 (K_1, x_2)$ for $x_2 > 0$ by hypothesis (2). Then $\dot{x}_1 < 0$ in around of $K_1$. Thus
\[
x_1 (t) \leq \max \left\{ K_1, x_{10} + \sum_{k=1}^{m} \alpha_{1k} x_1 (t_k) \right\}, \quad \dot{x}_1 < 0 \text{ for } x_1 > 1.
\]
Hence,
\[
\limsup_{t \to \infty} x_1 (t) \leq K_1.
\]
(3.2)

For
\[
\dot{x}_2 = B_2 (x_2) - D_2 (x_2) - h_2 (x_1, x_2)
\]
a similar analysis by assumptions (1)-(4) gives
\[
x_2 (t) \leq \max \left\{ K_2, x_{20} + \sum_{k=1}^{m} \alpha_{2k} x_2 (t_k) \right\},
\]
\[
\limsup_{t \to \infty} x_2 (t) \leq K_2.
\]
(3.3)

Now consider
\[
\dot{x}_3 = B_3 (x_1, x_3) - D_3 (x_3) - h_3 (x_1, x_3).
\]
From (3.1) by assumptions (5) and (6) we have
\[ x_3 < B_3 (x_1, x_3) - D_3 (x_3) < 0. \]

Then by reasoning as the case of \( x_1 \) we deduced

\[
x_3 (t) \leq \max \left\{ K_3, x_{30} + \sum_{k=1}^{m} \alpha_{1k} x_k (t_k) \right\},
\]

\[
\limsup_{t \to \infty} x_3 (t) \leq K_3. \tag{3.4}
\]

Hence, from (3.2) – (3.4) we obtain (1) and (2) assertions. Now, let us show (3). Let \( f_1, f_2, f_3 \) denote the right sides of the system (1.1). Since

\[
\frac{\partial f_1}{\partial x_1} + \frac{\partial f_2}{\partial x_2} + \frac{\partial f_3}{\partial x_3} = \frac{\partial}{\partial x_1} B_1 (x_1) - \frac{\partial}{\partial x_1} D_1 (x_1, x_2) - \frac{\partial}{\partial x_1} h_1 (x_1, x_3) +
\]

\[
\frac{d}{dx_2} B_2 (x_2) - \frac{d}{dx_2} D_2 (x_2) - \frac{\partial}{\partial x_2} h_2 (x_1, x_2) +
\]

\[
\frac{\partial}{\partial x_3} B_3 (x_1, x_3) - \frac{d}{dx_3} D_3 (x_3) - \frac{\partial}{\partial x_3} h_3 (x_1, x_3)
\]

by assumptions (1)-(6) we obtain

\[
\frac{\partial f_1}{\partial x_1} + \frac{\partial f_2}{\partial x_2} + \frac{\partial f_3}{\partial x_3} < 0 \text{ for } x \in O_K,
\]

i.e. the system (1.1) is dissipative.

4. The equilibria points

In this section we find the equilibria points of the system (1.1). The equilibria points of (1.1) are obtained by solving the system of corresponding isocline equations

\[
B_1 (x_1) - D_1 (x_1, x_2) - h_1 (x_1, x_3) = 0,
\]

\[
B_2 (x_2) - D_2 (x_2) - h_2 (x_1, x_2) = 0, \tag{4.1}
\]

\[
B_3 (x_1, x_3) - D_3 (x_3) - h_3 (x_1, x_3) = 0.
\]

Since we are interested in biologically relevant solutions of (4.1), we find sufficient conditions under which this system have positive solutions.

**Lemma 4.1.** Assume the assumptions (1)-(5) of the condition 3.1 are satisfied. Then

\[
E_1 (0, 0, 0), E_2 (\bar{x}_1, 0, 0), E_3 (0, \bar{x}_2, 0), E_4 (\bar{x}_1, 0, \bar{x}_3), E_5 (\bar{x}_1, \bar{x}_2, 0),
\]

\[
E_6 (0, \bar{x}_2, \bar{x}_3) \tag{4.2}
\]
are the equilibria points, where \( \bar{x}_1, \bar{x}_2, \bar{x}_3 \) will be defined below.

**Proof.** By assumption (4), \( E_1, E_2 \) and \( E_3 \) are equilibria points, where \( \bar{x}_1, \bar{x}_2 \) are solutions of the equations, respectively

\[
B_1(x_1) = D_1(x_1, 0), \quad B_2(x_2) = D_2(x_2).
\]

(4.3)

It remains to find the points

\[
E_4(\bar{x}_1, 0, \bar{x}_3), \quad E_5(\bar{x}_1, \bar{x}_2, 0), \quad E_6(0, \bar{x}_2, \bar{x}_3).
\]

Consider the point \( E_4(\bar{x}_1, 0, \bar{x}_3) \), i.e. \( x_2 = 0 \). Then, by assumption (4), we get that \( E_4(\bar{x}_1, 0, \bar{x}_3) \) is equilibrium point, when \( \bar{x}_1, \bar{x}_3 \) are solution of the following system of equations

\[
B_1(x_1) - D_1(x_1, 0) - h_1(x_1, x_3) = 0,
\]

(4.4)

\[
B_3(x_1, x_3) - D_3(x_3) - h_3(x_1, x_3) = 0.
\]

Consider the point \( E_5(\bar{x}_1, \bar{x}_2, 0) \), i.e. \( x_3 = 0 \). Then, by assumption (4), we get that \( E_5(\bar{x}_1, \bar{x}_2, 0) \) is equilibrium point, when \( \bar{x}_1, \bar{x}_2 \) are solution of the following system of equations

\[
B_1(x_1) - D_1(x_1, x_2) - h_1(x_1, 0) = 0,
\]

(4.5)

\[
B_2(x_2) - D_2(x_2) - h_2(x_1, x_2) = 0.
\]

The point \( E_6(0, \bar{x}_2, \bar{x}_3) \) is equilibrium point if \( \bar{x}_2, \bar{x}_3 \) are solution of the system

\[
B_2(x_2) - D_2(x_2) - h_2(x_1, x_2) = 0,
\]

(4.6)

\[
B_3(x_1, x_3) - D_3(x_3) - h_3(x_1, x_3) = 0.
\]

Let

\[
R_3^i = \{ x = (x_1, x_2, x_3) \in R^3 : x_i > 0, \ i = 1, 2, 3 \}.
\]

We now discuss the local linearized stability of the system (1.1) \( - (1.2) \) restricted to neighborhood of the equilibrium points (4.2). The linearized matrix of (1.1) about an arbitrary equilibrium point \( E(x_1, x_2, x_3) \) is given by

\[
A_{E(x_1, x_2, x_3)} =
\]

\[
\begin{bmatrix}
\frac{\partial D_1}{\partial x_1} & \frac{\partial D_1}{\partial x_2} & -\frac{\partial h_1}{\partial x_1} & -\frac{\partial D_1}{\partial x_3} & -\frac{\partial h_1}{\partial x_3} \\
\frac{\partial D_1}{\partial x_1} & \frac{\partial D_1}{\partial x_2} & 0 & -\frac{\partial h_2}{\partial x_1} & -\frac{\partial D_2}{\partial x_3} & -\frac{\partial h_2}{\partial x_3} \\
0 & \frac{\partial D_2}{\partial x_2} & \frac{\partial D_2}{\partial x_2} & 0 & -\frac{\partial h_2}{\partial x_3} & -\frac{\partial D_2}{\partial x_3} & -\frac{\partial h_3}{\partial x_3}
\end{bmatrix}.
\]

(4.7)

By assumption (4), the linearized matrices for equilibria points (4.2) will be correspondingly as:

\[
A_1 = \begin{bmatrix}
a_{11} & a_{12} & 0 \\
0 & a_{22} & 0 \\
a_{31} & 0 & a_{33}
\end{bmatrix}, \quad A_2 = \begin{bmatrix}
b_{11} & b_{12} & 0 \\
b_{21} & b_{22} & 0 \\
b_{31} & 0 & b_{33}
\end{bmatrix}, \quad A_3 = \begin{bmatrix}
c_{11} & c_{12} & 0 \\
c_{21} & c_{22} & 0 \\
c_{31} & 0 & c_{33}
\end{bmatrix}.
\]
\[
A_4 = \begin{bmatrix} d_{11} & d_{12} & d_{13} \\ d_{21} & d_{22} & 0 \\ d_{31} & 0 & d_{33} \end{bmatrix}, \quad A_5 = \begin{bmatrix} k_{11} & k_{12} & 0 \\ k_{21} & k_{22} & 0 \\ k_{31} & 0 & k_{33} \end{bmatrix}, \quad A_6 = \begin{bmatrix} l_{11} & l_{12} & 0 \\ l_{21} & l_{22} & 0 \\ l_{31} & 0 & l_{33} \end{bmatrix},
\]

where

\[
a_{11} = \frac{\partial}{\partial x_1} [B_1 - D_1](0) - \frac{\partial h_1}{\partial x_1}(0), \quad a_{12} = - \frac{\partial D_1}{\partial x_1}(0),
\]

\[
a_{22} = \frac{d}{dx_2} [B_2 - D_2](0), \quad a_{31} = \frac{\partial B_3}{\partial x_1}(0) - \frac{\partial h_1}{\partial x_1}(0),
\]

\[
a_{33} = \frac{d}{dx_3} [B_3 - D_3](0),
\]

\[
b_{11} = \frac{\partial}{\partial x_1} [B_1 - D_1](\bar{x}_1, 0) - \frac{\partial h_1}{\partial x_1}(\bar{x}_1, 0), \quad b_{12} = - \frac{\partial D_1}{\partial x_1}(\bar{x}_1, 0),
\]

\[
b_{21} = - \frac{\partial h_2}{\partial x_1}(\bar{x}_1, 0), \quad b_{22} = \frac{d}{dx_2} [B_2 - D_2](0) - \frac{\partial h_2}{\partial x_2}(\bar{x}_1, 0),
\]

\[
b_{31} = \frac{\partial}{\partial x_1} [B_3 - h_3](\bar{x}_1, 0), \quad b_{33} = \frac{d}{dx_3} [B_3 - D_3](\bar{x}_1, 0),
\]

\[
c_{11} = \frac{\partial}{\partial x_1} [B_1 - D_1](0, 0) - \frac{\partial h_1}{\partial x_1}(0, 0), \quad c_{12} = - \frac{\partial D_1}{\partial x_1}(0, 0),
\]

\[
c_{21} = - \frac{\partial h_2}{\partial x_1}(0, \bar{x}_2), \quad c_{22} = \frac{d}{dx_2} [B_2 - D_2](0), \quad c_{31} = \frac{\partial}{\partial x_1} B_3(0, 0),
\]

\[
c_{33} = \frac{d}{dx_3} [B_3 - D_3](0, 0),
\]

\[
d_{11} = \frac{\partial}{\partial x_1} [B_1 - D_1](\bar{x}_1, \bar{x}_3) - \frac{\partial h_1}{\partial x_1}(\bar{x}_1, \bar{x}_3), \quad d_{12} = - \frac{\partial D_1}{\partial x_1}(\bar{x}_1, \bar{x}_3), \quad d_{13} =
\]

