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Exponential Equilibria and Uniform Boundedness of HIV Infection Model

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1. Introduction

According to data and statistics in a global summary of the Acquired immune deficiency syndrome (AIDS) epidemic from The World Health Organization (WHO), by the end of 2007 an estimated 33 million people worldwide were living with human immunodeficiency virus, HIV. That same year, some 2 million died of AIDS, and the number of people receiving antiretroviral therapy (ART) was reported in 2.990.000, while an estimated of about 9.700.000 the people needing ART. In other words, globally, less than one person in five at risk of HIV has access to basic HIV prevention services. The same study indicates a total 31% as the ART coverage at that same period (WHO, 2007).
Highly Active Antiretroviral Therapy (HAART) has demonstrated to be effective at slowing the progression of (HIV) infection to Acquired immune deficiency syndrome (AIDS) and, subsequently, to improve quality of life for infected people. However, if on the one hand the cocktail of drugs has been making possible to extend patient's lives, on the other hand the many problems associated with it and its high cost, particularly to poor people are a clear indication that new approaches to address the situation are needed. Most efforts to control HIV replication has been focused on developing and optimizing antiretroviral therapies.
The immune system of human beings contains different types of cells that help protect the body from infections. One of these types of specialized cells are called Cluster of Differentiation Antigen 4 (CD4) or T-cells, by the fact that CD4 is a glycoprotein predominantly found on the surface of helper T cells. The Human Immunodeficiency Virus (HIV) is a retrovirus and therefore it needs cells from a host so that it can make copies of itself. The CD4 cells are receptors for HIV and they aid the virus to initiate its replication process by enabling it to enter into its host. HIV is essentially considered as an infection of the immune in the sense that this virus infects and damages CD4 during the virus replication process. The more virus is produced by infected cells, the higher is the viral load and consequently, lower will be the number of functioning CD4 cells. When this number of uninfected cells declines below a critical value, the immune system is seriously deteriorated by HIV.
In section 2, it is shown the theoretical reference used to analyze the asymptotic behavior of the solution to the nonlinear perturbed system. The analysis concerning the origin, x=0 as

a stable equilibrium point. On the other hand, the functions that represent the perturbation have the nonlinear dynamic and the function that force the localization of equilibrium point. That function allows to characterize the behavior of the trajectory around origin, x=0. In section 3 are analyzed the properties of the equilibrium in the origin that corresponds to the infected state and the asymptotic behavior of the solution to the model of 3 EDO presented by (Barao & Lemos, 2007; Perelson & Nelson, 1999; Santos & Middleton, 2008). The model is used to characterize the dynamic infection of the disease. In the last section are made some conclusions about exponential equilibrium and uniform boundedness of the model solution.

2. Perturbed system

Consider the following perturbed system

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

where $h : [0,\infty) \times D \rightarrow R^n$ is continuous and t is locally Lipschitz in x on domain $D \subset R^n$, and D is an open connected set that contains the origin $x = 0$. Now, consider the right-hand side of (1), then by adding and subtracting $f(x)$ known as the nominal system around the origin, we can rewrite the right-hand side as

$$h(t,x) = f(x) + [h(t,x) - f(x)],$$

and define

$$g(x) + d(t) = h(t,x) - f(x),$$

Hence, the perturbed system (1) can be written as

$$\begin{aligned} \dot{x} &= h(t,x) = f(x) + g(x) + d(t) \\ \dot{x} &= e(x) + d(t), \end{aligned} \tag{2}$$

where $f : D \rightarrow R^n$ and $g : D \rightarrow R^n$ are locally Lipschitz in x on domain $D \subset R^n$, $d(t)$ is a uniformly bounded disturbance that satisfies $|d(t)| \leq \delta$ for all $t \geq 0$ and $e(x) = f(x) + g(x)$. The nominal system in $f(x)$ could have a stable or asymptotically stable equilibrium point at the origin. The approach of the Lyapunov method will allow us to draw conclusions about the system when the nominal system is perturbed, whether such perturbation is an autonomous or a non autonomous perturbation respectively.

2.1 Nonlinear autonomous perturbation

Consider the autonomous system

$$\dot{x} = h(x), \tag{3}$$

where $h : D \rightarrow R^n$ is locally Lipschitz map from a domain $D \subset R^n$.

Suppose $\tilde{x} \in D$ is an equilibrium point of (3), that is $h(\tilde{x}) = 0$. The aim is to characterize the stability for the case when the equilibrium point is at the origin, that is $\tilde{x} = 0$. For autonomous system, there is a convergence of the trajectory to a set, the same as the asymptotic stability of the origin. A major concern in analysing the stability of dynamical system is the robustness of various stability properties to uncertainties in the system's model. In the following, it is introduced the stability definition.

Definition 1. *The equilibrium point $x = 0$ of (3) is*

- *Stable, if for each $\varepsilon > 0$, there is $\delta = \delta(\varepsilon) \geq 0$ such that*

$$\|x(0)\| < \delta \Rightarrow \|x(t)\| < \varepsilon, \;\; \forall t \geq 0.$$

- *Unstable, if not stable.*
- *Asymptotically stable if it is stable and $\delta > 0$ can be chosen such that*

$$\|x(0)\| < \delta \Rightarrow \lim_{t \to \infty} x(t) = 0.$$

Let $V : D \to R$ be a differentiable function defined in a domain $D \subset R^n$ that contains the origin. The derivative of $V(x)$ along the trajectories of (3), denoted by $\dot{V}(x)$, is given by

$$\dot{V}(x) = \sum_{i=1}^{n} \frac{\partial V}{\partial x_i} \dot{x}_i = \sum_{i=1}^{n} \frac{\partial V}{\partial x_i} h_i(x). \tag{4}$$

The function $\dot{V}(x)$ is dependent on the system's equation. Hence, if $\dot{V}(x)$ is negative, $V(x)$ will decrease along the solution of (3). The following lemma (Khalil, 2002) states Lyapunov's stability sense.

Lemma 1. *Let $x = 0$ be an equilibrium point for (3). Let $V : D \to R$ be a continuously differentiable function on a neighbourhood D of $x = 0$, such that*

$$\begin{aligned} V(0) = 0 \;\; and \;\; V(x) > 0 \;\; in \; D - \{0\}, \\ \dot{V}(x) \leq 0 \;\; in \; D. \end{aligned} \tag{5}$$

Then, $x = 0$ is stable. Moreover, if

$$\dot{V}(x) < 0 \;\; in \; D - \{0\}. \tag{6}$$

Then $x = 0$ is asymptotically stable.

