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ESTIMATING THE DOMAIN OF ATTRACTION OF HIV-1 SYSTEM BASED ON MOMENT METHOD

CHUNJI LI* AND HAN YAO

Abstract. In this article, we discuss the domain of attraction of HIV-1 system by using the moment theory. First, the asymptotic stabilities of the equilibrium point of the system are given, and then we introduce how to use the moment method to estimate domain of attraction. Finally, one simulation shows the effectiveness of moment method.

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1. Introduction

AIDS is a chronic virus that infects human immune system cells. The HIV-1 virus is the causative agent of AIDS. Once infected with the HIV-1 virus, the virus is brought to the body through the bloodstream, destroying lymphocytes in the body's immune system. The HIV-1 virus enters lymphocytes to self-replicate and destroy lymphocytes. This has caused great harm to human health. Therefore, many scholars have studied and solved a dynamic model problem which designed to meet the actual situation of HIV-1 virus. The works [2] and [7] provide a comprehensive overview of the different approaches used in the modeling of the HIV-1 system interaction dynamics.

In this paper, we use the moment theory to estimate domain of attraction of HIV-1 system on the equilibrium point. This method makes practical problems into application mathematical software to calculate and greatly reduce the computational difficulty, making computing more quickly and accurately, see [1], [5], [6] and [3]. We focus on the dynamic model of HIV-1 provided in the paper [7], it studies the relation between antiviral immune responses, virus load, and virus diversity. The paper is organized as follows: 1. Studied the equilibrium point of HIV-1 system, given the stability conditions for the equilibrium point and the

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corresponding proof. 2. Applied the moments theory, simulated to estimate the domain of attraction of HIV-1 system.

2. The domain of attraction of the system and Lyapunov function

Given the nonlinear polynomial autonomous system

$$\dot{x} = f(x), \tag{1}$$

with $x \in \mathbb{R}^n, f(0) = 0$, the domain of attraction of $x = 0$ is

$$S = \left\{ x^0 \in \mathbb{R}^n \middle| \lim_{t \to +\infty} x\left(t, x^0\right) = 0 \right\},$$

where $x\left(t, x^0\right)$ denotes the solution of (1) corresponding to the initial condition $x(0) = x^0$.

Definition 1. The function $V(x)$ is called a Lyapunov function for system (1), if

(i) $V(x)$ is positive definite, and continuously differentiable real-valued function defined on D, a domain containing the origin.

(ii) $\frac{\mathrm{d}V}{\mathrm{d}t}\Big|_{(1)} = \left(\frac{\partial V}{\partial x}\right)^{\mathrm{T}} f(x)$ is negative semidefinite on D.

Theorem 2. ([3, Theorem 2.3]) *Let $V(x)$ be a Lyapunov function for the system (1) in the domain*

$$\Omega_c = \{x \in \mathbb{R}^n | V(x) \leq c\}, \qquad c > 0.$$

Assume that Ω_c is bounded and $0 \in \Omega_c$. If $\dot{V}(x)$ is negative definite in Ω_c, then $\Omega_c \subset S$.

Let

$$V(x) = x^T P x, \quad P = P^T \in \mathbb{R}^{n \times n}, \quad P \succ 0.$$

Here, $P \succ 0$ means P is a positive definite matrix. The hypersurfaces given by $\dot{V}(x) = 0, x \neq 0$ define the boundary of the region of negative definiteness of $\dot{V}(x)$ in which we seek the guaranteed estimation Ω_c. In the case of quadratic Lyapunov functions such an estimation is the interior of the ellipsoid defined by (2). Our objective is to find the maximum value c^* of c such that $\dot{V}(x)$ is negative definite in Ω_c. This c^* is defined by the following optimization problem

$$\begin{cases} \text{find } c^* = \min V(x) \\ \text{subject to the constraint :} \\ \dot{V}(x) = 0, \qquad x \neq 0. \end{cases} \tag{2}$$