\[-\frac{\partial h_1}{\partial x_3}(\bar{x}_1, \bar{x}_3), \quad d_{21} = - \frac{\partial h_2}{\partial x_1}(\bar{x}_1, 0), \quad d_{22} = \frac{d}{dx_2} [B_2 - D_2](0) - \frac{\partial h_2}{\partial x_2}(\bar{x}_1, 0),
\]

\[
d_{31} = \frac{\partial}{\partial x_1} [B_3 - h_3](\bar{x}_1, \bar{x}_3), \quad d_{33} = \frac{d}{dx_3} [B_3 - D_3](\bar{x}_1, \bar{x}_3),
\]

\[
k_{11} = \frac{\partial}{\partial x_1} [B_1 - D_1](\bar{x}_1, 0) - \frac{\partial h_1}{\partial x_1}(\bar{x}_1, 0), \quad k_{12} = - \frac{\partial D_1}{\partial x_1}(\bar{x}_1, 0),
\]

\[
k_{21} = - \frac{\partial h_2}{\partial x_1}(\bar{x}_1, \bar{x}_2), \quad k_{22} = \frac{d}{dx_2} [B_2 - D_2](\bar{x}_2) - \frac{\partial h_2}{\partial x_2}(\bar{x}_1, \bar{x}_2),
\]

\[
(4.10)
\]
\[ k_{31} = \frac{\partial}{\partial x_1} B_3 (\bar{x}_1, 0), \quad k_{33} = \frac{d}{dx_3} [B_3 - D_3] (\bar{x}_1, 0), \]

\[ l_{11} = \frac{\partial}{\partial x_1} [B_1 - D_1] (0, \bar{x}_2) - \frac{\partial h_1}{\partial x_1} (0, \bar{x}_3), \quad l_{12} = -\frac{\partial D_1}{\partial x_1} (0, \bar{x}_2), \]

\[ l_{21} = -\frac{\partial h_2}{\partial x_1} (0, \bar{x}_2), \quad l_{22} = \frac{d}{dx_2} [B_2 - D_2] (\bar{x}_2) - \frac{\partial h_2}{\partial x_2} (0, \bar{x}_2), \quad (4.13) \]

\[ l_{31} = \frac{\partial}{\partial x_1} [B_3 (0, \bar{x}_3) - h_3 (0, \bar{x}_3)], \quad l_{33} = \frac{\partial}{\partial x_3} [B_3 - D_3] (0, \bar{x}_3), \]

\[ \bar{x}_1, \bar{x}_2 \text{ in (4.9) and (4.10) were defined respectively, by (4.3), } \bar{x}_1, \bar{x}_3 \text{ in (4.11) were defined by (4.4), } \bar{x}_1, \bar{x}_2 \text{ in (4.12) were defined by (4.5) and } \bar{x}_2, \bar{x}_3 \text{ in (4.13)} \]

5. Local stability analysis of equilibria points

In this section, we derive local stability of the system (1.1) at equilibria points (4.2). Eigenvalues of the Jacobian matrices \( A_j \) corresponding to equilibria points (4.2) (defined by (4.7)–(4.9)) are found as roots of the equations \( |A_j - \lambda| = 0 \). Consider the equilibria point \( E_1 (0, 0, 0) \). Let \( a_{ij} \) are defined by (4.8).

**Theorem 5.1.** Assume the assumptions (1)-(5) of Condition 3.1 are satisfied. If \( a_{ii} < 0 \) for \( i = 1, 2, 3 \), then the system (1.1) is local stable at the point \( E_1 (0, 0, 0) \); if \( a_{ii} > 0 \), then the system (1.1) is local unstable at \( E_1 \).

**Proof.** The eigenvalues of the Jacobian matrix \( A_1 \) are found as roots of the equation

\[ |A_1 - \lambda| = \begin{bmatrix} a_{11} - \lambda & a_{12} & 0 \\ 0 & a_{22} - \lambda & 0 \\ a_{31} & 0 & a_{33} - \lambda \end{bmatrix} = (a_{11} - \lambda) (a_{22} - \lambda) (a_{33} - \lambda) = 0. \]

Hence, \( \lambda_1 = a_{11}, \lambda_2 = a_{22}, \lambda_3 = a_{33} \) are the eigenvalues of the matrix \( A_1 \).

By first assumption all eigenvalues are negative, i.e. the system (1.1) is local stable at the point \( E_1 \); if \( a_{ii} > 0 \), then all eigenvalues are positive, i.e. the system (1.1) is local unstable at \( E_1 \).

Consider the equilibria point \( E_2 (\bar{x}_1, 0, 0) \). Let \( b_{ij} \) are defined by (4.9).

**Theorem 5.2.** Assume the assumptions (1)-(5) of the Condition 3.1 are satisfied. Let \( b_{12}^2 \leq b_{11} b_{22} \). If \( b_{33} < 0 \) and \( b_{11} + b_{22} < 0 \), then the system (1.1) is local stable at the point \( E_2 (\bar{x}_1, 0, 0) \); if \( b_{33} > 0 \) or \( b_{33} (b_{11} + b_{22}) < 0 \), then the system (1.1) is local unstable at \( E_2 \).

**Proof.** The eigenvalues of the Jacobian matrix \( A_2 \) are found as roots of the equation

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are positive, i.e. the system (1) are roots of the equation

\[ (b_{11} - \lambda) (b_{22} - \lambda) (b_{33} - \lambda) - b_{12}^2 (b_{33} - \lambda) = 0. \]

Thus, \( \lambda_1 = b_{33}, \lambda_2, \lambda_3 \) are the eigenvalues of the matrix \( A_2 \), where \( \lambda_2, \lambda_3 \)
are roots of the equation

\[ \lambda^2 - (b_{11} + b_{22}) \lambda + b_{11} b_{22} - b_{12}^2 = 0, \]

i.e.

\[ \lambda_2, \lambda_3 = \frac{(b_{11} + b_{22}) \pm \sqrt{(b_{11} + b_{22})^2 + 4 (b_{11} b_{22} - b_{12}^2)}}{2}. \]

That is, if \( b_{33} < 0 \) and \( b_{11} + b_{22} < 0 \), then the all eigenvalues of the matrix \( A_2 \) are negative, i.e. the system (1.1) is local stabile at the point \( E_2 \); if \( b_{33} > 0 \), \( b_{11} + b_{22} > 0 \) or \( b_{33} (b_{11} + b_{22}) < 0 \), then the all eigenvalues of the matrix \( A_2 \) are positive, i.e. the system (1.1) is local unstable at \( E_2 \).

Consider the equilibria point \( E_3 (0, \bar{x}_2, 0) \). Let \( c_{ij} \) are defined by (4.10).

**Theorem 5.3.** Assume the assumptions (1)-(5) of the Condition 3.1 are satisfied. Let \( c_{12}^2 \leq c_{11} c_{22}, c_{33} < 0 \) and \( c_{11} + c_{22} < 0 \), then the system (1.1) is local stabile at the point \( E_3 (0, \bar{x}_2, 0) \); if \( c_{33} > 0 \) or \( c_{33} (c_{11} + c_{22}) < 0 \), then the system (1.1) is local unstable at \( E_3 \).

**Proof.** The eigenvalues of the Jacobian matrix \( A_3 \) are found as roots

\[ |A_3 - \lambda| = \begin{bmatrix} c_{11} - \lambda & c_{12} & 0 \\ c_{12} & c_{22} - \lambda & 0 \\ c_{31} & 0 & c_{33} - \lambda \end{bmatrix} = \]

\[ (c_{11} - \lambda) (c_{22} - \lambda) (c_{33} - \lambda) - c_{12}^2 (c_{33} - \lambda) = \]

\[ (c_{33} - \lambda) [(c_{11} - \lambda) (c_{22} - \lambda) - c_{12}^2] = 0. \]

Thus, \( \lambda_1 = c_{33}, \lambda_2, \lambda_3 \) are the eigenvalues of the matrix \( A_3 \), where \( \lambda_2, \lambda_3 \)
are roots of the equation

\[ \lambda^2 - (c_{11} + c_{22}) \lambda + c_{11} c_{22} - c_{12}^2 = 0, \]

i.e.

\[ \lambda_2, \lambda_3 = \frac{c_{11} + c_{22} \pm \sqrt{(c_{11} + c_{22})^2 - 4 (c_{11} c_{22} - c_{12}^2)}}{2}. \]

That is, if \( c_{33} < 0 \) and \( c_{11} + c_{22} < 0 \), then the all eigenvalues of the matrix \( A_2 \) are negative, i.e. the system (1.1) is local stabile at the point \( E_3 \); if \( c_{33} > 0 \),
By the second assumption the all eigenvalues of the matrix $A_k$ satisfied. Let $\lambda$ the roots of the equation
\[
|A_k - \lambda| = \begin{vmatrix}
  d_{11} - \lambda & d_{12} & d_{13} \\
  d_{12} & d_{22} - \lambda & 0 \\
  d_{13} & 0 & d_{33} - \lambda
\end{vmatrix} = 0
\]
Then by the fundamental theorem of algebra we have
\[
\lambda_1 + \lambda_2 + \lambda_3 = d_{11} + d_{22} + d_{33},
\]
\[
\sum_{i,j=1}^{3} \lambda_i \lambda_j = (d_{11}d_{33} + d_{11}d_{22} + d_{22}d_{33} - d_{12}^2 - d_{13}d_{31}) ,
\]
\[
\lambda_1 \lambda_2 \lambda_3 = - [d_{12}^2 d_{33} + d_{13}d_{31}d_{22}] .
\]
The roots $\lambda_1$, $\lambda_2$, $\lambda_3$ of (5.1) are the eigenvalues of the matrix $A_k$. Then by the fundamental theorem of algebra we have
\[
\lambda_1 + \lambda_2 + \lambda_3 = d_{11} + d_{22} + d_{33},
\]
\[
\sum_{i,j=1}^{3} \lambda_i \lambda_j = (d_{11}d_{33} + d_{11}d_{22} + d_{22}d_{33} - d_{12}^2 - d_{13}d_{31}) ,
\]
\[
\lambda_1 \lambda_2 \lambda_3 = - [d_{12}^2 d_{33} + d_{13}d_{31}d_{22}] .
\]
By the second assumption the all eigenvalues of the matrix $A_k$ are negative, i.e. (1.1) is local stable at $E_4(\bar{x}_1, \bar{x}_3)$.

Consider the point $E_5(\bar{x}_1, \bar{x}_3, 0)$. Let $k_{ij}$ are defined by (4.12).

**Theorem 5.5.** Assume the assumptions (1)-(5) of the Condition 3.1 are satisfied. Let $k_{12}^2 \leq k_{11}k_{22}$. If $k_{33} < 0$ and $k_{11} + k_{22} < 0$, then the system (1.1) is local stable at the point $E_5(\bar{x}_1, \bar{x}_3, 0)$; if $k_{33} > 0$ or $k_{33}(k_{11} + k_{22}) < 0$, then the system (1.1) is local unstable at $E_5$.