Proof. Given $\varepsilon > 0$, choose $r \in (0, \varepsilon]$ such that

$$B_r = \{x \in R^n | \|x\| \leq r\} \subset D.$$

Let $\alpha = min_{\|x\|=r} V(x)$. Then, $\alpha > 0$ by (5). Take $\beta \in (0, \alpha)$, and let

$$\Omega_\beta = \{x \in B_r | V(x) \leq \beta\}.$$

The set Ω_β has the property that any trajectory starting in Ω_β at $t = 0$, stays in Ω_β for all $t \geq 0$. This follows from (5) since

$$\dot{V}(x(t)) \leq 0 \Rightarrow V(x(t)) \leq V(x(0)) \leq \beta, \;\; \forall t \geq 0.$$

Since Ω_β is a compact set (is closed and bounded since it is contained in B_r), the system in (3) has a unique solution defined for all $t \geq 0$, whenever $x(0) \in \Omega_\beta$. Since $V(x)$ is continuous and $V(0) = 0$, there is $\delta > 0$ such that

$$\|x\| \leq \delta \Rightarrow V(x) < \beta.$$

Then

$$B_\delta \subset \Omega_\beta \subset B_r,$$

and

$$x(0) \in \beta_\delta \Rightarrow x(0) \in \Omega_\beta \Rightarrow x(t) \in \Omega_\beta \Rightarrow x(t) \in B_r.$$

Therefore,

$$\|x(0)\| < \delta \Rightarrow \|x(t)\| < r \leq \varepsilon, \ \ \forall t \geq 0.$$

which shows that the equilibrium point $x = 0$ is stable. Now, to show asymptotic stability it is necessary to show that $x(t) \to 0$ as $t \to \infty$, that is, for every $a > 0$, there is $T > 0$ such that $\|x(t)\| < a$, for all $t > T$. For every $a < 0$, we can choose $b > 0$ such that $\Omega_b \subset B_a$. Therefore, it is sufficient to show that $V(x(t)) \to 0$ as $t \to \infty$. Since $V(x)$ is monotonically decreasing and bounded from below by zero,

$$V(x(t)) \to c \geq 0 \ \ as \ \ t \to \infty.$$

To show that $c = 0$, suppose by contradiction $c > 0$. By continuity of $V(x)$, there is $d > 0$ such that $B_d \subset \Omega_c$. The limit $V(x(t)) \to c > 0$ implies that the trajectory $x(t)$ lies outside the ball $B_d \subset \Omega_c$ for all $t \geq 0$. When $\dot{V}(x)$ is integrated on t, it follows by (6) that

$$V(x(t)) = V(x(0)) + \int_0^t \dot{V}(x(\tau))d\tau \leq V(x(0)) + kt,$$

where $k = -max_{a \leq \|x\| \leq r} \dot{V}(x) < 0$. Since the right-hand side will eventually become negative, the inequality contradicts the assumption that $c > 0$. □

Remark 1. *The origin is stable if there is a continuously differentiable positive definite function* $V(x)$ *so that* $\dot{V}(x)$ *is negative semi-definite, and it is asymptotically stable if* $\dot{V}(x)$ *is negative definite.*

Remark 2. *The theorem's conditions are only sufficient. Failure of a Lyapunov function candidate to satisfy the conditions for stability or asymptotic stability does not mean that the equilibrium is not stable or asymptotically stable. It only means that such a stability property cannot be established by using this Lyapunov function candidate.*

For the case when the origin $x = 0$ is asymptotically stable, it is often interesting to determine how far from the origin can the trajectory be and still converges to the origin as $t \to \infty$. This gives rise to the definition of the region of attraction or basin.

Definition 2. *Let* $x(t, x(0))$ *be the solution of (3) that starts at initial state* x_0 *at time* $t = 0$. *Then, the region of attraction is defined as the set of all points x such that* $\lim_{t \to \infty} x(t, x(0)) = 0$.

To find the exact region of attraction analytically might be difficult or even impossible. However, Lyapunov functions can be used to estimate the region of attraction, that is, to find sets contained in the region of attraction. From the proof of Lemma 1, we say that if there is a Lyapunov function that satisfies the conditions of asymptotic stability over a domain D, and if

$$\Omega_c = \{x \in R^n | V(x) \leq c\}, \tag{7}$$

is bounded and contained in D, then every trajectory starting in Ω_c remains in Ω_c, and approaches the origin as $t \to \infty$. The set in (7) with $\dot{V}(x) \leq 0, \forall x \in \Omega_c$ is a positively invariant set, since, as we showed in the proof of Lemma 1, a solution starting in Ω_c remains in Ω_c for all $t \geq 0$. Now, it is introduced the following corollaries known as the LaSalle invariance principle and the Barbashin-Krasovskii theorem.

Corollary 1. *Let Ω_c be a compact (closed and bounded) set with the property that every solution of (3) which starts in Ω_c remains for all future time in Ω_c. Let $V : \Omega_c \to R$ be a continuously differentiable function such that $\dot{V}(x) \leq 0, \forall x \in \Omega_c$. Let E be the set of all points in Ω_c where $\dot{V}(x) = 0$. Let M be the largest invariant set in E. Then every solution starting in Ω_c approaches M as $t \to \infty$.*

Corollary 2. *Let $x = 0$ be an equilibrium point for (1). Let $V : \Omega_c \to R$ be a continuously differentiable positive definite function on a neighbourhood Ω_c of $x = 0$, such that $\dot{V}(x) \leq 0, \forall x \in \Omega_c$. Let $S = \{x \in \Omega_c | \dot{V}(x) = 0\}$, and suppose that no solution can stay forever in S, other than the trivial solution. Then, the origin $x = 0$ is asymptotically stable.*

Remark 3. *When $\dot{V}(x)$ is negative definite, $S = 0$. Then, corollary 2 coincide with lemma 1.*

With the previous stability criteria for equilibria point about the origin, it is necessary to introduce the specific analysis for autonomous perturbed system.

2.1.1 Mean value

Consider the autonomous case in (2), when $d(t) = 0$ for all $t \geq 0$. Suppose that the origin $x = 0$ is inside of D and is an equilibrium point for the nominal system $f(x)$, that is, $f(0) = 0$. By the mean value

$$f(x) = f(0) + \frac{\partial f(z)}{\partial x}x,$$

where z is a point on the line segment connecting x to the origin. The above equality is valid for any point $x \in D$ such that the line segment connecting x to the origin lies entirely in D. Since $f(0) = 0$, we can write $f(x)$ as

$$f(x) = \frac{\partial f(z)}{\partial x}x = \frac{\partial f(0)}{\partial x}x + \left[\frac{\partial f(z)}{\partial x} - \frac{\partial f(0)}{\partial x}\right]x,$$
$$f(x) = Ax + g(x),$$

where

$$A = \frac{\partial f(0)}{\partial x}, \quad and \quad g(x) = \left[\frac{\partial f(z)}{\partial x} - \frac{\partial f(0)}{\partial x}\right]x.$$

The function $g(x)$ satisfies

$$\|g(x)\|_2 \leq \left|\frac{\partial f(z)}{\partial x} - \frac{\partial f(0)}{\partial x}\right|_2 \|x\|_2 \leq k\|x\|_2,$$

for any $k > 0$, there exists $r > 0$, such that $\forall \|x\|_2 < r$. It is possible to approximate in a small neighbourhood of the origin the nonlinear system $f(x)$ by its linearization about the origin

$$\dot{(x)} = Ax, \quad where \quad A = \frac{\partial f(0)}{\partial x}. \tag{8}$$

The following corollary characterizes the stability properties of the origin.