3. The description of the HIV-1 system

The HIV-1 system contains three variables: uninfected cells x, infected cells y, and free virus particles v. The system model is

$$\begin{cases} \dot{x} = s - dx(t) - \beta x(t) v(t), \\ \dot{y} = \beta x(t) v(t) - py(t), \\ \dot{v} = ky(t) - uv(t), \end{cases} \tag{3}$$

where infected cells are produced from uninfected cells and free virus at rate βxv and die at rate py. Free virus is produced from infected cells at rate ky and declines at rate uv. Therefore, the average lifetime of an infected cell is $\frac{1}{p}$ and the average lifetime of a free virus particle is $\frac{1}{u}$; the total number of virus particles produced from one cell is $\frac{k}{p}$. Uninfected cells are produced at a constant rate s, from a pool of precursor cells and die at rate dx. This is the simplest possible host cell dynamics, which leads to a stable equilibrium of host cells in the absence of virus.

System (3) has two equilibrium points:

$$E_1 = \left(\frac{s}{d}, 0, 0\right) \text{ and } E_2 = \left(\frac{pu}{k\beta}, \frac{s}{p} - \frac{du}{k\beta}, \frac{ks}{pu} - \frac{d}{\beta}\right).$$

4. Stability of equilibrium points

Let $R_0 = \frac{ks\beta}{dpu}$ be the basic reproductive ratio of system (3).

Theorem 3. *For system (3), if $R_0 < 1$, then the equilibrium points E_2 is unstable, and E_1 is locally asymptotically stable.*

Proof. Only discuss the stability of the equilibrium point E_1. First, we obtain the Jacobian matrix of system (3)

$$J = \begin{bmatrix} -d - \beta v(t) & 0 & -\beta x(t) \\ \beta v(t) & -p & \beta x(t) \\ 0 & k & -u \end{bmatrix}. \tag{4}$$

For equilibrium point E_1, we have the corresponding characteristic polynomial

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0, \tag{5}$$

where

$$\begin{aligned} a_1 &= d + p + u > 0, \\ a_2 &= d(p + u) + pu(1 - R_0), \\ a_3 &= (1 - R_0)\, dpu > 0. \end{aligned}$$

According to Routh Hurwitz Criterion, for system (3), the equilibrium point is locally asymptotically stable if and only if

$$a_1 > 0, a_3 > 0, a_1a_2 - a_3 > 0. \tag{6}$$

In fact, since $R_0 < 1$,

$$a_1 a_2 - a_3 = (p+u)\left(d\left(p+u+d\right) + pu\left(1 - R_0\right)\right) > 0.$$

Hence the equilibrium point E_1 is locally asymptotically stable. □

Theorem 4. *For system (3), if $R_0 > 1$, then the equilibrium points E_1 is unstable, and E_2 is locally asymptotically stable.*

Proof. Only discuss the stability of the equilibrium point E_2. First, we obtain the Jacobian matrix of system (3)

$$J = \begin{bmatrix} -d - \beta v\left(t\right) & 0 & -\beta x\left(t\right) \\ \beta v\left(t\right) & -p & \beta x\left(t\right) \\ 0 & k & -u \end{bmatrix}. \tag{7}$$

For equilibrium point E_2, we have the corresponding characteristic polynomial

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0, \tag{8}$$

where

$$\begin{aligned} a_1 &= p + u + \frac{k}{p}\frac{s}{u}\beta > 0, \\ a_2 &= ks\beta\left(\frac{1}{p} + \frac{1}{u}\right), \\ a_3 &= \left(R_0 - 1\right) dpu > 0. \end{aligned}$$

According to Routh Hurwitz Criterion, for system (3), the equilibrium point is locally asymptotically stable if and only if

$$a_1 > 0, a_3 > 0, a_1a_2 - a_3 > 0. \tag{9}$$

In fact, since $R_0 > 1$, we have $a_3 > 0$, and

$$a_1a_2 - a_3 = \frac{1}{p^2u^2}\left(k^2s^2\beta^2\left(p+u\right) + kpsu\beta\left(pu + p^2 + u^2\right) + dp^3u^3\right) > 0.$$