**Proof.** The eigenvalues of the Jacobian matrix $A_5$ are found as roots of the equation
\[
|A_5 - \lambda| = \begin{vmatrix}
  k_{11} - \lambda & k_{12} & 0 \\
  k_{12} & k_{22} - \lambda & 0 \\
  k_{31} & 0 & k_{33} - \lambda
\end{vmatrix} = 0
\]
\[
(k_{11} - \lambda) (k_{22} - \lambda) (k_{33} - \lambda) - k_{12}^2 (k_{33} - \lambda) = 0.
\]
Thus, $\lambda_1 = k_{33}$, $\lambda_2$, $\lambda_3$ are the eigenvalues of the matrix $A_5$, where $\lambda_2$, $\lambda_3$ are roots of the equation

$$
\lambda^2 - (k_{11} + k_{22}) \lambda + k_{11} k_{22} - k_{12}^2 = 0,
$$
i.e.

$$
\lambda_2, \lambda_3 = \frac{k_{11} + k_{22} \pm \sqrt{(k_{11} + k_{22})^2 - 4(k_{11} k_{22} - k_{12}^2)}}{2}.
$$

That is, if $k_{33} < 0$ and $k_{11} + k_{22} < 0$, then the all eigenvalues of the matrix $A_2$ are negative, i.e. the system (1.1) is local stable at the point $E_5$; if $k_{33} > 0$, $k_{11} + k_{22} > 0$ or $k_{33} (k_{11} + k_{22}) < 0$, then the eigenvalues of the matrix $A_2$ are positive, i.e. the system (1.1) is local unstable at $E_5$.

Consider the equilibria point $E_6 (0, \bar{x}_2, \bar{x}_3)$, where $\bar{x}_2$, $\bar{x}_3$ is a positive solution of (4.6). Let $l_{ij}$ are defined by (4.13).

**Theorem 5.6.** Assume the assumptions (1)-(5) of the Condition 3.1 are satisfied. Let $l_{12} l_{21} \leq l_{11} l_{22}$. If $l_{33} < 0$ and $l_{11} + l_{22} < 0$, then the system (1.1) is local stable at the point $E_6 (0, \bar{x}_2, \bar{x}_3)$; if $l_{33} > 0$ or $l_{33} (l_{11} + l_{22}) < 0$, then the system (1.1) is local unstable at $E_6$.

**Proof.** The eigenvalues of the Jacobian matrix $A_5$ are found as roots of the equation

$$
|A_6 - \lambda| = \begin{vmatrix}
    l_{11} - \lambda & l_{12} & 0 \\
    l_{21} & l_{22} - \lambda & 0 \\
    l_{31} & 0 & l_{33} - \lambda
\end{vmatrix} =
$$

$$(l_{11} - \lambda) (l_{22} - \lambda) (l_{33} - \lambda) - l_{12} l_{21} (l_{33} - \lambda) =
$$

$$(l_{33} - \lambda) [(l_{11} - \lambda) (l_{22} - \lambda) - l_{12} l_{21}] = 0.
$$

Thus, $\lambda_1 = l_{33}$, $\lambda_2$, $\lambda_3$ are the eigenvalues of the matrix $A_6$, where $\lambda_2$, $\lambda_3$ are roots of the equation

$$
\lambda^2 - (l_{11} + l_{22}) \lambda + l_{11} l_{22} - l_{12} l_{21} = 0,
$$
i.e.

$$
\lambda_2, \lambda_3 = \frac{l_{11} + l_{22} \pm \sqrt{(l_{11} + l_{22})^2 - 4(l_{11} l_{22} - l_{12} l_{21})}}{2}.
$$

That is, if $l_{33} < 0$ and $l_{11} + l_{22} < 0$, then the all eigenvalues of the matrix $A_2$ are negative, i.e. the system (1.1) is local stable at the point $E_6$; if $l_{33} > 0$, $l_{11} + l_{22} > 0$ or $l_{33} (l_{11} + l_{22}) < 0$, then the all eigenvalues of the matrix $A_2$ are positive, i.e. the system (1.1) is local unstable at $E_6$. 

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6. The Lyapunov stability of equilibria points

In this section, we will derive the stability properties of the system (1.1) at points (4.2) in the Lyapunov sense.

Let 

\[ R_+^3 = \{ x \in R^3: x_i \geq 0, i = 1, 2, 3 \} , \quad B_r (\bar{x}) = \{ x \in R^3, \| x - \bar{x} \|^2 \leq r^2 \} . \]

Let \( a_{ij} \) be the real numbers defined by (4.8). In this section we show the following results:

**Theorem 6.1.** Assume the assumptions (1)-(5) of the Condition 3.1 are satisfied and \( a_{ii} < 0 \) for \( i = 1, 2, 3 \). Then the system (1.1) is asymptotically stable at the equilibria point \( E_1 (0, 0, 0) \) in the Lyapunov sense.

**Proof.** Let \( A_1 \) be the linearized matrix with respect to equilibria point \( E_1 (0, 0, 0) \), i.e.

\[ A_1 = \begin{bmatrix} a_{11} & a_{12} & 0 \\ a_{21} & a_{22} & 0 \\ a_{31} & a_{32} & a_{33} \end{bmatrix} , \quad A_1^T = \begin{bmatrix} a_{11} & 0 & a_{31} \\ a_{12} & a_{22} & 0 \\ 0 & 0 & a_{33} \end{bmatrix} . \]

We consider the Lyapunov equation

\[ P_1 A_1 + A_1^T P_1 = -I , \quad P_1 = \begin{bmatrix} p_{11} & p_{12} & p_{13} \\ p_{21} & p_{22} & p_{23} \\ p_{31} & p_{32} & p_{33} \end{bmatrix} , \quad p_{ij} = p_{ji} , \]

here

\[ P_1 A_1 = \begin{bmatrix} p_{11}a_{11} + p_{13}a_{31} & p_{11}a_{12} + p_{12}a_{22} + p_{13}a_{33} \\ p_{21}a_{11} + p_{23}a_{31} & p_{21}a_{12} + p_{22}a_{22} + p_{23}a_{33} \\ p_{31}a_{11} + p_{33}a_{31} & p_{31}a_{12} + p_{32}a_{22} + p_{33}a_{33} \end{bmatrix} , \]

\[ A_1^T P_1 = \begin{bmatrix} a_{11}p_{11} + a_{13}p_{31} & a_{11}p_{12} + a_{13}p_{32} & a_{11}p_{13} + a_{13}p_{33} \\ a_{12}p_{11} + a_{22}p_{21} & a_{12}p_{12} + a_{22}p_{22} & a_{12}p_{13} + a_{22}p_{23} \\ a_{33}p_{31} & a_{33}p_{32} & a_{33}p_{33} \end{bmatrix} , \]

\[ P_1 A_1 + A_1^T P_1 = -I . \quad (6.1) \]

The matrix equation (6.1) is equivalent to system of algebraic equations with respect to \( p_{ij} \):

\[ 2 (a_{11}p_{11} + a_{31}p_{33}) = -1 , \quad a_{12}p_{11} + (a_{22} + a_{11}) p_{12} + a_{31}p_{23} = 0 , \]

\[ (a_{33} + a_{11}) p_{13} + a_{31}p_{33} = 0 , \quad 2 (a_{12}p_{12} + a_{22}p_{22}) = -1 , \]

\[ (a_{22} + a_{33}) p_{23} + a_{12}p_{13} = 0 , \]

\[ a_{12}p_{13} + (a_{22} + a_{33}) p_{23} = 0 , \quad 2p_{33}a_{33} = -1 . \]
By solving this system we obtain

$$p_{33} = -\frac{1}{2a_{33}}, \quad p_{13} = \frac{a_{31}}{2(a_{11} + a_{33})a_{33}}, \quad p_{11} = -\frac{1}{a_{11}} \left( \frac{1}{2} + a_{31} p_{13} \right), \quad (6.2)$$

$$p_{23} = -\frac{a_{12} p_{13}}{a_{22} + a_{33}}, \quad p_{12} = -\left( \frac{a_{12} p_{11} + a_{31} p_{23}}{a_{11} + a_{22}} \right) / a_{22}, \quad p_{22} = -\left( \frac{1}{2} + a_{12} p_{12} \right).$$

Hence, the eigenvalues of $A$ are positive if the quadratic function

$$V_1 (x) = X^T P_1 X = p_{11} x_1^2 + p_{22} x_2^2 + p_{33} x_3^2 + 2p_{13} x_1 x_3 +$$

$$2p_{13} x_1 x_3 + 2p_{23} x_2 x_3, \quad X = [x_1, x_2, x_3]$$

is positive defined. It is clear to see that

$$V_1 (x) = \frac{1}{2} p_{11} x_1^2 + 2p_{12} x_1 x_2 + \frac{1}{2} p_{22} x_2^2 + \frac{1}{2} p_{11} x_1^2 + 2p_{13} x_1 x_3 +$$

$$\frac{1}{2} p_{22} x_2^2 + 2p_{23} x_2 x_3 + p_{33} x_3^2 = \frac{1}{2} p_{11} \left( x_1 + 2 \frac{p_{12}}{p_{11}} x_2 \right)^2 + \left( \frac{1}{2} p_{22} - \frac{2p_{12}^2}{p_{11}} \right) x_2^2 +$$

$$\frac{1}{2} p_{11} \left( x_1 + 2 \frac{p_{12}}{p_{11}} x_3 \right)^2 + \left( \frac{1}{2} p_{33} - \frac{2p_{12}^2}{p_{11}} \right) x_3^2 +$$

$$\frac{1}{2} p_{22} \left( x_2 + 2 \frac{p_{23}}{p_{22}} x_3 \right)^2 + \left( \frac{1}{2} p_{33} - \frac{2p_{23}^2}{p_{22}} \right) x_3^2 > 0,$$

when

$$p_{11} > 0, \quad 4p_{12}^2 \leq p_{11} p_{22}, \quad 4p_{12}^2 \leq p_{11} p_{33}, \quad 4p_{23}^2 \leq p_{22} p_{33},$$

i.e., the matrix $P_1$ is positive defined under the condition (6.4). Hence, the quadratic function $V_1 (x)$ is a positive defined Lyapunov function candidate in the certain neighborhood of $E_1 (0, 0, 0)$. By [12, Corollary 8.2] we need now to determine a domain $\Omega_1$ about the point $E_1$, where $\dot{V}_1 (x)$ is negatively defined and a constant $C$ such that $\Omega_C$ is a subset of $\Omega_1$. By assuming $x_k \geq 0, k = 1, 2, 3$, we will find the solution set of the following inequality

$$\dot{V}_1 (x) = \sum_{k=1}^{3} \frac{\partial V_1}{\partial x_k} \frac{dx_k}{dt} =$$

$$2 (p_{11} x_1 + p_{12} x_2 + p_{13} x_3) [B_1 (x_1) - D_1 (x_1, x_2) - h_1 (x_1, x_3)] +$$

$$2 (p_{12} x_1 + p_{22} x_2 + p_{23} x_3) [B_2 (x_2) - D_2 (x_2) - h_2 (x_1, x_2)] +$$

$$2 (p_{13} x_1 + p_{23} x_2 + p_{33} x_3) [B_3 (x_1, x_3) - D_3 (x_3) - h_3 (x_1, x_3)] \leq 0.$$
Hence, (6.5) is satisfied if the following hold
\[ p_{11}x_1 + p_{12}x_2 + p_{13}x_3 \geq 0, \quad p_{12}x_1 + p_{22}x_2 + p_{23}x_3 \geq 0, \quad p_{13}x_1 + p_{23}x_2 + p_{33}x_3 \geq 0, \quad B_1(x_1)-D_1(x_1,x_2)-h_1(x_1,x_3) \leq 0, \quad B_2(x_2)-D_2(x_2)-h_2(x_1,x_2) \leq 0, \]
\[ B_3(x_1,x_3)-D_3(x_3)-h_3(x_1,x_3) \leq 0. \quad (6.6) \]