Corollary 3. *The equilibrium point $x = 0$ of (8) is stable if and only if all eigenvalues of A satisfy $Re(\lambda_i) \leq 0$. The equilibrium point $x = 0$ is asymptotically stable if and only if all eigenvalues of A satisfy $Re(\lambda_i) < 0$. When all eigenvalues of A satisfy $Re(\lambda_i) < 0$, A is called a stability matrix or a Hurwitz matrix. The origin of (8) is asymptotically stable if and only if A is a stability matrix.*

Consider a quadratic Lyapunov function candidate

$$V(x) = x^T P x,$$

where P is a real symmetric positive definite matrix. The derivative of V along the trajectories of the linear system (8) is given by

$$\dot{V}(x) = \dot{x}^T P x + x^T P \dot{x} = x^T \left(PA + A^T P \right) x = -x^T Q x.$$

Asymptotic stability of the origin can be also investigated using Lyapunov's equation, as it is shown on corollary 4.

Corollary 4. *A matrix A is a stability matrix, that is, $Re(\lambda_i) < 0$ for all eigenvalues of A, if and only if for any given positive definite symmetric matrix Q there exists a positive definite symmetric matrix P that satisfies the Lyapunov equation*

$$PA + A^T P = -Q. \tag{9}$$

If Q is positive definite, then the origin is asymptotically stable, that is, $Re(\lambda_i) < 0$, for all eigenvalues of A. Here it follows the usual procedure of Lyapunov's method, where it choose $V(x)$ to be positive definite and then check negative definiteness of $\dot{V}(x)$.

Remark 4. *If matrix A is a stability matrix, then P is a unique solution of (9).*

The Lyapunov equation can be used to test whether or not a matrix A is a stability matrix, as an alternative to calculating the eigenvalues of A. The existence of a Lyapunov function will allow us to draw conslusions about the system when the linear term Ax is perturbed, whether such perturbation is a linear perturbation in the coefficients of A or a nonlinear autonomous perturbation. The following lemma is known as Lyapunov's indirect method or Lyapunov first method.

Lemma 2. *Let $x = 0$ be an equilibrium point for the nonlinear system*

$$\dot{x} = f(x), \tag{10}$$

where $f : D \to R^n$ is continuously differentiable and D is a neighbourhood of the origin. Let

$$A = \left. \frac{\delta f(x)}{\delta x} \right|_{x=0}.$$

Then, the origin is asymptotically stable if $Re(\lambda_i) < 0$ for all eigenvalues of A.

Proof. Let A be a stability matrix. Then, by corollary 4 it is known that for any positive definite symmetric matrix Q, the solution P of the Lyapunov equation (9) is positive definite. Consider

$$V(x) = x^T P x,$$

as a Lyapunov function candidate for the nonlinear system. The derivative of $V(x)$ along the trajectories of the system is given by

$$\dot{V}(x) = x^T P e(x) + e^T(x) P x = x^T P \left(Ax + g(x) \right) + \left(x^T A^T + g^T(x) \right) P x,$$
$$\dot{V}(x) = x^T \left(PA + A^T P \right) x + 2x^T P g(x) = -x^T Q x + 2x^T P g(x).$$

The first term on the right-hand side is negative definite, while the second term is indefinite. But the function $g(x)$ satisfies

$$\|g(x)\|_2 \leq k\|x\|_2, \;\; \forall \|x\|_2 < r.$$

For any $k > 0$, there exists $r > 0$. Hence, after majorize the right-hand side

$$\dot{V}(x) \leq -x^T Q x + 2k\|P\|_2\|x\|_2^2,$$

but

$$x^T Q x \geq \lambda_{min}(Q)\|x\|_2^2,$$

where $\lambda_{min}(\cdot)$ denotes the minimum eigenvalue of a matrix. Note that $\lambda_{min}(Q)$ is real and positive since Q is symmetric and positive definite. Thus

$$\dot{V}(x) \leq -\left(\lambda_{min}(Q) - 2k\|P\|_2\|\right)\|x\|_2^2.$$

By choosing

$$k < \frac{1}{2}\frac{\lambda_{min}(Q)}{\|P\|_2},$$

ensures that $\dot{V}(x)$ is negative definite. By lemma 1, we conclude that the origin is asymptotically stable. □

2.2 Non linear non autonomous perturbation

Consider the system given in (2)

$$\dot{x} = h(t,x) = f(x) + g(x) + d(t),$$
$$\dot{x} = e(x) + d(t),$$

where $f : D \to R^n$ and $g : D \to R^n$ are locally Lipschitz in x on domain $D \subset R^n$, $d(t)$ is a uniformly bounded disturbance that satisfies $|d(t)| \leq \delta$ for all $t \geq 0$ and $e(x) = f(x) + g(x)$.
The notions of stability and asymptotic stability of the equilibrium of a non autonomous system are basically the same as Definition 1 for autonomous system, see (Khalil, 2002). The difference here is that, while the solution of an autonomous system depends only on $(t - t_0)$, the solution of a non autonomous system may depend on both t and t_0. Here, in that case the function $d(t) \neq 0$ for all $t \geq 0$ about the origin.
Therefore, the stability behavior of the equilibrium point will be dependent on t_0.

Definition 3. *The equilibrium point $x = 0$ of (2) is*

- *Stable, if for each $\varepsilon > 0$, and any $t_0 \geq 0$ there is $\delta = \delta(\varepsilon, t_0) \geq 0$ such that*

$$\|x(t_0)\| < \delta \Rightarrow \|x(t)\| < \varepsilon, \;\; \forall t \geq 0.$$

- *Unstable, if not stable.*
- *Asymptotically stable if it is stable and $\delta > 0$ can be chosen such that*

$$\|x(t_0)\| < \delta \Rightarrow \lim_{t\to\infty} x(t) = 0.$$

It is necessary to introduce special scalar functions that will help to characterize and study the behavior of a solution for the non autonomous system.

Definition 4. *A scalar function $w(r) \in R$ is said to be positive definite, if it is continuous and $w(r) > 0$ for $|r| > 0$ and $w(0) = 0$. The scalar function is radially unbounded if $w(r) \to \infty$ as $|r| \to \infty$.*

Definition 5. *A scalar function $u(r,s) \in R$ is said to be positive definite and decreasing, if for each fixed s, the function $u(r,s) > 0$ and $u(r,0) = 0$ is continuous with respect to r, and for each fixed r the function $u(r,s)$ is continuous and decreasing with respect to s and $u(r,s) \to 0$ as $|s| \to \infty$.*

The following corollary states some properties of positive definite functions.

Corollary 5. *Let $w_1(\cdot)$ and $w_2(\cdot)$ be positive definite functions on domain $D = \{x \in R^n, \|x\| < r\}$. Consider the following difference between scalar functions*

$$k_1 w_1(r) - k_2 w_2(\|x\|) \geq 0, \text{ where } \|x\| < r.$$

If the leading term can be factorized, then the bound is given by

$$\|x\| \leq \gamma, \text{ where } \gamma = w_2^{-1}[w_1(r)].$$

The following stability properties of the origin are given.

