Numerical analysis of three-dimensional leukemia model’s equilibrium points

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Abstract. The results of numerical analysis of a mathematical model for chronic myelogenous leukemia (CML) equilibrium points quantity are presented. Considering a control example, the condition for the system without bistable equilibrium points was reached, so the system is supposed to have only those equilibrium points which are asymptotically stable.

1. Introduction

The study on mathematical model for chronic myelogenous leukemia (CML) equilibrium points quantity, suggested by N. Li and H. Moore in 2003 [1] is undertaken. Similar model was reviewed before [2, 3].

It was found, that with any allowable of the system parameters values, at least one equilibrium point exists. A method for searching of the parameters, with which the considered system is supposed to have three balancing points is suggested. Numerical calculation of balancing points was subsequently performed and system phase portrait was visualized using MatLab software for a control example. The analysis taken out revealed bistable situation of the system: the trajectory asymptotically strives to one of the two stable equilibrium points depending on the initial conditions.

2. Mathematical model

Consider the following mathematical model, given in dimensionless view:

\[
\begin{align*}
\dot{x} &= 1 - x - \frac{\xi_1 x z}{\xi_2 + z} \\
\dot{y} &= \frac{\xi_3 x z}{\xi_2 + z} + \frac{\xi_4 y z}{\xi_3 + z} - \xi_1 y - y z \\
\dot{z} &= (\xi_6 \ln \xi_7 - \xi_9) z - \xi_8 \ln z - y z,
\end{align*}
\]

where: \(x\) – initial number of cells, \(y\) – number of effector cells, \(z\) – number of cancer cells.

All system parameters are positive and are not equal to zero. Every equation describes cell population rate of change. Problem’s domain is \(D = \{x \geq 0, y \geq 0, z \geq 0\}\).

3. Equilibrium points estimation

Consider the equilibrium points for the system (1). One equilibrium point is obvious when \(z = (1, 0, 0)\). However, the not trivial case is more interesting. After transformations got the following non-linear equations in terms of \(z\) variable, represented as the equality of the two functions set \(f_1(z) = f_2(z)\):

\[
\begin{align*}
\frac{\xi_3 x z}{\xi_2 + z} + \frac{\xi_4 y z}{\xi_3 + z} - \xi_1 y - y z &= 0 \\
(\xi_6 \ln \xi_7 - \xi_9) z - \xi_8 \ln z - y z &= 0.
\end{align*}
\]
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$f_1 = \xi_6 \ln \xi_7 - \xi_8 - \xi_6 \ln z.$

$$f_2 = \frac{\xi_5 (\xi_2 + z)}{(z^2 + (\xi_2 + \xi_3) z + \xi_4)(\xi_2 + \xi_5 z + z)}.$$ Qualitative behavior of the function graph $f_1(z)$ is shown in figure 1.

![Figure 1. Qualitative behavior of $f_1(z)$.](image1)

Qualitative behavior of $f_2(z)$ is determined by quadratic trinomial in denominator. Consider cases of qualitative behavior of $f_2(z)$ marking quadratic trinomial discriminant as D:

1. Roots are real, different and positive (the first case) when $D > 0$, $\xi_2 \xi_5 > 0$ (figure 2), where $z_1, z_2$ — quadratic trinomial roots. Concurring positive roots take place when $D = 0$, $\xi_2 \xi_5 > 0$ (figure 2).

![Figure 2. Qualitative behavior of $f_2(z)$ for the first case.](image2a) ![Figure 2. Qualitative behavior of $f_2(z)$ for the first case.](image2b)

2. Roots are negative (the second case) when $D > 0$, $\xi_2 \xi_5 > 0$, $-(\xi_2 + \xi_5 - \xi_4) < 0$ (figure 3). Multiple root takes place for the same conditions, but at $D=0$. Situation with complex roots is implemented when $D < 0$. Qualitative behavior of $f_2(z)$ for the discussed conditions is presented in figure 3.

![Figure 3. Qualitative behavior of $f_2(z)$ for the second case.](image3)
Other cases are not possible because all system parameters are positive, so absolute term in trinomial cannot be equal to zero.

From the visualized functions behavior, it can be revealed that functions $f_1(z)$ and $f_2(z)$ have at least one cross point. It means that there will be always not less than one equilibrium point. Suppose, that the functions can have more than one equilibrium point.

Confronting the plots for $f_1(z)$ and $f_2(z)$ (when the roots of trinomial are different and positive) it can be revealed that the two functions can cross each other in three points, varying the parameter $\xi_8$ of $f_1(z)$. Taking into consideration the biological formulation of the problem, select the certain values of the parameters to make $f_1(z)$ and $f_2(z)$ plots cross each other in three points.

4. Control example

Set the following values of the system parameters:
$$\begin{align*}
\xi_1 &= 0.004, \xi_2 = 0.0228, \xi_3 = 9.5776E-06, \xi_4 = 1,
\xi_5 = 0.5, \xi_6 = 0.12, \xi_7 = 13.68, \xi_8 = 0.12.
\end{align*}$$

After calculations got
$$\begin{align*}
\xi_3 \xi_5 &= 0.0114 > 0,
\xi_2 + \xi_3 - \xi_4 &= -0.4772 < 0,
D &= 0.18212 > 0
\end{align*}$$

and so the roots $z_1 = 0.0252225, z_2 = 0.451978$ are positive and different.

On the next step the cross points for the graphs of $f_1(z)$ and $f_2(z)$ are suitably matched equilibrium points for the system (1) using MatLab software. The equilibrium points are given in table 1.

Table 1. The equilibrium points calculation.

| Point | Value | Type |
|-------|-------|------|
| $P_1$ | (0.99603383, 2.0931368E-06, 0.052503) | Stable knot |
| $P_2$ | (0.99790355, 0.63527278, 0.025221605) | Asymptotically stable |
| $P_3$ | (0.94839882, 0.2892583717, 0.4520125) | Not stable, has stable 2-dimensional manifold, and unstable 1-dimensional one |

Considering the system’s phase portrait, all phase curves can be separated into two parts (figure 4). In the first part (a) all trajectories strive to $P_1$. From the biological point of view, it means that the illness is progressing and the number of cancer cells is increasing. All phase curves in the second part (b) of the dimensional phase curves strive to $P_2$. From the biological point of view, it means that a patient feels better and the number of cancer cells is decreasing.
5. Conclusion
As a result, the condition for the system without bistable equilibrium points was reached, so it can be concluded, that the system is supposed to have only those equilibrium points which are asymptotically stable. From the biological point of view, it means that a patient’s condition aims to stability. The previously obtained results [3] are in accordance with ours.

References
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