**Remark 6.1.** By (6.2) the sign of \( p_{13} \) is the same as the sign of \( a_{31} \) and the sign of \( p_{23} \) is the same as the sign of \( a_{12}a_{31} \). So, \( p_{13} > 0 \), when \( a_{31} > 0 \); hence, \( p_{23} > 0, p_{12} > 0 \) when \( a_{31} > 0 \) and \( a_{12} > 0 \). By assumption \( a_{ii} < 0 \) and (6.2) we get \( p_{11} = \frac{1}{a_{11}} \left( \frac{1}{3} + a_{31}p_{13} \right) > 0, \quad p_{33} > 0. \) Since \( a_{22} < 0 \) we get that \( p_{22} = \frac{1}{2a_{22}} > 0 \), when \( a_{31} > 0 \) and \( a_{12} > 0 \). Moreover, by using (6.2) we can derive the conditions on \( a_{ij} \) that the assumptions (6.4) are hold.

Here, \( b_{ij} \) are real numbers defined by (4.9). Let
\[ d = (b_{11} + b_{33})(b_{22} + b_{33}) - b_{12}b_{21}, \]
\[ D = b_{11}b_{22}(b_{11} + b_{22}) - b_{11}b_{12}b_{21} - b_{11}b_{22}b_{12}. \]

**Theorem 6.2.** Assume the assumptions (1)-(5) of the Condition 3.1 are satisfied. Suppose \( b_{ii} < 0 \) for \( i = 1, 2, 3, \quad d \neq 0 \) and \( D \neq 0 \). Then the system (1.1) is asymptotically stable at the equilibria point \( E_2(\bar{x}_1, 0, 0) \) in the Lyapunov sense.

**Proof.** Let \( A_2 \) be the linearized matrix with respect to equilibria point \( E_2(\bar{x}_1, 0, 0) \), i.e.
\[ A_2 = \begin{bmatrix} b_{11} & b_{12} & 0 \\ b_{21} & b_{22} & 0 \\ b_{31} & 0 & b_{33} \end{bmatrix}, \quad A_2^T = \begin{bmatrix} b_{11} & b_{12} & b_{31} \\ b_{21} & b_{22} & 0 \\ 0 & 0 & b_{33} \end{bmatrix}. \]

We consider the Lyapunov equation
\[ P_2A_2 + A_2^TP_2 = -I, \quad P_2 = \begin{bmatrix} p_{11} & p_{12} & p_{13} \\ p_{21} & p_{22} & p_{23} \\ p_{31} & p_{32} & p_{33} \end{bmatrix}, \quad p_{ij} = p_{ji}, \quad (6.7) \]
where
\[ P_2A_2 = \begin{bmatrix} p_{11}b_{11} + p_{12}b_{21} + p_{13}b_{31} & p_{11}b_{12} + p_{12}b_{22} & p_{11}b_{13} + p_{12}b_{23} \\ p_{21}b_{11} + p_{22}b_{21} + p_{23}b_{31} & p_{21}b_{12} + p_{22}b_{22} & p_{21}b_{13} + p_{22}b_{23} \\ p_{31}b_{11} + p_{32}b_{21} + p_{33}b_{31} & p_{31}b_{12} + p_{32}b_{22} & p_{31}b_{13} + p_{32}b_{23} \end{bmatrix} \]
\[ A_2^TP_2 = \begin{bmatrix} b_{11}p_{11} + b_{21}p_{21} + b_{31}p_{31} & b_{11}p_{12} + b_{21}p_{22} + b_{31}p_{32} & b_{11}p_{13} + b_{21}p_{23} + b_{31}p_{33} \\ b_{12}p_{11} + b_{22}p_{21} & b_{12}p_{12} + b_{22}p_{22} & b_{12}p_{13} + b_{22}p_{23} \\ b_{33}p_{31} & b_{33}p_{32} & b_{33}p_{33} \end{bmatrix}, \]
\[ 18 \]
\[ P_2 A_2 + A_2^T P_2 = -I. \] (6.8)

The matrix equation (6.1) is equivalent to system of algebraic equations with respect to \( p_{ij} \)

\[ \begin{align*}
2 (b_{11} p_{11} + b_{21} p_{12} + b_{31} p_{13}) &= -1, \quad b_{12} p_{11} + (b_{22} + b_{11}) p_{12} + b_{21} p_{22} + \\
\quad b_{31} p_{23} &= 0, \quad (b_{33} + b_{11}) p_{13} + b_{21} p_{23} + b_{31} p_{33} = 0, \\
2 (b_{12} p_{12} + b_{22} p_{22}) &= -1, \quad (b_{33} + b_{22}) p_{23} + b_{12} p_{13} = 0, \\
(b_{11} + b_{33}) p_{13} + b_{21} p_{23} + b_{31} p_{33} &= 0, \\
2 (b_{12} p_{13} + b_{22} p_{23}) &= 0, \quad 2 p_{33} b_{21} = -1.
\end{align*} \]

By solving this system we obtain

\[ \begin{align*}
p_{33} &= \frac{1}{2 b_{33}}, \quad p_{13} = \frac{d_1}{d}, \quad p_{23} = \frac{d_2}{d}, \quad p_{11} = \frac{D_1}{D}, \quad p_{12} = \frac{D_2}{D}, \quad p_{22} = \frac{D_3}{D},
\end{align*} \]

where

\[ \begin{align*}
d_1 &= -\frac{b_{21} b_{31}}{2 b_{33}}, \quad d_2 = \frac{b_{31}}{2 b_{33}} (b_{11} + b_{33}), \\
D_1 &= -\frac{1}{2} b_{21}^2 + b_{22} (b_{11} + b_{22}) \left( \frac{1}{2} + b_{31} p_{13} \right) + \\
&\quad \left( \frac{1}{2} + b_{31} p_{13} \right) b_{12} b_{21} + b_{21} b_{22} b_{31} p_{23}, \\
D_2 &= \frac{1}{2} b_{11} b_{21} + b_{12} b_{22} \left( \frac{1}{2} + b_{31} p_{13} \right) - b_{11} b_{22} b_{31} p_{23}, \\
D_3 &= b_{11} b_{12} b_{31} p_{23} + \frac{1}{2} b_{12} b_{21} - \frac{1}{2} b_{11} (b_{11} + b_{22}) - b_{12}^2 \left( \frac{1}{2} + b_{31} p_{13} \right).
\end{align*} \] (6.9)

Hence, the eigenvalues of \( A_2 \) are positive if the quadratic function

\[ V_2 (x) = X^T P_2 X = p_{11} x_1^2 + p_{22} x_2^2 + p_{33} x_3^2 + 2 p_{12} x_1 x_2 + 2 p_{13} x_1 x_3 + 2 p_{23} x_2 x_3 \]

is positive defined. By assumption we get that \( p_{33} > 0 \). Moreover, \( p_{kk} > 0 \) for \( k = 1, 2 \), when \( \frac{D_1}{D} > 0, \frac{D_3}{D} > 0 \). Hence, in a similar way we obtain that \( V_2 (x) \) is positive defined, if \( \frac{D_1}{D} > 0, \frac{D_3}{D} > 0 \) and when the estimate of type (6.4) is satisfied.

By reasoning as in the proof of Theorem 6.1 we obtain that the inequality

\[ \dot{V}_2 (x) = \sum_{k=1}^3 \frac{\partial V_2}{\partial x_k} \frac{d x_k}{dt} \leq 0 \] (6.10)
is valid if the following holds

\[ p_{11}x_1 + p_{12}x_2 + p_{13}x_3 \geq 0, \quad p_{12}x_1 + p_{22}x_2 + p_{23}x_3 \geq 0, \quad p_{13}x_1 + p_{23}x_2 + p_{33}x_3 \geq 0, \]

\[ B_1(x_1) - D_1(x_1, x_2) - h_1(x_1, x_3) \leq 0, \quad B_2(x_2) - D_2(x_2) - h_2(x_1, x_2) \leq 0, \]

\[ B_3(x_1, x_3) - D_3(x_3) - h_3(x_1, x_3) \leq 0. \quad (6.11) \]

**Remark 6.2.** In view of (6.2), \( p_{kk} > 0 \) when \( (b_{12}^2 - b_{11}b_{22}) < 0, \ D_1 > 0, \ D_3 > 0 \) or \( (b_{12}^2 - b_{11}b_{22}) > 0, \ D_1 < 0, \ D_3 < 0 \). Moreover, by using (6.9) we can derived the conditions on \( b_{ij} \) so that the assumptions of type (6.4) are hold.

Here, \( c_{ij} \) are real numbers defined by (4.10). Let

\[ d = (c_{11} + c_{33})(c_{22} + c_{33}) - c_{12}c_{21}, \]

\[ D = c_{11}c_{22}(c_{11} + c_{22}) - c_{11}c_{12}c_{21} - c_{11}c_{22}c_{12}. \]

**Theorem 6.3.** Assume the assumptions (1)-(5) of the Condition 3.1 are satisfied. Suppose \( c_{ii} < 0 \) for \( i = 1, 2, 3 \), \( d \neq 0 \) and \( D \neq 0 \). Then the system (1.1) is asymptotically stable at the equilibria point \( E_2(x_1, 0, 0) \) in the Lyapunov sense.

**Proof.** Let \( A_3 \) be the linearized matrix with respect to equilibria point \( E_3(0, x_2, 0) \), i.e.

\[ A_3 = \begin{bmatrix} c_{11} & c_{12} & 0 \\ c_{12} & c_{22} & 0 \\ c_{31} & 0 & c_{33} \end{bmatrix}, \quad A_3^T = \begin{bmatrix} c_{11} & c_{12} & c_{31} \\ c_{12} & c_{22} & 0 \\ 0 & 0 & c_{33} \end{bmatrix}. \]

We consider the Lyapunov equation

\[ P_3A_3 + A_3^TP_3 = -I, \quad P_3 = \begin{bmatrix} p_{11} & p_{12} & p_{13} \\ p_{21} & p_{22} & p_{23} \\ p_{31} & p_{32} & p_{33} \end{bmatrix}, \quad p_{ij} = p_{ji}. \quad (6.12) \]

By solving (6.12) as in the Theorem 6.2 we obtain

\[ p_{33} = -\frac{1}{2c_{33}}, \quad p_{13} = \frac{d_1}{d}, \quad p_{23} = \frac{d_2}{d}, \quad p_{11} = \frac{D_1}{D}, \quad p_{12} = \frac{D_2}{D}, \quad p_{22} = \frac{D_3}{D}, \]

where

\[ d_1 = -\frac{c_{21}c_{31}}{2c_{33}}, \quad d_2 = \frac{c_{31}}{2c_{33}}(c_{11} + c_{33}), \quad (6.13) \]

\[ D_1 = -\frac{1}{2}c_{21}^2 + c_{22}(c_{11} + c_{22}) \left( \frac{1}{2} + c_{31}p_{13} \right) + \left( \frac{1}{2} + c_{31}p_{13} \right)c_{12}c_{21} + c_{21}c_{22}c_{31}p_{23}, \]
$D_2 = \frac{1}{2} c_{11}c_{21} + c_{12}c_{22} \left( \frac{1}{2} + c_{31}p_{13} \right) - c_{11}c_{22}c_{31}p_{23}$.