Definition 6. *The equilibrium point $x = 0$ of (2) is*

1. *Uniformly stable, if there exists a positive definite function $w(\cdot)$ and a positive constant r, independent of t_0 such that*

$$\|x(t)\| \leq w(\|x(t_0)\|), \forall t \geq t_0 > 0, \forall \|x(t_0)\| < r. \tag{11}$$

2. *Uniformly asymptotically stable, if there exist a positive definite and decreasing function $u(\cdot,\cdot)$ and a positive constant r, independent of t_0 such that*

$$\|x(t)\| \leq u(\|x(t_0)\|, t - t_0), \forall t \geq t_0 > 0, \forall \|x(t_0)\| < r. \tag{12}$$

3. *Globally uniformly asymptotically stable, if inequality (12) is satisfied for any initial state $x(t_0)$.*
4. *Exponentially stable if inequality (12) is satisfied with*

$$u(r,s) = kre^{-\alpha s}, \ k > 0, \ \alpha > 0. \tag{13}$$

To establish uniform asymptotic stability of the origin, it is necessary to verify inequality (12) with the aid of an auxiliary scalar differential equation. The following corollary defines a scalar solution of a special equation.

Corollary 6. *Consider the scalar differential equation*

$$\dot{y} = -w(y), \ y(t_0) = y_0.$$

where $w(\cdot)$ is a locally Lipschitz positive definite function. Then, this equation has a unique solution $y(t)$ defined for all $t \geq t_0$

$$y(t) = \sigma\big(y(t_0), t - t_0\big)$$

where $\sigma(r,s)$ is a positive definite and decreasing function, see Definition 5.

Lyapunov stability theorems give sufficient conditions for stability, asymptotic stability, and so on. They do not say whether the given conditions are also necessary. There are converse theorems which establish, that for many Lyapunov stability theorems the given conditions are indeed necessary (Hahn, 1967; Krasovskii, 1967). The converse theorems are proved by actually constructing auxiliary functions that satisfy the conditions of the respective theorems. Almost always this construction assumes the knowledge of the solution of the differential equation. The origin $x = 0$ of the perturbed non-autonomous system (2), may not be an equilibrium point. We can no longer study stability of the origin as an equilibrium point, nor should we expect the solution of the perturbed system to approach the origin as $t \to \infty$. If the perturbation terms $g(x)$ and $d(t)$ are small in some sense, then the solution $x(t)$ will be bounded by a small bound, that is $\|x(t)\|$ will be small for sufficiently large t.

Definition 7. *The solution of $\dot{x} = h(t, x)$ is said to be uniformly bounded if there exist constants a and b, and for every $\mu \in (0, b)$ there is a constant T such that*

$$\|x(t_0)\| < \mu \Rightarrow \|x(t)\| < a, \quad \forall t > t_0 + T. \tag{14}$$

It is said globally uniformly bounded if (14) holds for arbitrarily large μ.

The following Lyapunov like theorem is useful to show uniform boundedness.

Theorem 1. *Let $D = \{x \in R^n \mid \|x\| < r\}$ and $h : [0, \infty) \times D \to R^n$ be continuous in t and locally Lipschitz in x. Let $V : [0, \infty) \times D \to R$ be a continuously differentiable function such that*

$$w_1(\|x\|) \leq V(t, x) \leq w_2(\|x\|), \tag{15}$$

$$\frac{\partial V}{\partial t} + \frac{\partial V}{\partial x} h(t, x) \leq w_3(x), \tag{16}$$

for all $\|x\| \geq \mu > 0$, and for all $x \in D$, where $w_1(\cdot)$, $w_2(\cdot)$ and $w_3(\cdot)$ are positive definite functions and $\mu < w_2^{-1}(w_1(r))$. Then, there exists a positive definite and decreasing function $u(\cdot, \cdot)$ and a finite time t_1 (dependent on $x(t_0)$ and μ) such that

$$\|x(t)\| \leq u(\|x(t_0)\|, t - t_0), \quad \forall t_0 \leq t < t_1, \tag{17}$$

$$\|x(t)\| \leq w_1^{-1}(w_2(\mu)), \quad \forall t \geq t_1, \tag{18}$$

for all $\|x(t_0)\| < w_2^{-1}(w_1(r))$. Furthermore, if $w_i(r) = k_i r^c$, for some positive constants k_i and c, then $u(r, s) = kre^{-\alpha s}$, with $k = (k_2/k_1)^{1/c}$, and $\alpha = (k_3/k_2 c)$.

Proof. By definition 6, it is necessary to prove that the origin is uniformly asymptotically stable in order to have an uniformly bounded solution. First, consider the derivative of $V(t, x)$ along the trajectories of (2)

$$\dot{V}(t, x) = \frac{\partial V}{\partial t} + \frac{\partial V}{\partial x} h(t, x) \leq -w_3(\|x\|).$$

Let $\rho < r$, and define a time-dependent set $\Omega_{t,\rho}$ by

$$\Omega_{t,\rho} = \{x \in D | V(t, x) \leq w_1(\rho)\}.$$

The set $\Omega_{t,\rho}$ contains the ball $\left\{\|x\| \leq w_2^{-1}(w_1(\rho))\right\}$ since

$$w_2(\|x\|) \leq w_1(\rho) \;\; and \;\; V(t, x) \leq w_1(\rho).$$

Also, the set $\Omega_{t,\rho}$ is a subset of the ball $\{\|x\| \leq \rho\}$ since $w_1(\|x\|) \leq w_1(\rho)$. Thus

$$\left\{x \in R^n | \|x\| \leq w_2^{-1}(w_1(\rho))\right\} \subset \Omega_{t,\rho},$$
$$\Omega_{t,\rho} \subset \{x \in R^n | \|x\| \leq \rho\} \subset D,$$

for all $t \geq 0$. For any $t_0 \geq 0$ and any $x(t_0) \in \Omega_{t,\rho}$, the solution starting at $(t_0, x(t_0))$ stays in $\Omega_{t,\rho}$ for all $t_0 \geq 0$. This follows from the fact that $\dot{V}(t,x)$ is negative on $D - \{0\}$; hence $V(t,x)$ is decreasing. Therefore, the solution starting at $(t_0, x(t_0))$ is defined for all $t \geq t_0$ and $x(t) \in D$. Now, it will assume that $\left\{\|x(t_0)\| \leq w_2^{-1}(w_1(\rho))\right\}$. Then

$$\dot{V}(t,x) \leq -w_3(\|x(t_0)\|) \leq -w_3\left(w_2^{-1}(w_1(\rho))\right).$$