Hence the equilibrium point E_2 is locally asymptotically stable. □

5. Estimating the domain of attraction via moment method

5.1. Moment method. In [6] Lasserre considers the following two classical problems

- global optimization

$$P \mapsto p^* := \min_{x\in\mathbb{R}^n} p(x)$$

- constrained optimization

$$P_K \mapsto p_K^* := \min_{x\in K} p(x) \tag{10}$$

where $p(x)$ is m-degree real-valued polynomial, and K is a compact set in $\mathbb{R}^n$ defined by polynomial inequalities

$$K = \{ x \in \mathbb{R}^n |\, g_i(x) \geq 0, i = 1, \ldots, r\}. \tag{11}$$

Let

$$1, x_1, \ldots, x_n, x_1^2, x_1x_2, \ldots, x_1x_n, \ldots, x_1^m, \ldots, x_n^m$$

be a basis for the m-degree real-valued polynomials $p(x)$, and let $s\,(2m)$ be its dimension, where $s\,(m) := \begin{pmatrix} n+m \\ n \end{pmatrix} = \frac{(n+m)!}{n!m!}$. Let

$$p(x) = \sum_{\alpha} p_\alpha x^\alpha, \tag{12}$$

where $\alpha := (\alpha_1, \alpha_2, \ldots, \alpha_n)$, and

$$x^\alpha := x_1^{\alpha_1} x_2^{\alpha_2} \cdots x_n^{\alpha_n}, \quad \sum_{i=1}^{n} \alpha_i \leq m.$$

Given an $s\,(2m)$-vector $y := \{y_\alpha\}$ with first element $y_{0,\ldots,0} = 1$, let $M_m(y)$ be the moment matrix of dimension $s\,(m)$.

For $n = 3, s\,(m) = \frac{(m+1)(m+2)(m+3)}{6}$. In this case the matrix $M_m(y)$ consists of the block matrices defined by

$$M_{i,0,k}(y) = \begin{bmatrix} y_{i+k,0,0} & y_{i+k-1,1,0} & y_{i+k-1,0,1} & \cdots & y_{i,0,k} \\ y_{i+k-1,1,0} & y_{i+k-2,2,0} & y_{i+k-2,1,1} & \cdots & y_{i-1,1,k} \\ y_{i+k-1,0,1} & y_{i+k-2,1,1} & y_{i+k-2,0,2} & \cdots & y_{i-1,0,k+1} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ y_{k,0,i} & y_{k-1,1,i} & y_{k-1,0,i+1} & \cdots & y_{0,0,i+k} \end{bmatrix}, \tag{13}$$

where $y_{i,j,k}$ represents the $(i + j + k)$ order moment

$$y_{i,j,k} = \int x_1^i x_2^j x_3^k \mu\left(\mathrm{d}\left(x_1, x_2, x_3\right)\right), \tag{14}$$

for some probability measure μ.

For the case $n = 3, m = 1$, one obtain

$$M_1(y) = \begin{bmatrix} 1 & y_{1,0,0} & y_{0,1,0} & y_{0,0,1} \\ y_{1,0,0} & y_{2,0,0} & y_{1,1,0} & y_{1,0,1} \\ y_{0,1,0} & y_{1,1,0} & y_{0,2,0} & y_{0,1,1} \\ y_{0,0,1} & y_{1,0,1} & y_{0,1,1} & y_{0,0,2} \end{bmatrix}.$$

Let $g(x) : \mathbb{R}^n \to \mathbb{R}$ be a real valued polynomial of degree w with coefficient vector $g \in \mathbb{R}^{s(w)}$. If the entry (i, j, k) of the matrix $M_m\,(y)$ is y_β, let $\beta\,(i, j, k)$

denote the subscript β of y_β. Then $M_m(gy)$ is defined by

$$M_m(gy)(i,j,k) = \sum_{\alpha} g_\alpha y_{\{\beta(i,j,k)+\alpha\}}. \tag{15}$$