$D_3 = c_{11}c_{12}c_{31}p_{23} + \frac{1}{2} c_{12}c_{21} - \frac{1}{2} c_{11} (c_{11} + c_{22}) - c_{12}^2 \left( \frac{1}{2} + c_{31}p_{13} \right).$

Hence, the eigenvalues of $A_3$ are positive if the quadratic function

$$V_3 (x) = X^T P_2 X = p_{11}x_1^2 + p_{22}x_2^2 + p_{33}x_3^2 + 2p_{12}x_1x_2 + 2p_{13}x_1x_3 + 2p_{23}x_2x_3$$

is positive defined. In a similar way we obtain that $V_3 (x)$ is positive defined, when $\frac{D_1}{D_3} > 0$, $\frac{D_2}{D_3} > 0$ and the conditions of type (6.4) are hold.

By reasoning as in the proof of Theorem 6.1 we obtain that the inequality

$$\dot{V}_3 (x) = \sum_{k=1}^{3} \frac{\partial V_3}{\partial x_k} dx_k dt \leq 0$$

is valid if the following are hold

$$p_{11}x_1 + p_{12}x_2 + p_{13}x_3 \geq 0, \quad p_{12}x_1 + p_{22}x_2 + p_{23}x_3 \geq 0, \quad p_{13}x_1 + p_{23}x_2 + p_{33}x_3 \geq 0,$$

$$B_1 (x_1) - D_1 (x_1, x_2) - h_1 (x_1, x_3) \leq 0, \quad B_2 (x_2) - D_2 (x_2) - h_2 (x_1, x_2) \leq 0,$$

$$B_3 (x_1, x_3) - D_3 (x_3) - h_3 (x_1, x_3) \leq 0. \quad (6.14)$$

**Remark 6.3.** By (6.13), $p_{kk} > 0$ when $(c_{11}^2 - c_{11}c_{22}) < 0$, $D_1 > 0$, $D_3 > 0$ or $(c_{12}^2 - c_{11}c_{22}) > 0$, $D_1 < 0$, $D_3 < 0$. Moreover, by using (6.13) we can derived the conditions on $c_{ij}$ that the assumptions of type (6.4) are hold.

Consider the stable point $E_4 (\bar{x}_1, 0, \bar{x}_3)$. Here, $d_{ij}$ are real numbers defined by (4.11). Let

$$d = (d_{11} + d_{33}) (d_{22} + d_{33}) - d_{12}d_{21},$$

$$D = d_{11}d_{22} (d_{11} + d_{22}) - d_{11}d_{12}d_{21} - d_{11}d_{22}d_{12}.$$  

**Theorem 6.4.** Assume the assumptions (1)-(5) of the Condition 3.1 are satisfied. Suppose $d_{ii} < 0$ for $i = 1, 2, 3, d \neq 0$ and $D \neq 0$. Then the system (1.1) is asymptotically stable at the equilibria point $E_4 (\bar{x}_1, 0, \bar{x}_3)$ in the Lyapunov sense.

**Proof.** Let $A_4$ be the linearized matrix with respect to equilibria point $E_4 (\bar{x}_1, 0, \bar{x}_3)$, i.e.

$$A_4 = \begin{bmatrix} d_{11} & d_{12} & d_{13} \\ d_{21} & d_{22} & 0 \\ d_{31} & 0 & d_{33} \end{bmatrix}, \quad A_4^T = \begin{bmatrix} d_{11} & d_{12} & d_{13} \\ d_{21} & d_{22} & 0 \\ d_{31} & 0 & d_{33} \end{bmatrix}.$$
We consider the Lyapunov equation
\[ P_A + A_T P = -I, \quad P_4 = \begin{bmatrix} p_{11} & p_{12} & p_{13} \\ p_{21} & p_{22} & p_{23} \\ p_{31} & p_{32} & p_{33} \end{bmatrix}, \quad p_{ij} = p_{ji}. \] (6.15)

It is clear that
\[ P_4 A_4 = \begin{bmatrix} d_{11} p_{11} + d_{21} p_{21} + d_{31} p_{31} & d_{12} p_{12} + d_{22} p_{22} + d_{32} p_{32} & d_{13} p_{13} + d_{33} p_{33} \\ d_{11} p_{21} + d_{21} p_{22} + d_{31} p_{32} + d_{33} p_{33} & d_{12} p_{12} + d_{22} p_{22} + d_{32} p_{32} + d_{33} p_{33} & d_{13} p_{13} + d_{33} p_{33} \\ d_{11} p_{31} + d_{21} p_{32} + d_{31} p_{33} & d_{12} p_{12} + d_{22} p_{22} + d_{32} p_{32} + d_{33} p_{33} & d_{13} p_{13} + d_{33} p_{33} \end{bmatrix}, \]

\[ A_4^T P_4 = \begin{bmatrix} d_{11} p_{11} + d_{21} p_{21} + d_{31} p_{31} & d_{12} p_{12} + d_{22} p_{22} + d_{32} p_{32} & d_{13} p_{13} + d_{33} p_{33} \\ d_{12} p_{11} + d_{22} p_{21} & d_{12} p_{12} + d_{22} p_{22} & d_{12} p_{13} + d_{22} p_{23} \\ d_{13} p_{11} + d_{33} p_{31} & d_{13} p_{12} + d_{33} p_{32} & d_{13} p_{13} + d_{33} p_{33} \end{bmatrix}, \]

\[ P_A^4 + A_4^T P_4 = \begin{bmatrix} d_{11} p_{11} + d_{21} p_{21} + d_{31} p_{31} & d_{12} p_{12} + d_{22} p_{22} + d_{32} p_{32} & d_{13} p_{13} + d_{33} p_{33} \\ d_{11} p_{21} + d_{21} p_{22} + d_{31} p_{33} & d_{12} p_{12} + d_{22} p_{22} + d_{32} p_{33} & d_{13} p_{13} + d_{33} p_{33} \\ d_{11} p_{31} + d_{21} p_{32} + d_{31} p_{33} & d_{12} p_{12} + d_{22} p_{22} + d_{32} p_{33} & d_{13} p_{13} + d_{33} p_{33} \end{bmatrix}. \]

From (6.15) we obtain the following system of the equations in \( p_{ij} \):

\[
2 (d_{11} p_{11} + d_{21} p_{21} + d_{31} p_{31}) = -1, \quad d_{21} p_{11} + (d_{22} + d_{11}) p_{12} + d_{21} p_{22} + d_{31} p_{32} = 0, \\
d_{13} p_{11} + (d_{33} + d_{11}) p_{13} + d_{21} p_{23} + d_{31} p_{33} = 0, \quad 2 (d_{12} p_{12} + d_{22} p_{22}) = -1, \\
d_{12} p_{13} + (d_{33} + d_{22}) p_{23} + d_{13} p_{12} = 0, \quad 2 (d_{13} p_{13} + d_{33} p_{33}) = -1.
\]

By taking
\[ p_{22} = -\frac{1}{d_{22}} \left( \frac{1}{2} + d_{12} p_{12} \right), \quad p_{33} = -\frac{1}{d_{33}} \left( \frac{1}{2} + d_{13} p_{13} \right) \]
in the other equations we get
\[ 2 (d_{11} p_{11} + d_{21} p_{21} + d_{31} p_{31}) = -1, \]
\[
d_{21} p_{11} + \left( d_{22} + d_{11} - \frac{d_{12} d_{21}}{d_{22}} \right) p_{12} + d_{31} p_{23} = \frac{d_{12}}{2 d_{22}}, \] (6.16)
\[
d_{13} p_{11} + \left( d_{33} + d_{11} - \frac{d_{13} d_{31}}{d_{33}} \right) p_{13} + d_{21} p_{23} = \frac{d_{13}}{2 d_{33}} \]
\[ d_{12} p_{13} + (d_{33} + d_{22}) p_{23} + d_{13} p_{12} = 0. \]

By solving the system (6.16) we get
\[ p_{11} = \frac{D_1}{D}, \quad p_{12} = \frac{D_2}{D}, \quad p_{13} = \frac{D_3}{D}, \quad p_{23} = \frac{D_4}{D}. \]
where

\[ D = \begin{vmatrix} 2d_{11} & 2d_{21} & 2d_{31} & 0 \\ d_{21} & d_0 & 0 & d_{31} \\ 0 & d_{12} & d_{22} + d_{33} \\ 0 & d_{13} & d_{12} & d_{22} + d_{33} \end{vmatrix}, \]

\[ D_1 = \begin{vmatrix} -1 & 2d_{21} & 2d_{31} & 0 \\ \frac{d_{12}}{2d_{22}} & d_0 & 0 & d_{31} \\ \frac{d_{13}}{d_{22}} & d_{12} & d_{22} + d_{33} & 0 \\ 0 & d_{13} & d_{12} & d_{22} + d_{33} \end{vmatrix}, \quad D_2 = \begin{vmatrix} 2d_{11} & -1 & 2d_{31} & 0 \\ d_{21} & \frac{d_{12}}{2d_{22}} & 0 & d_{31} \\ 0 & \frac{d_{13}}{d_{22}} & d_{12} & d_{22} + d_{33} \\ 0 & 0 & d_{12} & d_{22} + d_{33} \end{vmatrix} \]

\[ D_3 = \begin{vmatrix} 2d_{11} & 2d_{21} & -1 & 0 \\ \frac{d_{12}}{2d_{22}} & d_0 & \frac{d_{13}}{d_{22}} & d_{31} \\ 0 & d_{13} & \frac{d_{12}}{2d_{22}} & d_{22} + d_{33} \\ 0 & d_{13} & 0 & d_{22} + d_{33} \end{vmatrix}, \quad D_4 = \begin{vmatrix} 2d_{11} & 2d_{21} & 2d_{31} & -1 \\ \frac{d_{12}}{2d_{22}} & d_0 & \frac{d_{13}}{d_{22}} & d_{31} \\ 0 & \frac{d_{13}}{d_{22}} & d_{12} & \frac{d_{12}}{2d_{22}} \\ 0 & 0 & d_{13} & d_{22} + d_{33} \end{vmatrix}. \]

Here,

\[ d_0 = d_{22} + d_{11} - \frac{d_{12}d_{21}}{d_{22}}, \quad b_0 = d_{33} + d_{11} - \frac{d_{13}d_{31}}{d_{33}}, \quad (6.17) \]

\[ p_{22} = -\frac{1}{d_{22}} \left( \frac{1}{2} + d_{12}p_{12} \right) = -\frac{1}{d_{22}} \left( \frac{1}{2} + d_{12} \frac{D_2}{D} \right), \quad p_{33} = -\frac{1}{d_{33}} \left( \frac{1}{2} + d_{13} \frac{D_3}{D} \right). \]

Thus, the eigenvalues of \( A_4 \) are positive if the quadratic function

\[ V_4 (x) = \mathbf{x}^T P_2 \mathbf{x} = p_{11}x_1^2 + p_{22}x_2^2 + p_{33}x_3^2 + 2p_{12}x_1x_2 + 2p_{13}x_1x_3 + 2p_{23}x_2x_3 \]

is positive defined. In a similar way we obtain that \( V_4 (x) \) is positive defined, when the conditions of type (6.4) are hold.