Let $y(t)$ satisfy the auxiliary autonomous first order differential equation

$$\dot{y} = w(y), \;\; y(t_0) = V(t_0, x(t_0)) \geq 0.$$

It is clear that

$$V(t, x(t)) \leq y(t), \;\; \forall t \geq t_0.$$

By corollary 6, there exists a positive definite and decreasing function $\sigma(r,s)$ such that

$$V(t, x(t)) \leq \sigma(V(t_0, x(t_0)), t - t_0), \;\; \forall t \geq t_0.$$

Therefore, any solution starting in $\Omega_{t,\rho}$ satisfies the inequality

$$\begin{aligned} w_1(\|x(t)\|) &\leq V(t, x(t)), \\ \|x(t)\| &\leq w_1^{-1}(V(t, x(t))), \\ \|x(t)\| &\leq w_1^{-1}(\sigma(V(t_0, x(t_0)), t - t_0)), \\ \|x(t)\| &\leq w_1^{-1}(\sigma(w_2(\|x(t_0)\|), t - t_0)), \\ \|x(t)\| &\leq u(\|x(t_0)\|, t - t_0). \end{aligned}$$

Since $\mu < w_2^{-1}(w_1(r))$, we can choose $\rho < r$ such that $\mu < w_2^{-1}(w_1(\rho))$.
Furthermore, for any $\|x(t_0)\| < w_2^{-1}(w_1(r))$, we can choose ρ close enough to r such that $\|x(t_0)\| < w_2^{-1}(w_1(\rho))$. Let $\eta = w_1^{-1}(w_2(\mu))$. Then

$$B_\mu \subset \Omega_{t,\eta} \subset B_\eta \subset B_\rho \subset D,$$

and

$$\Omega_{t,\eta} \subset \Omega_{t,\rho} \subset B_\rho \subset D.$$

The sets $\Omega_{t,\rho}$ and $\Omega_{t,\eta}$ have the property that a solution starting inside either set cannot leave it because $\dot{V}(t,x)$ is negative on the boundary. Therefore, if $\|x(t_0)\| \leq w_2^{-1}(w_1(\rho))$, the solution $x(t)$ will belong to $\Omega_{t,\rho}$ for all $t \geq t_0$. For a solution starting inside $\Omega_{t,\eta}$, the inequality (18) is satisfied for all $t \geq t_0$. For a solution starting inside $\Omega_{t,\rho}$, but outside $\Omega_{t,\eta}$, let t_1 be the first time it enters $\Omega_{t,\eta}$. This time t_1 could be t_0 (if the solution starts inside $\Omega_{t,\eta}$) or infinite (if it never enters $\Omega_{t,\eta}$). Since $u(\|x(t_0)\|, t - t_0) \to 0$ as $t \to \infty$, there is a finite time after which $u(\|x(t_0)\|, t - t_0) < \mu$ for all t. Therefore, the time t_1 must be finite; that is, the solution must enter the set $\Omega_{t,\eta}$ in finite time. Once inside the set, the solution remains inside for all $t \geq t_1$. Therefore,

$$V(t, x(t)) \leq w_1(\eta), \;\; \forall t \geq t_1,$$

and

$$\|x(t)\| \leq \eta, \;\; \forall t \geq t_1.$$

Hence, any initial state $x(t_0)$ can be included in the set $\{\|x\| \leq w_2^{-1}(w_1(\rho))\}$. Thus, inequality (12) is satisfied for all $\{\|x(t_0)\| \leq w_2^{-1}(w_1(\rho))\}$, which implies that the origin $x = 0$ is uniformly asymptotically stable. The exponentially decaying for $w_1(\cdot)$, $w_2(\cdot)$ and $w_3(\cdot)$ is given by

$$w_i(r) = k_i r^c, \;\; k_i > 0, \;\; c > 0, \;\; i = 1, 2, 3.$$

Further, for scalar function

$$w(r) = k_3 \left[\left(\frac{r}{k_2} \right)^{1/c} \right]^c = \frac{k_3}{k_2} r.$$

Hence, the positive definite and decreasing function $\sigma(\cdot, \cdot)$ is given by

$$\sigma(r, s) = r e^{-(k_3/k_2)s}.$$

Subsequently, the function $u(\cdot, \cdot)$ is given by

$$u(r, s) = \left[\frac{k_2 r^c e^{-(k_3/k_2)s}}{k_1} \right]^{1/c}.$$

Hence, the origin is exponentially stable. The property completes the proof. □

Inequalities (17) and (18) show that the solution $x(t)$ is uniformly bounded for all $t \geq t_0$.

Remark 5. *Let $w_1^{-1}(w_2(\mu))$ be a positive definite function called the bound of μ. As $\mu \to 0$, the bound approaches zero. Sometimes, it is possible to combine inequalities (17) and (18) in one inequality*

$$\|x(t)\| \leq u\big(\|x(t_0)\|, t - t_0\big) + w_1^{-1}(w_2(\mu)), \;\; \forall t \geq t_0. \tag{19}$$

Now, let us illustrate how Theorem 1 is used in the analysis of the perturbed system (2), when the origin of the nominal system is exponentially stable and the system has a uniform bounded solution.

Lemma 3. *Let $x = 0$ be an exponentially stable equilibrium point of the nominal system (8). Let $V : [0, \infty) \times D \to R$ be a Lyapunov function of the nominal system that satisfies inequalities (15) and (16), where $D = \{x \in R^n, \; \|x\| < r\}$. Suppose the perturbation term $g(x) + d(t)$ satisfies*

$$\|g(x)\| \leq c_4 \|x\|, \;\; \|d(t)\| \leq \delta < \frac{\zeta}{c_5} r\theta \sqrt{\frac{c_1}{c_2}},$$

for all $t \geq 0$, $x(t) \in D$, and some positive constants $0 < \theta < 1$, $0 < \zeta < 1$, $c_2 > 0$, $c_4 > 0$, $c_5 > 0$ respectively. Then, for all $\|x(t_0)\| < r\sqrt{c_1/c_2}$, the solution of the perturbed system $x(t)$ satisfies

$$\|x(t)\| \leq k\|x(t_0)\| exp(-\alpha(t - t_0)), \;\; \forall t_0 \leq t < t_1,$$

and

$$\|x(t)\| \leq b, \;\; \forall t \geq t_1,$$

for some finite time t_1, where

$$k = \sqrt{\frac{c_2}{c_1}}, \ \alpha = \frac{(1-\theta)\zeta}{2c_2}, \ b = \frac{c_5}{\zeta}\frac{\delta}{\theta}k,$$
$$c_1 = \lambda_{min}(P), \ c_2 = \lambda_{max}(P),$$
$$c_3 = \lambda_{min}(Q), \ c_4 \leq c_3 - \zeta.$$

Proof. Consider $V(t,x)$ as a Lyapunov function candidate. The derivative of $V(t,x)$ along the trajectories of (2) satisfies

$$\dot{V}(t,x) \leq -c_3\|x\|_2^2 + \left\|\frac{\partial V}{\partial x}\right\|_2 \|g(x)\|_2 + \left\|\frac{\partial V}{\partial x}\right\|_2 \|d(t)\|_2,$$
$$\dot{V}(t,x) \leq -c_3\|x\|_2^2 + c_4\|x\|_2^2 + c_5\delta\|x\|_2,$$
$$\dot{V}(t,x) \leq -(c_3 - c_4 - \zeta)\|x\|_2^2 - \zeta\|x\|_2^2 + c_5\delta\|x\|_2,$$
$$\dot{V}(t,x) \leq -\zeta\|x\|_2^2 + c_5\delta\|x\|_2, \ 0 < \zeta < 1,$$
$$\dot{V}(t,x) \leq -(1-\theta)\zeta\|x\|_2^2 - \theta\zeta\|x\|_2^2 + c_5\delta\|x\|_2,$$
$$\dot{V}(t,x) \leq -(1-\theta)\zeta\|x\|_2^2, \ 0 < \theta < 1, \ \forall\|x\|_2 \geq \delta c_5/\theta\zeta.$$

By following application of theorem 1 completes the proof. □

The bound b is proportional to the upper bound on the perturbation δ. Once again, this result can be viewed as a robustness property of nominal system having exponentially uniform equilibria at the origin, because it shows that arbitrarily small (uniformly bounded) perturbations, will not result in large steady-state derivations from the origin.