Let $\deg g_i(x) = w_i$, and define

$$\tilde{w}_i = \left\lceil \frac{w_i}{2} \right\rceil$$

which is *the smallest integer larger than* $\frac{w_i}{2}$. Then optimization problem (10) is equivalent to the following problem

$$Q_K^N \mapsto \begin{cases} \inf_y \sum_\alpha p_\alpha y_\alpha \\ \text{subject to the constraints :} \\ M_N(y) \geq 0 \\ M_{N-\tilde{w}_i}(g_i y) \geq 0, i = 1, \ldots, r. \end{cases} \tag{16}$$

The number N has to be chosen according to the following conditions

$$N \geq \left\lceil \frac{m}{2} \right\rceil \text{ and } N \geq \max_i \tilde{w}_i.$$

Lasserre [6] proves that

$$\inf Q_K^N \uparrow p_K^* \quad \text{as } N \to \infty.$$

Algorithm 5. *The Algorithm for The Estimation*

- *Step 1*: Rewrite Ω_c as
$$\Omega_c = \{x | V(x) \leq c_0\} \cup \{x | c_0 \leq V(x) \leq c\}, \tag{17}$$
such that $\dot{V}(x) < 0$ in $\Omega_{c_0} \backslash \{0\}$.
- *Step 2*: Rewrite (2) as
$$\begin{cases} \text{find } c^* = \min V(x) \\ \text{subject to the constraints :} \\ g_1(x) = \dot{V}(x) \geq 0, \\ g_2(x) = x^T x - c_0 \geq 0, \\ g_3(x) = -x^T x + R \geq 0. \end{cases} \tag{18}$$
- *Step 3*: Translation (18) as (16).
- *Step 4*: Use an LMI-solver to compute c^*.

5.2. Estimating the domain of attraction of HIV-1 system. For E_1, we select the appropriate parameter values for the dynamic model of HIV-1 system as follows:

$$d = 2, p = 1, u = 1, k = 1, s = 1, \beta = 1.$$

Then $R_0 < 1$ is satisfied, and we obtain

$$\begin{cases} \dot{x} = 1 - 2x - xv, \\ \dot{y} = xv - y, \\ \dot{v} = y - v. \end{cases} \tag{19}$$

and $E_1 = \left(\frac{1}{2}, 0, 0\right)$.

Let $m = x - \frac{1}{2}, n = y, q = v$, and for conveniently we also write (m, n, q) as (x, y, v). Then we can rewrite (19) as

$$\begin{cases} \dot{x} = -\frac{1}{2}v - 2x - vx, \\ \dot{y} = \frac{1}{2}v - y + vx, \\ \dot{v} = y - v. \end{cases} \tag{20}$$

Hence the linearized system is

$$\begin{cases} \dot{x} = -\frac{1}{2}v - 2x, \\ \dot{y} = \frac{1}{2}v - y, \\ \dot{v} = y - v. \end{cases} \tag{21}$$

The following function

$$V(x, y, v) = \frac{34}{136}x^2 + \frac{174}{136}y^2 + \frac{124}{136}v^2 - \frac{4}{136}xy - \frac{12}{136}xv + \frac{212}{136}yv$$

is a Lyapunov function for system (21), since V is positive definite, and

$$\left.\frac{\mathrm{d}V}{\mathrm{d}t}\right|_{(21)} = -x^2 - y^2 - v^2.$$

Furthermore,

$$\left.\frac{\mathrm{d}V}{\mathrm{d}t}\right|_{(20)} = -x^2 - y^2 - v^2 + \frac{224}{136}v^2x - \frac{72}{136}vx^2 + \frac{352}{136}vxy.$$