By reasoning as in the proof of Theorem 6.1 we obtain that the inequality

\[ \dot{V}_4 (x) = \sum_{k=1}^3 \frac{\partial V_4}{\partial x_k} dx_k dt \leq 0 \]

is valid if the following are satisfied

\[ p_{11}x_1 + p_{12}x_2 + p_{13}x_3 \geq 0, \quad p_{12}x_1 + p_{22}x_2 + p_{23}x_3 \geq 0, \quad p_{13}x_1 + p_{23}x_2 + p_{33}x_3 \geq 0, \]

\[ B_1 (x_1) - D_1 (x_1, x_2) - h_1 (x_1, x_3) \leq 0, \quad B_2 (x_2) - D_2 (x_2) - h_2 (x_1, x_2) \leq 0, \]

\[ B_3 (x_1, x_3) - D_3 (x_3) - h_3 (x_1, x_3) \leq 0. \quad (6.18) \]

**Remark 6.4.** By (6.17), \( p_{kk} > 0 \) when \( \frac{\partial p_{kk}}{\partial D} > 0 \), \(-\frac{1}{d_{22}} \left( \frac{1}{2} + d_{12} \frac{D_2}{D} \right) > 0,\)

\(-\frac{1}{d_{33}} \left( \frac{1}{2} + d_{13} \frac{D_3}{D} \right) > 0.\) Moreover, by using (6.17) we can derived the conditions on \( d_{ij} \) that the assumptions of type (6.4) are hold.

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Here, $k_{ij}$ are real numbers defined by (4.12). Let

$$d = (k_{11} + k_{33})(k_{22} + k_{33}) - k_{12}k_{21},$$

$$D = k_{11}k_{22}(k_{11} + k_{22}) - k_{11}k_{12}k_{21} - k_{11}k_{22}k_{12}.$$

**Theorem 6.5.** Assume the assumptions (1)-(5) of the Condition 3.1 are satisfied. Suppose $k_{ii} < 0$ for $i = 1, 2, 3$, $d \neq 0$ and $D \neq 0$. Then the system (1.1) is asymptotically stable at the equilibria point $E_5(\bar{x}_1, \bar{x}_2, 0)$ in the Lyapunov sense.

**Proof.** Let $A_5$ be the linearized matrix with respect to equilibria point $E_5(\bar{x}_1, \bar{x}_2, 0)$, i.e.

$$A_5 = \begin{bmatrix} k_{11} & k_{12} & 0 \\ k_{21} & k_{22} & 0 \\ k_{31} & 0 & k_{33} \end{bmatrix}, \quad A_5^T = \begin{bmatrix} k_{11} & k_{12} & k_{31} \\ k_{12} & k_{22} & 0 \\ 0 & 0 & k_{33} \end{bmatrix}.$$  

We consider the Lyapunov equation

$$P_5A_5 + A_5^TP_5 = -I, \quad P_5 = \begin{bmatrix} p_{11} & p_{12} & p_{13} \\ p_{21} & p_{22} & p_{23} \\ p_{31} & p_{32} & p_{33} \end{bmatrix}, \quad p_{ij} = p_{ji}. \quad (6.19)$$

By solving (6.19), in a similar way as in the Theorem 6.2 we obtain

$$p_{33} = -\frac{1}{2k_{33}}, \quad p_{13} = \frac{d_1}{d}, \quad p_{23} = \frac{d_2}{d}, \quad p_{11} = \frac{D_1}{D}, \quad p_{12} = \frac{D_2}{D}, \quad p_{22} = \frac{D_3}{D},$$

where

$$d_1 = \frac{k_{21}k_{31}}{2k_{33}}, \quad d_2 = \frac{k_{31}}{2k_{33}}(k_{11} + k_{33}), \quad (6.20)$$

$$D_1 = -\frac{1}{2}k_{21}^2 + k_{22}(k_{11} + k_{22})\left(\frac{1}{2} + k_{31}p_{13}\right) +$$

$$\left(\frac{1}{2} + k_{31}p_{13}\right)k_{12}k_{21} + k_{21}k_{22}k_{31}p_{23},$$

$$D_2 = \frac{1}{2}k_{11}k_{21} + k_{12}k_{22}\left(\frac{1}{2} + k_{31}p_{13}\right) - k_{11}k_{22}k_{31}p_{23},$$

$$D_3 = k_{11}k_{12}k_{31}p_{23} + \frac{1}{2}k_{12}k_{21} - \frac{1}{2}k_{11}(k_{11} + k_{22}) - k_{12}\left(\frac{1}{2} + k_{31}p_{13}\right).$$

Hence, the eigenvalues of $A_5$ are positive if the quadratic function

$$V_5(x) = X^TP_2X = p_{11}x_1^2 + p_{22}x_2^2 + p_{33}x_3^2 + 2p_{12}x_1x_2 +$$

$$2p_{13}x_1x_3 + 2p_{23}x_2x_3$$

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is positive defined. In a similar way we obtain that \( V_5(x) \) is positive defined, when \( \frac{D_1}{D} > 0, \frac{D_2}{D} > 0 \) and the conditions of type (6.4) are satisfied. By reasoning as in the proof of Theorem 6.1 we obtain that the inequality

\[
\dot{V}_5(x) = \sum_{k=1}^{3} \frac{\partial V_5}{\partial x_k} \frac{dx_k}{dt} \leq 0
\]

is valid if the following holds

\[
p_{11}x_1 + p_{12}x_2 + p_{13}x_3 \geq 0, \quad p_{12}x_1 + p_{22}x_2 + p_{23}x_3 \geq 0, \quad p_{13}x_1 + p_{23}x_2 + p_{33}x_3 \geq 0,
\]

\[
B_1(x_1) - D_1(x_1, x_2) - h_1(x_1, x_3) \leq 0, \quad B_2(x_2) - D_2(x_2) - h_2(x_1, x_2) \leq 0,
\]

\[
B_3(x_1, x_3) - D_3(x_3) - h_3(x_1, x_3) \leq 0. \quad (6.21)
\]

**Remark 6.5.** In view of (6.17), \( p_{kk} > 0 \) when \( (k_1^2 - k_{11}, k_{22}) < 0, \ D_1 > 0, \ D_3 > 0 \) or \( (k_1^2 - k_{11}, k_{22}) > 0, \ D_1 < 0, \ D_3 < 0 \). Moreover, by using (6.20) we can derived the conditions on \( k_{ij} \) that the assumptions of type (6.4) are hold.

Here, \( l_{ij} \) are real numbers defined by (4.13). Let

\[
d = (l_{11} + l_{33})(l_{22} + l_{33}) - l_{12}l_{21},
\]

\[
D = l_{11}l_{22}(l_{11} + l_{22}) - l_{11}l_{22}l_{21} - l_{11}l_{22}l_{21}.
\]

**Theorem 6.6.** Assume the assumptions (1)-(5) of the Condition 3.1 are satisfied. Suppose \( l_{ii} < 0 \) for \( i = 1, 2, 3, d \neq 0 \) and \( D \neq 0 \). Then the system (1.1) is asymptotically stable at the equilibria point \( E_6(0, \bar{x}_2, \bar{x}_3) \) in the Lyapunov sense.

**Proof.** Let \( A_6 \) be the linearized matrix with respect to equilibria point \( E_6(0, \bar{x}_2, \bar{x}_3) \), i.e.

\[
A_6 = \begin{bmatrix}
l_{11} & l_{12} & 0 \\
l_{21} & l_{22} & 0 \\
l_{31} & 0 & l_{33}
\end{bmatrix}, \quad A_6^T = \begin{bmatrix}
l_{11} & l_{21} & l_{31} \\
l_{12} & l_{22} & 0 \\
0 & 0 & l_{33}
\end{bmatrix}.
\]

We consider the Lyapunov equation

\[
P_5 A_5 + A_6^T P_5 = -I, \quad P_5 = \begin{bmatrix}
p_{11} & p_{12} & p_{13} \\
p_{21} & p_{22} & p_{23} \\
p_{31} & p_{32} & p_{33}
\end{bmatrix}, \quad p_{ij} = p_{ji}.
\]  \quad (6.22)

By solving (6.22), in a similar way as in the Theorem 6.2 we obtain

\[
p_{33} = -\frac{1}{2d_{33}}, \quad p_{13} = \frac{d_1}{d}, \quad p_{23} = \frac{d_2}{d}, \quad p_{11} = \frac{D_1}{D}, \quad p_{12} = \frac{D_2}{D}, \quad p_{22} = \frac{D_3}{D},
\]

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where
\[ d_1 = -\frac{l_{21}l_{31}}{2l_{33}}, \quad d_2 = \frac{l_{31}}{2l_{33}}(l_{11} + l_{33}), \]  
(6.23)
\[ D_1 = -\frac{1}{2}l_{21}^2 + l_{22}(l_{11} + l_{22})\left(\frac{1}{2} + l_{31}p_{13}\right) + \]  
\[ \left(\frac{1}{2} + l_{31}p_{13}\right)l_{12l_{21}} + l_{21l_{31}}l_{33}, \]  
\[ D_2 = \frac{1}{2}l_{11}l_{21} + l_{12l_{22}}\left(\frac{1}{2} + l_{31}p_{13}\right) - l_{11l_{22}}l_{31}, \]  
\[ D_3 = l_{11l_{12l_{31}}}l_{23} + \frac{1}{2}l_{12l_{21}} - \frac{1}{2}l_{11}(l_{11} + l_{22}) - k_{12}^2\left(\frac{1}{2} + l_{31}p_{13}\right). \]  

Hence, the eigenvalues of \( A_6 \) are positive if the quadratic function
\[ V_5(x) = X^TP_2X = p_{11}x_1^2 + p_{22}x_2^2 + p_{33}x_3^2 + 2p_{12}x_1x_2 + 2p_{13}x_1x_3 + 2p_{23}x_2x_3 \]
is positive defined. In a similar way we obtain that \( V_6(x) \) is positive defined, when \( \frac{D_k}{p_{kk}} > 0, k = 1, 3 \) and the assumptions of type (6.23) are hold.