3. HIV infection model approximation: Third order ODE

Consider the following model for HIV infection that involves a 3rd order ODE (Barao & Lemos, 2007), (Perelson & Nelson, 1999), and (Santos & Middleton, 2008)

$$\begin{aligned} \frac{dT}{dt} &= s - d_\tau T - \beta T V, \\ \frac{d\tilde{T}}{dt} &= \beta T V - \delta \tilde{T}, \\ \frac{dV}{dt} &= p\tilde{T} - cV, \end{aligned} \tag{20}$$

where T denotes the concentration of uninfected target cells (specially, CD4+helper T cells), $\tilde{T}$ is the concentration of infected target cells and V denotes the concentration of virions. There are two equilibrium points for the system given in (20). One of these is termed the uninfected state and is given by

$$T = \frac{s}{d_T}, \ \tilde{T} = 0, \ V = 0. \tag{21}$$

The other equilibrium is termed the infected state and is given by

$$T = \frac{\delta c}{\beta p}, \ \tilde{T} = \frac{s}{\delta} - \frac{c d_\tau}{\beta p}, \ V = \frac{ps}{\delta c} - \frac{d_\tau}{\beta}. \tag{22}$$

Parameter	Description	Value/units
s	Source term for uninfected cells	10mm^{-3} per day
d_T	Death rate of uninfected cells	0.02 per day
β	Infection rate of free virus particles	2.4×10^{-5} mm^{-3} per day
δ	Death rate of infected cell	0.24 per day
p	Rate of virions produced per infected cells	100 per day
c	Death rate of free particle virions	2.4 per day
t	Time	days

Table 1. Parameters for HIV model

3.1 Linearisation on infected and uninfected equilibrium point

On reference (Santos & Middleton, 2008), both equilibrium points (21) and (22) were studied. The uninfected state (21), see parameter values on Table 1, is an unstable equilibrium, where even a small perturbation (e.g introduction of HIV virus to system's dynamic) leads to divergence. For infected state in (22), it is concluded that the infected equilibrium is locally stable for the parameter values given on Table 1. The qualitative behavior of a non linear system near an equilibrium point can be determined via linearisation (Khalil, 2002). The system can be linearised by computing the Jacobian which for (20) is given by

$$A = \left.\frac{\partial f}{\partial x}\right|_{x=[T,\tilde{T},V]} = \begin{bmatrix} -(d_T + \beta V) & 0 & -\beta T \\ \beta V & -\delta & \beta T \\ 0 & p & -c \end{bmatrix}, \tag{23}$$

where A is a stability matrix for the evaluation of infected state given in (22) that leads to the characteristic polynomial

$$|\lambda I - A| = \lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 \tag{24}$$

where $a_1 = \left(c + \delta + \frac{\beta sp}{\delta c}\right)$, $a_2 = \frac{\beta sp}{\delta c}(c + \delta)$, and $a_3 = (\beta sp - \delta c d_T)$.

From (24), the Hurwitz stability conditions are $a_k > 0$, for $k = 1, 2, 3$ and $a_1 a_2 - a_3 > 0$. This stability domain is very conservative, because of the local behavior about the equilibrium point in (22). In next subsection, for equilibrium point in (22), we need to probe the exponentially uniform stable property and describe boundedness of the region of attraction. We propose to work with the converse Lyapunov stability analysis in order to obtain a uniformly bounded estimation for the equilibria point behavior at perturbation.

3.2 Non autonomous perturbation analysis

Now, it is necessary to study the dynamics for the perturbation and to determine the extent of stability region to know how large a perturbation from the equilibrium can be allowed and it can still be sure that the solution remains toward the equilibrium (Hahn, 1967), (Khalil, 2002). Consider the following change of variables in (20)

$$x = [T, \tilde{T}, V]^T = [x_1, x_2, x_3]^T.$$

The HIV model equations (20) can be rewritten as a perturbed model

$$\begin{aligned} \dot{x}_1 &= s - d_T x_1 - \beta x_1 x_3 = -d_T x_1 + (s - \beta x_1 x_3), \\ \dot{x}_2 &= \beta x_1 x_3 - \delta x_2 = -\delta x_2 + (\beta x_1 x_3), \\ \dot{x}_3 &= p x_2 - c x_3. \end{aligned} \tag{25}$$

The compact form of (25) is

$$\dot{x} = f(x) + g(x) + d(t), \tag{26}$$

where $\beta \geq 0$ is unknown, d is bounded disturbance that satisfies $|d(t)| \leq \delta$, for $t \geq 0$, and

$$f(x) = Ax = \left.\frac{\partial f}{\partial x}\right|_{x=0} x = \begin{bmatrix} -d_T & 0 & 0 \\ 0 & -\delta & 0 \\ 0 & p & -c \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix},$$

$$g(x) = \begin{bmatrix} -\beta x_1 x_3 \\ \beta x_1 x_3 \\ 0 \end{bmatrix}, \quad d(t) = \begin{bmatrix} s \\ 0 \\ 0 \end{bmatrix}. \tag{27}$$

Suppose the perturbation $g(x)$ satisfies the uniform bound

$$\|g(x)\|_2 \leq \beta \begin{bmatrix} |x_1||x_3| \\ |x_1||x_3| \\ 0 \end{bmatrix} \leq \frac{\beta}{2} \begin{bmatrix} \|x\|_2 \\ \|x\|_2 \\ 0 \end{bmatrix}. \tag{28}$$

The linearisation about the origin $x = 0$ for the perturbed system in (20) is described by matrix A in (27). The stability analysis of matrix A is given by the eigenvalues

$$|\lambda I - A| = \begin{vmatrix} \lambda + d_T & 0 & 0 \\ 0 & \lambda + \delta & 0 \\ 0 & -p & \lambda + c \end{vmatrix},$$

$$|\lambda I - A| = (\lambda + d_T)(\lambda + \delta)(\lambda + c).$$

Matrix A is Hurwitz when $d_T > 0, \delta > 0, c > 0$.
The converse theorem of Lyapunov is based on linearisation about the origin, $x = 0$. The theorem supposes that matrix A is Hurwitz, in other words the nominal system. Then, there exists a candidate Lyapunov function $V(x) = x^T P x$, which permit to analyse the stability by evaluating its derivative along the trajectories of the nominal system (27) such that

$$\begin{aligned} \dot{V}(x) &= \dot{x}^T P x + x^T P \dot{x}, \\ \dot{V}(x) &= x^T A^T P x + x^T P A x, \\ \dot{V}(x) &= x^T [A^T P + PA] x. \end{aligned}$$