Now using Algorithm 4, we obtain

N	3	4	5
$M_N(y)$	$\mathbb{R}^{20\times 20}$	$\mathbb{R}^{35\times 35}$	$\mathbb{R}^{56\times 56}$
c^*	0.6990	1.0811	1.0811

Therefore, the set

$$\left\{ \begin{array}{c} (x, y, v) : x \geq -\frac{1}{2}, y \geq 0, v \geq 0, \text{and} \\ \frac{34}{136}x^2 + \frac{174}{136}y^2 + \frac{124}{136}v^2 - \frac{4}{136}xy - \frac{12}{136}xv + \frac{212}{136}yv \leq 1.0811 \end{array} \right\}$$

is a subset of the domain of attraction for system (20).

We can obtain the domain of attraction of simulated images for system (20), as shown right one in Figure 1, while the left one is its extension.

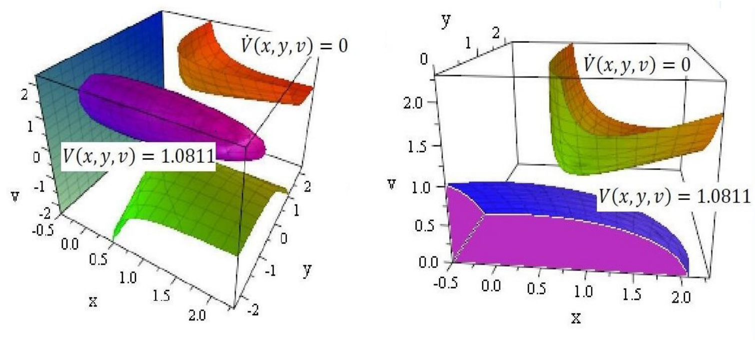

Figure 1. The domain of attraction of the equilibrium point E_1 of HIV-1 system (20)

For E_2, we select the appropriate parameter values for the dynamic model of HIV-1 system as follows:

$$d = 1, p = 1, u = 1, k = 2, s = 1, \beta = 1.$$

Then $R_0 > 1$ is satisfied, and we obtain

$$\begin{cases} \dot{x} = 1 - x - xv, \\ \dot{y} = xv - y, \\ \dot{v} = 2y - v. \end{cases} \tag{22}$$

and $E_2 = \left(\frac{1}{2}, \frac{1}{2}, 1\right)$.

Let $m = x - \frac{1}{2}, n = y - \frac{1}{2}, q = v - 1$, and for conveniently we also write (m, n, q) as (x, y, v). Then we can rewrite (22) as

$$\begin{cases} \dot{x} = -\frac{1}{2}v - 2x - xv, \\ \dot{y} = \frac{1}{2}v + x - y + xv, \\ \dot{v} = 2y - v. \end{cases} \tag{23}$$

Hence the linearized system is

$$\begin{cases} \dot{x} = -\frac{1}{2}v - 2x, \\ \dot{y} = \frac{1}{2}v + x - y, \\ \dot{v} = 2y - v. \end{cases} \tag{24}$$

The following function

$$V(x, y, v) = \frac{29}{30}x^2 + \frac{97}{30}y^2 + \frac{11}{12}v^2 + \frac{43}{15}xy + \frac{16}{15}xv + \frac{41}{15}yv$$

is a Lyapunov function for system (24), since V is positive definite, and

$$\left.\frac{\mathrm{d}V}{\mathrm{d}t}\right|_{(24)} = -x^2 - y^2 - v^2.$$

Furthermore,

$$\left.\frac{\mathrm{d}V}{\mathrm{d}t}\right|_{(23)} = -x^2 - y^2 - v^2 + \frac{5}{3}v^2x + \frac{14}{15}vx^2 + \frac{18}{5}vxy.$$

Now using Algorithm 4, we obtain

N	3	4	5
$M_N(y)$	$\mathbb{R}^{20\times 20}$	$\mathbb{R}^{35\times 35}$	$\mathbb{R}^{56\times 56}$
c^*	1.3414	1.4738	1.4738

Therefore, the set

$$\left\{ \begin{array}{c} (x,y,v) : x \geq -\frac{1}{2}, y \geq -\frac{1}{2}, v \geq -1, \text{and} \\ \frac{29}{30}x^2 + \frac{97}{30}y^2 + \frac{11}{12}v^2 + \frac{43}{15}xy + \frac{16}{15}xv + \frac{41}{15}yv \leq 1.4738 \end{array} \right\}$$

is a subset of the domain of attraction for system (23).