By reasoning as in the proof of Theorem 6.1 we obtain that the inequality
\[ \dot{V}_6(x) = \sum_{k=1}^{3} \frac{\partial V_6}{\partial x_k} \frac{dx_k}{dt} \leq 0 \]
is valid if the following holds
\[ p_{11}x_1 + p_{12}x_2 + p_{13}x_3 \geq 0, \quad p_{12}x_1 + p_{22}x_2 + p_{23}x_3 \geq 0, \quad p_{13}x_1 + p_{23}x_2 + p_{33}x_3 \geq 0, \]
\[ B_1(x_1) - D_1(x_1, x_2) - h_1(x_1, x_3) \leq 0, \quad B_2(x_2) - D_2(x_2) - h_2(x_1, x_2) \leq 0, \]
\[ B_3(x_1, x_3) - D_3(x_3) - h_3(x_1, x_3) \leq 0. \]  
(6.24)

**Remark 6.6.** By assumption \( p_{33} > 0 \) and by (6.23), \( p_{kk} > 0 \) when \( \frac{D_k}{p_{kk}} > 0, \) \( k = 1, 3. \) Moreover, by using (6.23) we can deduced the conditions on \( l_{ij} \) that the assumptions of type (6.24) are hold.

7. Basins of multiphase attractions

In this section we will derived the domains of multipoint attraction sets of the problem (1.3) – (1.4) at the the following attractor points (4.2), where \( a_{\pm}, b_{\pm}, x_1, \bar{x}, x_{1i}, x_{2j}, x_{3ij} \) were defined by (4.16) and (4.24).

Lyapunov’s method can be used to find the region of attraction or an estimate of it. We show in this section the following results:
Theorem 7.1. Assume that the all conditions of Theorem 6.1 are satisfied. Then the basin of multiphase attraction set of (1.3) – (1.4) at \( \vec{x} = (1, 0, 0) \) belongs to the set \( \Omega C \subset \Omega_1 \), where \( \Omega_1 \) was defined by (4.8) and
\[
\Omega C = \{ x \in \mathbb{R}^3_+ : V_1 (x) \leq C \},
\]
here a positive constant \( C \) is defined in bellow.

Proof. We are interested in the largest set \( \Omega C \) that we can determine the largest value for the constant \( C \) such that \( \Omega C \subset D (V_1) \), where
\[
D (V_1) = \left\{ x \in \mathbb{R}^3, V_1 (x) \geq 0, V_1 (x) < 0 \right\}.
\]

Let us now find the set \( \Omega C \subset B_r (\vec{x}) \), where
\[
C < \min_{|x-x|=r} V_1 (x) = \lambda_{\min} (P_1) r^2,
\]
here \( P_1 \) was defined by (4.1), \( \lambda_{\min} (P_1) \) denotes a minimum eigenvalue of the corresponding matrix \( A_1 \).

Moreover, for some \( C > 0 \) the inclusion \( \Omega C \subset \Omega_1 \) means the existence of \( C > 0 \) such that \( x \in \Omega C \) implies \( x \in \Omega_1 \), where
\[
\Omega_1 = \left\{ x \in \mathbb{R}^3_+, x_j = x_{j0} + \sum_{k=1}^{m} \alpha_{jk} x_j (t_k) \geq 0, j = 1, 2, 3, x_2 \geq \eta_2, \right\}
\]
p_{11} x_1 + p_{12} x_2 + p_{13} x_3 \geq 0, p_{12} x_1 + p_{22} x_2 + p_{23} x_3 \geq 0, p_{13} x_1 + p_{23} x_2 + p_{33} x_3 \geq 0,
P_1 (x_1) - D_1 (x_1, x_2) - h_1 (x_1, x_3) \leq 0, P_2 (x_2) - D_2 (x_2) - h_2 (x_1, x_2) \leq 0,
P_3 (x_1, x_3) - D_3 (x_3) - h_3 (x_1, x_3) \leq 0.
\]

where \( \Omega_1 (t_0) \) was defined by (1.3), \( p_{ij} \), \( a_{ij} \) were defined by (6.2) and (4.8), respectively, i.e.
\[
p_{33} = -\frac{1}{2a_{33}}, p_{13} = \frac{a_{31}}{2(a_{11} + a_{33}) a_{33}}, p_{11} = -\frac{1}{a_{11}} \left( \frac{1}{2} + a_{31} p_{13} \right),
\]
\[
p_{23} = -\frac{a_{12} p_{13}}{a_{22} + a_{33}}, p_{12} = -\frac{(a_{12} p_{11} + a_{31} p_{23})}{(a_{11} + a_{22})}, p_{22} = -\frac{(\frac{1}{2} + a_{12} p_{12})}{a_{22}}.
\]
\[
a_{11} = \frac{\partial}{\partial x_1} [B_1 - D_1] (0) - \frac{\partial h_1}{\partial x_1} (0), a_{12} = -\frac{\partial D_1}{\partial x_1} (0),
\]
\[
a_{22} = \frac{d}{dx_2} [B_2 - D_2] (0), a_{31} = \frac{\partial B_3}{\partial x_1} (0) - \frac{\partial h_1}{\partial x_1} (0),
\]
\[
a_{33} = \frac{d}{dx_3} [B_3 - D_3] (0).
\]

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Remark 7.1. By assumptions of theorem $p_{ii} > 0$. By Remark 6.1 if $a_{31} > 0$, then $p_{13} > 0$; moreover, $p_{23} > 0$, $p_{12} > 0$ when $a_{31} > 0$ and $a_{12} > 0$. Then (7.1) holds if

$$B_1 (x_1) - D_1 (x_1, x_2) - h_1 (x_1, x_3) \leq 0, \ B_2 (x_2) - D_2 (x_2) - h_2 (x_1, x_2) \leq 0,$$

$$B_3 (x_1, x_3) - D_3 (x_3) - h_3 (x_1, x_3) \leq 0 \right\} \quad (7.2)$$

In view of (4.8), $a_{31} > 0$, $a_{12} > 0$, when $\frac{\partial B}{\partial x_1}(0) > \frac{\partial h_1}{\partial x_1} (0)$ and $\frac{\partial D_1}{\partial x_1} (0) < 0$.

Hence,

$$\Omega_{10} = \left\{ x \in \mathbb{R}^3_+, \ b_{11} (x_1 - 1)^2 + (b_{22} + b_{12}) x_2^2 + x_3^2 \leq 0 \right\}$$

$$b_{11} + (\beta_1 + \beta_2 \eta_2)^2, \ x_1 \geq 1 \right\} \subset \Omega_1.$$

So, it is not hard to see that

$$B_\bar{r} = \left\{ x \in \mathbb{R}^3, \ |x - \bar{x}| < \bar{r} \right\} \subset \Omega_1,$$

where

$$\bar{r} = \eta_0 \left[ b_{11} + (\beta_1 + \beta_2 \eta_2)^2 \right]^{\frac{1}{2}}, \ \eta_0 = \max \{ b_{11}, b_{22} + b_{12}, 1 \}.$$  

Then we obtain

$$C < \min_{|x|=r_1} V_1 (x) = \lambda_{\min} (P_1) \bar{r}^2,$$

i.e.

$$C < \lambda_{\min} (P_1) r_0^2, \ r_0 = \min \{ r, \ \bar{r} \}.$$  

Now, we consider the equilibria point $E_2 (0, 1, 0)$ and prove the following result

**Theorem 5.2.** Assume that the all conditions of Theorem 4.2 and (4.15) are satisfied. Then the basin of multiphase attraction set of (1.3)–(1.4) at $E_2 (0, 1, 0)$ is whole $\mathbb{R}^3_+$.

**Proof.** Indeed, by Theorem 4.2 the system (1.3) is global stabile at $E_2 (0, 1, 0)$. Thus, the basin of multiphase attraction set coincides with $\mathbb{R}^3_+$.

**Theorem 5.3.** Assume that the all conditions of Theorem 4.3 are satisfied. Then the basin of multiphase attraction set of (1.3)–(1.4) at $E_3 (a_\pm, 0, b_\pm)$ belongs to the set $\Omega_C \subset \Omega_3$, where $\Omega_3$ was defined by (4.23), here $V_3 (x)$ was defined by (4.15).

**Proof.** We will find $C > 0$ such that $\Omega_C \subset B_r (E_3) \cap \Omega_3$. It is clear to see that $\Omega_C \subset B_r (E_3)$ for

$$C < \min_{|x - \bar{x}| = r} V_3 (x) = \lambda_{\min} (P_3) r^2, \ \bar{x} = (a_\pm, 0, b_\pm).$$
here $\lambda_{\min}(P_3)$ denotes a minimum eigenvalue of $A_3$. Let $\Omega_3$ is a domain defined by (4.23), i.e.

$$\Omega_3 = \left\{ x \in \mathbb{R}_3^3 : x_j = x_{j0} + \sum_{k=1}^m \alpha_{jk} x_j (t_k) \geq 0, j = 1, 2, 3, \right\}$$

where

$$\alpha_1 x_1 + \alpha_2 x_2 + \alpha_3 x_3 \geq \gamma_0, x_1 \geq \gamma_1, x_2 \leq \gamma_2 x_3, x_3 \leq \gamma_3 x_1,$$

$$(b_{11} + b_{11} a_+ + b_{13} b_+) (x_1 - a_+)^2 + r_2 (b_{12} a_+ + b_{23} b_+ + b_{22}) x_2^2 \leq r_2 (b_{12} a_+ + b_{23} b_+ + b_{22}) x_2^2 + b_{11} x_1^3,$$

and

\begin{align*}
\alpha_1 &= \min \left\{ [b_{11} a_+ + b_{13} b_+] - 2a_+ (b_{11} + b_{11} a_+ + b_{13} b_+) \right\}, \\
\alpha_2 &= \min \left\{ r_2 (b_{12} a_+ + b_{23} b_+) - 2a_+ r_2 (b_{12} a_+ + b_{23} b_+ + b_{22}) \right\}, \\
\alpha_3 &= \min \left\{ b_{13} a_{12} - b_{23} a_{21}, b_{12}, b_{13} \right\}, \\
\gamma_0 &= (b_{11} a_{12} + b_{12} + b_{13} a_{12} b_+ + a_{21} b_{12} a_+ + a_{21} b_{13} b_+), \\
\gamma_1 &= \left( b_{11} a_+ + b_{13} b_+ \right) a_{13} + b_{13}, \\
\gamma_2 &= \frac{a_{13} b_{13} x_3}{-a_{21} b_{23}}, \\
\gamma_3 &= \frac{b_{11} a_{13}}{-b_{23} a_{21}}.
\end{align*}

It is clear that $\alpha_2, \alpha_3 \leq 0$ and $\alpha_1 > 0$. Hence, $\alpha_1 x_1 - \gamma_0 > 0$. Moreover, since

$$\alpha_1 x_1 + \alpha_2 x_2 + \alpha_3 x_3 \geq \gamma_0, x_1 \geq \gamma_1, x_2 \leq \gamma_2 x_3, x_3 \leq \gamma_3 x_1$$

we get

$$0 \leq x_3 \leq \beta_1 \gamma_1 - \beta_2,$$

where

$$\beta_1 = -\frac{\alpha_1}{\alpha_2 \gamma_2 + \alpha_3}, \quad \beta_2 = -\frac{\gamma_0}{\alpha_2 \gamma_2 + \alpha_3}.$$ 