By solving the Lyapunov equation

$$A^T P + PA = -Q, \;\; Q = Q^T > 0. \tag{29}$$

It is possible to find the unique solution with matrix $P = P^T > 0$ be positive definite. By taking the parameter values in Table 1 the matrix P is

$$P = \begin{bmatrix} 25 & 0 & 0 \\ 0 & 3.2902 \times 10^3 & 7.8914 \\ 0 & 7.8914 & 0.2083 \end{bmatrix}. \tag{30}$$

The candidate Lyapunov function $V(x) = x^T Px$ needs to satisfy the following four conditions, for being a positive definite scalar function

1. $\lambda_{min}(P)\|x\|_2^2 \leq V(x) \leq \lambda_{max}(P)\|x\|_2^2$,
   $\lambda_{min}(P) = 0.1894, \ \ \lambda_{max}(P) = 3.2902 \times 10^3$.

2. $\frac{\partial V}{\partial x} f(x) = \frac{\partial V}{\partial x} Ax = -x^T Qx$,
   $\|\frac{\partial V}{\partial x}\|_2 \|Ax\|_2 \leq -\lambda_{min}(Q)\|x\|_2^2$,
   $\lambda_{min}(Q) = 1, \ \ Q = I = Q^T > 0$.

3. $\|\frac{\partial V}{\partial x}\|_2 = \|2x^T P\|_2 \leq 2\|P\|_2\|x\|_2 \leq 2\lambda_{max}(P)\|x\|_2$,
   $2\lambda_{max}(P) = 6.5804 \times 10^3$.

4. $\|\frac{\partial V}{\partial x}\|_2 |d(t)| = |2x^T P||d(t)|$,
   $\|\frac{\partial V}{\partial x}\|_2 |d(t)| \leq 2|P||x||d(t)|$,
   $\leq 2\sum_{i=1}^{3} \lambda_i(P)|x_i||d_i(t)| = 0.5|x_1|$.

Remark 6. *A candidate Lyapunov function $V(x)$ is used to investigate for the nominal system and its stable or asymptotically stable equilibrium point at the origin, and determine if perturbed system (26) can obtain a uniform bounded value.*

By evaluation the derivative of $V(x)$ along the trajectories of perturbed system (26)

$$\dot{V}(x) = \frac{\partial V}{\partial x}\dot{x} = \frac{\partial V}{\partial x} f(x) + \frac{\partial V}{\partial x} g(x) + \frac{\partial V}{\partial x} d(t), \tag{31}$$

where $f(x)$ is a function which describes the nominal system in (26), $g(x)$ is a function which describes the perturbation about the origin in (26) and satisfy the growing bound given in (28) and $d(t)$ is a function for a bounded perturbation in (26). Hence, by using the bound (28) given for $g(x)$, their corresponding results for the function $V(x)$ are given by

$$\begin{aligned} \dot{V}(x) &\leq -\|x\|_2^2 + \left\|\frac{\partial V}{\partial x}\right\|_2 \|g(x)\|_2 + \left\|\frac{\partial V}{\partial x}\right\|_2 \|d(t)\|_2, \\ \dot{V}(x) &\leq -\|x\|_2^2 + \frac{6.5804 \times 10^3}{2}\beta\|x\|_2^3 + 50s\|x\|_2, \\ \dot{V}(x) &\leq -\zeta\|x\|_2^2 + 50s\|x\|_2^2; \ \ 0 < \zeta < 1, \ \ M > 0, \\ \dot{V}(x) &\leq (1-\theta)\zeta\|x\|_2^2; \ \ 0 < \theta < 1. \end{aligned}$$

Then, the function $\dot{V}(x)$ will be negative definite if the following conditions are satisfied

$$\forall\|x\|_2 \geq \min\left\{\frac{50s}{\theta\zeta}, M\right\}, \tag{32}$$

where

$$M = \frac{\beta 6.5804 \times 10^3}{2(1-\zeta)} > 0, \ \ 0 < \theta < 1, \ \ 0 < \zeta < 1.$$

Therefore, the function $\dot{V}(x)$ is negative definite inside the ball $\|x\| < r\sqrt{c_1/c_2}$. The ball defines the region of attraction for the solution, when condition (32) is satisfied. It is concluded that the origin $x = 0$ is exponentially uniform stable and the solution for system (20) is uniformly bounded in the large for disturbances that satisfy $|d(t)| \leq \delta$, for all $t \geq 0$.

3.3 Simulation of trajectories and the region of attraction

For the bound given in (32), the following simulations are shown, with initial condition $T(0) = 520$, $\tilde{T}(0) = 0$ and $V(0) = 1$. The phase space for system (20) is depicted in Figure 1 for parameter values $s = 10$, and $\beta = 2.4 \times 10^{-5}$.

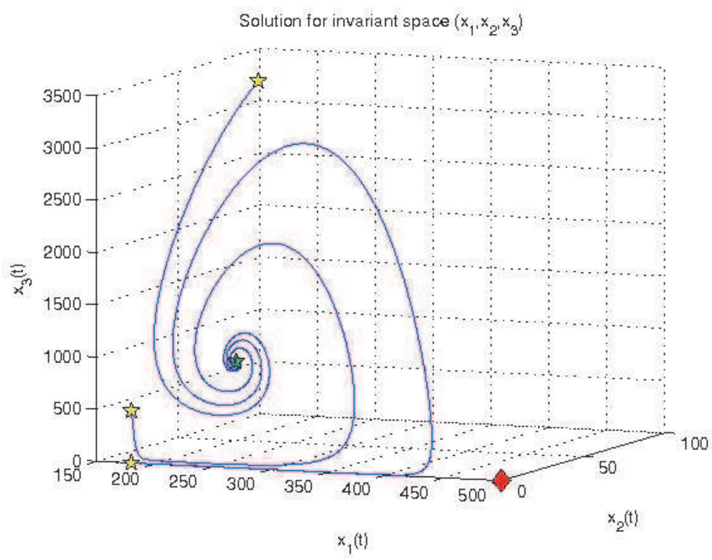

Fig. 1. Phase space for: $s = 10$, $\beta = 2.4 \times 10^{-5}$ with three initial conditions (order from above to bottom): a) $T(0) = 180.2$, $\tilde{T}(0) = 77.6$, $V(0) = 3305$; b) $T(0) = 180.2$, $\tilde{T}(0) = 0$, $V(0) = 500$; c) $T(0) = 180.2$, $\tilde{T}(0) = 0$, $V(0) = 1$.