We can obtain the domain of attraction of simulated images for system (23), as shown right one in Figure 2, while the left one is its extension.

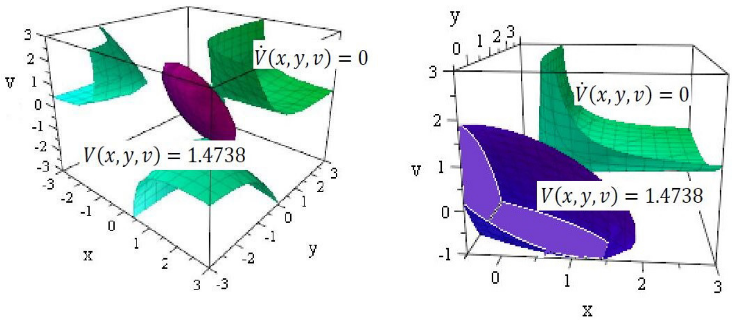

Figure 2. The domain of attraction of the equilibrium point E_2 of HIV-1 system (23)

6. Conclusions

This paper considered the domain of attraction of HIV-1 system by using the moments theory, which discuss the great harm to human health. Finally, one simulation shows the effectiveness of moment method. It is beneficial to the study of HIV-1 virus, while this will usually result in large virus load, severe tissue damage, or both. The proposed method makes practical problems can be calculated using the software, which greatly reduces the computational difficulty, making computing more quickly and accurately.

References

1. X. Chen, C. Li, J. Lü and Y. Jing, *The domain of attraction for a SEIR epidemic model based on sum of square optimization*, Bull. Korean Math. Soc. **49**(2012), no. 3, 517-528.
2. W. Cheng, W. Ma and S. Guo, *Estimation of the attractive region of a class of delayed virus dynamics model with apoptosis of uninfected T cells by infected T cells*, J. Sichuan Normal Univ. Nat. Sci. Ed. **39**(2016), no. 2, 202-208.

3. O. Hachicho, *A noble LMI-based optimization algorithm for the guaranteed estimation of the domain of attraction using rational Lyapunov functions,* J. Franklin Inst. **344**(2007), no. 5, 535-552.
4. C. Li, W. Wang and C.S. Ryoo, *Estimating the domain of attraction of tumor-immune system based moment method*, Far East J. Math. Sci. **100**(2016), no. 11, 1951-1963.
5. C. Li, C.S. Ryoo, N. Li and L. Cao, *Estimating the domain of attraction via moment matrices*, Bull. Korean Math. Soc. **46**(2009), no. 6, 1237-1248.
6. J.B. Lasserre, *Global optimization with polynomials and the problem of moments*, SIAM J. Optim. **11**(2001), no. 3, 796-817.
7. M.A. Nowak and C.R. Bangham, *Population dynamics of immune responses to persistent viruses*, Science **272**(1996), 74-79.

Chunji Li received Ph.D. degree from Kyungpook National University, Korea. His research interests focus on the control theory, moment method, and unilateral weighted shifts.

Department of Mathematics, Northeastern University, Shenyang 110004, R. R. China.
e-mail: lichunji@mail.neu.edu.cn

Han Yao is a Master course student of Northeastern University. Her research interests focus on the control theory.

Department of Mathematics, Northeastern University, Shenyang 110004, R. R. China.
e-mail: Alice9312@sina.com