Thus,

$$\Omega_{30} = \left\{ x \in \mathbb{R}_3^3 : x_j = x_{j0} + \sum_{k=1}^m \alpha_{jk} x_j (t_k) \geq 0, j = 1, 2, 3, \right\}$$

from (4.23) it is not hard to see that

$$B_\Omega(x) = \left\{ x \in \mathbb{R}_+^3, |x - \bar{x}| < \bar{r} \right\} \subset \Omega_3$$

for $\bar{x} = (0, a_+, b_+)$, where

$$\bar{r} = \frac{1}{\eta} \left[ r_2 (b_{12} a_+ + b_{23} b_+ + b_{22}) + b_{11} \gamma_1 + (\beta_1 \gamma_1 - \beta_2)^2 \right].$$
\[ \eta = \max \{ (b_{11} + b_{11}a_+ + b_{13}b_+) \cdot r_2 (b_{12}a_+ + b_{23}b_+ + b_{22}), 1 \}. \]

Then we obtain that
\[ C < \min_{|x - \bar{x}| = \bar{r}} V_3 (x) = \lambda_{\min} (P_3) \bar{r}^2, \]
i.e.
\[ C < \lambda_{\min} (P_3) \bar{r}^2 \text{ for } r_0 = \min \{ r, \bar{r} \}. \]

Consider the point \( E_4 (\bar{x}_1, \bar{x}_2, 0) \). By reasoning as the above we prove the following result:

**Theorem 5.4.** Assume that the all conditions of Theorem 4.4 are satisfied. Then the basin of multiphase attraction sets of (1.3) – (1.4) at \( E_4 (\bar{x}_1, \bar{x}_2, 0) \) belongs to the set \( \Omega_4 \), where \( \Omega_4 \) was defined by (4.31).

**Proof.** We will find \( C > 0 \) such that \( \Omega_C \subset B_r (E_4) \subset \Omega_4 \). It is clear to see that \( \Omega_C \subset B_r (\bar{x}) \) for
\[ C < \min_{|x - \bar{x}| = r} V_4 (x) = \lambda_{\min} (P_4) r^2, \quad \bar{x} = (\bar{x}_1, \bar{x}_2, 0), \]
here \( \lambda_{\min} (P_4) \) denotes a minimum eigenvalue of \( A_4 \). From (4.31) we get
\[ \Omega_{40} = \{ x \in \mathbb{R}_+^3 : x_j = x_{j0} + \sum_{k=1}^{m} a_{jk} x_j (t_k) \geq 0, j = 1, 2, 3, \quad (5.4) \]
where
\[ \begin{align*}
\gamma_1 &= \frac{b_{12} - r_2 (b_{12}b_1 + b_{22}b_2)}{b_{12}}, \quad \gamma_2 = \frac{(b_{11}\bar{x}_1 + b_{12}\bar{x}_2)}{a_{13} (b_{11}\bar{x}_1 + b_{12}\bar{x}_2)}, \\
\gamma_3 &= \frac{b_{22} - r_2 (b_{12}b_1 + b_{22}b_2)}{a_{13} (b_{11}\bar{x}_1 + b_{12}\bar{x}_2)}, \quad \alpha_1 = \min \{ b_{11}, b_{13} \}, \quad \alpha_3 = \min \{ b_{13}, b_{23} \}, \\
\alpha_2 &= \min \{ (b_{12} + a_{12}b_{11} + a_{21}b_{22}) \cdot a_{12} (b_{11}\bar{x}_1 + b_{12}\bar{x}_2), a_{12}b_{12} + a_{21}b_{23} \}. \\
\end{align*} \]

From (5.4) It is not hard to see that \( \gamma_1 \leq \frac{\alpha_2 \gamma_2}{b_{12}} \) and
\[ B_r (\bar{x}) = \{ x \in R_+^3, |x - \bar{x}| < \bar{r} \} \subset \Omega_{40} \text{ for } \bar{x} = (\bar{x}_1, \bar{x}_2, 0), \]
where
\[ \bar{r}^2 = \frac{1}{\eta} \left[ (b_{11}\bar{x}_1 + b_{12}\bar{x}_2) \bar{x}_1^2 + r_2 (b_{12}\bar{x}_1 + b_{22}\bar{x}_2) \bar{x}_2^2 + b_{22}r_2 \gamma_2^3 + d^2 \right], \]

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Then we obtain that
\[ i.e. \quad C < \min_{|x-\bar{x}|=\bar{r}} V_4(x) = \lambda_{\min}(P_4) \bar{r}^2, \]
i.e.
\[ C < \lambda_{\min}(P_4) \bar{r}^2 \text{ for } r_0 = \min \{ r, \bar{r} \}. \]

Consider the points \( E_{ij} \).

**Theorem 5.5.** Assume that all conditions of Theorem 4.5 are satisfied. Then the basin of multiphase attraction sets of (1.3) - (1.4) at points \( E_{ij} \) belong to the \( \Omega_{ij} \), where \( \Omega_{ij} \) was defined by (4.38).

**Proof.** We will find \( C > 0 \) such that \( \Omega_C \subset B_r(E_{ij}) \subset \Omega_{ij} \). It is clear to see that \( \Omega_C \subset B_r(\bar{x}) \) for
\[ C < \min_{|x-\bar{x}|=r} V_5(x) = \lambda_{\min}(P_5) r^2, \]
here \( \lambda_{\min}(P_5) \) denotes a minimum eigenvalue of \( A_5 \). Assume \( a_{13} > 1 \). Then from (4.38) it is not hard to see that

\[ B_r(E_{ij}) \subset \Omega_{ij0} = \left\{ x \in \mathbb{R}^3_+: x_j = x_{j0} + \sum_{k=1}^{m} a_{jk} x_j(t_k) \geq 0, j = 1, 2, 3, \right\} \]
\[ \text{ (5.5) } \]
\[ x_1 \leq \gamma_1, \quad x_2 \geq 1, \quad x_3 \leq \frac{1}{a_{13}}, \]
\[ \left[ Q_1(x_1-x_{1i})^2 + Q_2(x_2-x_{2j})^2 + (x_3-x_{3ij})^2 \leq Q_1x_{1i}^2 + Q_1x_{2j}^2 \right. \]
\[ + \left. \left( \frac{1}{a_{13}} - x_{3ij} \right)^2 + p_{22}r_2 + d^2, \quad \gamma_3 \leq \alpha_1 x_1 + \alpha_2 x_2 \right\}, \]
where
\[ \alpha_1 = \min \{ p_{11}, \ p_{23}a_{21} + p_{13}a_{13}, \ p_{12}a_{21} + p_{13} \}, \]
\[ \alpha_2 = \min \{ p_{11}a_{12} + p_{12}, \ p_{12}a_{13}, \ p_{12} (a_{12} + r_2) + p_{22}a_{21} + p_{23} \}, \]
\[ \alpha_3 = \min \{ p_{11}a_{13}, \ p_{13}a_{13}, \ p_{13}a_{12}, p_{33} \}, \quad d = \frac{-p_{12}}{a_3} (1 + \gamma_1), \]
\[ a = \max \{ a_{21}, \ a_{12}r_2 \}, \]
\[ \gamma_1 = \frac{r_2}{(a_{13} + 2x_{1i})Q_1 + (a_{21} + r_2 + 2x_{2j})Q_2}. \]
\[ (\bar{r})^2 = \frac{1}{\eta} \left[ Q_1x_{1i}^2 + Q_1x_{2j}^2 + \left( \frac{1}{a_{13}} - x_{3ij} \right)^2 + p_{22}r_2 + d^2 \right] \]
\[ \eta = \max \{ Q_1, \ Q_2, \ 1 \}. \]
Then we obtain that

\[ C < \min_{\|x-x_0\|=\bar{r}} V_5(x) = \lambda_{\min}(P_5)^2, \]

i.e.

\[ C < \lambda_{\min}(P_5)^2 \text{ for } r_0 = \min\{r, \bar{r}\}. \]

**Conclusion.** Taking into account different and effective features of mathematical modelling and its possibilities to figure out a problem in dynamics on the basis of its logic properties, it was surely pointed out the characteristics of a mathematical model to use in description of needed processes of a given dynamic system with identified problems. In this paper, a three dimensional model was devoted to mathematical description and regulation possibilities of uncontrolled tumor processes by organism as a complex system. The dynamics of interactions of the dimensions corresponded to tumor cells, immune cells and healthy – “host” – cells were given as forces of vectors, negatively or positively converging to basins of attractions, depending on their importance for the complex system. In order to make the model subjected to control, there was included multiphase IVP, describing the system’s important parameters to operate with it in the farther processes of stages of development. The model was undergone different changes to determine its limits of survival: it was determined the conditions of boundedness the system can be restricted, invariance in non-negativity, which means the model keeps its properties of reactions to changing in proper way, being subjected to different analysis, and the circumstances the system can be forced to be dissipated in. The system was exposed to changing pressures to estimate its convenience to biologically important properties as points of equilibria and Lyapunov stability conditions. The next step in exploring of the model were very complex and logistic approaches to its properties for verification of the conditions, providing the global equilibria points and multimodal attraction sets, having biologically strong value in regulation of the processes towards the positive effects of feasible medical external implementation at the convenient stages, determined by multimodal attraction basins.

**Biological implications.** Here we study a multiphase host-tumor model that enhances the type of effector immune cells that can fight a tumor, and stimulates effector immune cells to proliferate. Interactions between cancer tumor cells, healthy host cells and the effector immune cells can explain long-term tumor relapse. Here, the sufficient conditions is derived that under which the possible biologically feasible dynamics is stable in the Lyapunov sense, and a converges to one of equilibrium points. Since these equilibrium points have a biological sense, we notice that understanding limit properties of dynamics of cells populations based on solving the problem (1.3) – (1.4) may be of an essential interest for the prediction of health conditions of a patient without a treatment, when the data (e.g. the status of blood cells shown above) that determines the condition of the patient are compared at various times \( t_0, t_1, ..., t_m \) and correlated. In the section 3, we find the positively invariant domain \( B_{a,m} \)
that depend on multipoint IVP condition parameters $\alpha_k$, $t_k$ and $m$. Moreover, the boundedness of orbits of the system (1.3) – (1.4) is derived. As a result, the future evolution of cells populations involved in this model is completely predictable in the following sense: by knowing the specific linear connection between the tumor, guest and immune cells at the $t_0, t_1, \ldots, t_m$ time phase densities, populations has an accurate and predictable estimate of its change. In the section 4, Lyapunov stability of the system (1.3) at the corresponding equilibria points are studied. We show that the system (1.3) is global stable at the “free tumor” equilibria point $E_2(0, 1, 0)$. In the section 5, the basins of multiphase attractors of the system (1.3) – (1.4) (dependent on multipoint parameters of IVP) are constructed.

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