The result describing the region of attraction is useful for the clinical personal studying HIV behavior, since it allows to predict the infection development and then choose treatment options. This model does not describe the infection behavior when AIDS has already developed. The region of attraction describes the zone for which, given any initial state condition within it, its future dynamics will be particularly slow, i.e. exponentially uniform. In the positive sector ($x_i > 0, i = 1, 2, 3$) of the trajectory space, the solutions will be exponentially uniform, but two different types of conditions are analysed: those starting outside and those starting inside of the domain. The latter are from an invariant set. In Fig. 2, the trajectory corresponds to initial condition given in the paper (Barao & Lemos, 2007). That trajectory belongs to solution with fast dynamics that becomes slow as soon as it traverses the invariant set.

One point which is closer to conditions found in reality is the point $(180.2, 0, 1)$, which is depicted in Fig. 1, c). Here, the viral load is small, but the number of uninfected cells is zero. This makes us think of an HIV-infected patient who is not having a large viral load. This information may be useful to configure control law that locate the starting condition at a point such that no large viral load is generated. It is important to keep in mind that the attraction

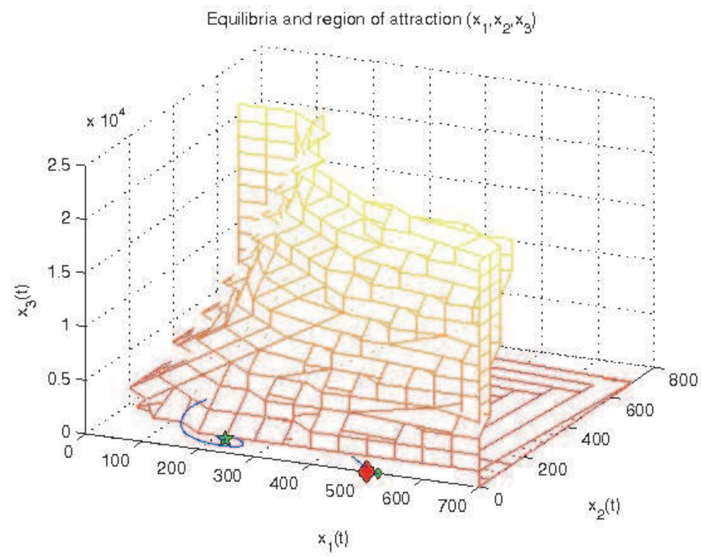

Fig. 2. Region of attraction for: $T(0) = 520$, $\tilde{T}(0) = 0$, $V(0) = 1$.

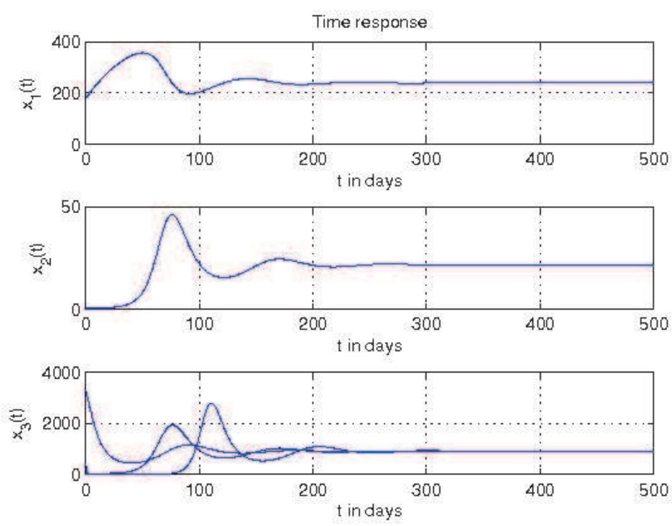

Fig. 3. Time response for three initial conditions: a) $T(0) = 180.2$, $\tilde{T}(0) = 77.6$, $V(0) = 3305$; b) $T(0) = 180.2$, $\tilde{T}(0) = 0$, $V(0) = 500$; c) $T(0) = 180.2$, $\tilde{T}(0) = 0$, $V(0) = 1$.

point is the same, regardless of the the given initial condition. The proposed change in the values causes a shift in the response for the viral load for variable V, without modifying the time response for T and $\tilde{T}$, see Fig. 3. Also, the possibility of the initial condition $(180.2, 0, 500)$ is worth considering in Fig. 1,b) and Fig. 3. That represents the beginning of an infection with a high viral load. This generates a more benign transient concerning the viral load dynamics. The aim of plotting the trajectories generated from different initial conditions is to depict the dynamics generated by the three state HIV model. Remember that the perturbation term $d(t)$ is constant.

4. Conclusions

In the paper of (Barao & Lemos, 2007), the study is made for 3rd order ODE, which focus on the analysis of eigenvalues resulting from linearisation around the equilibrium points (Santos

& Middleton, 2008). The disadvantage of linearizing about the equilibrium point when it is not the origin, is that the non linearities of the system are not taken into account.
Lyapunov converse analysis allows to obtain bounds on the phase space so that the exponential stability of the equilibrium point at the origin is guaranteed.
This means that the system trajectory describes an exponentially uniform trajectory as it approaches to stable equilibrium point. It can be seen that, there are initial conditions which are not within the given sets but their respective trajectories eventually reach the stable equilibrium point.
This dynamic characteristic is studied for the kind of nonlinear system which is studied in this chapter. It must be emphasized that the region of attraction will always determined by the initial conditions and the parameter values. It is also interesting in the future, to study the repulsion region, that means, the region which corresponds to the unstable equilibrium region. Both regions, attraction and repulsion are located in a manifold. The closer the initial condition is to the manifold in which the equilibrium point is located, the less stressful will the patient suffer from the dynamics. That is the main reason to justify the search for manifolds where the uniformly exponentially stable trajectories are found.

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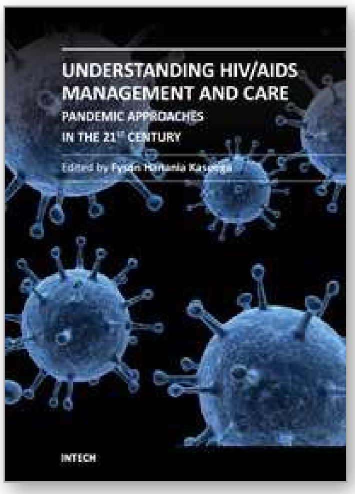

Understanding HIV/AIDS Management and Care - Pandemic Approaches in the 21st Century
Edited by Dr. Fyson Kasenga

ISBN 978-953-307-603-4
Hard cover, 384 pages
Publisher InTech
Published online 14, December, 2011
Published in print edition December, 2011

Like any other book on the subject of HIV/AIDS, this book is not a substitute or exhausting the subject in question. It aims at complementing what is already in circulation and adds value to clarification of certain concepts to create more room for reasoning and being part of the solution to this global pandemic. It is further expected to complement a wide range of studies done on this subject, and provide a platform for the more updated information on this subject. It is the hope of the authors that the book will provide the readers with more knowledge and skills to do more to reduce HIV transmission and improve the quality of life of those that are infected or affected by HIV/AIDS.