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journal homepage: [www.elsevier.com/locate/apm](http://www.elsevier.com/locate/apm)Global dynamics of a mathematical model for HTLV-I infection of CD4<sup>+</sup> T-cells <sup>☆</sup>Liming Cai <sup>a,b,\*</sup>, Xuezhi Li <sup>b</sup>, Mini Ghosh <sup>c</sup><sup>a</sup> College of Mathematics and Information Science, Xinyang Normal University, Xinyang 464000, China<sup>b</sup> Academy of Mathematics and Systems Science, Academia Sinica, Beijing 100190, PR China<sup>c</sup> School of Advanced Sciences, VIT University, Chennai Campus, India

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## ABSTRACT

In this paper, a mathematical model for HTLV-I infection of CD4<sup>+</sup> T-cells is investigated. The force of infection is assumed to be a function in general form, and the resulting incidence term contains, as special cases, the bilinear and the saturation incidences. The model can be seen as an extension of the model [Wang et al. *Mathematical analysis of the global dynamics of a model for HTLV-I infection and ATL progression*, *Math. Biosci.* 179 (2002) 207–217; Song, Li, *Global stability and periodic solution of a model for HTLV-I infection and ATL progression*, *Appl. Math. Comput.* 180(1) (2006) 401–410]. Mathematical analysis establishes that the global dynamics of T-cells infection is completely determined by a basic reproduction number  $\mathcal{R}_0$ . If  $\mathcal{R}_0 \leq 1$ , the infection-free equilibrium is globally stable; if  $\mathcal{R}_0 > 1$ , the unique infected equilibrium is globally stable in the interior of the feasible region.

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## 1. Introduction

Human T-cell lymphotropic virus I (HTLV-I), which is a single-stranded RNA retrovirus, is linked to the development of Adult T-cell leukemia (ATL), among many diseases. HTLV-I Infection is achieved through cell-to-cell contact [1,2]. To describe the T-cell dynamics of the HTLV-I infection and the development of ATL, a mathematical model was first proposed by Stilianakis and Seydel [3]. The model consists of a system of nonlinear ordinary differential equations that divides CD4<sup>+</sup> T cells into four compartments: uninfected CD4<sup>+</sup> T cells, latently infected cells, actively infected cells, and leukemia cells. Let  $T$ ,  $T_L$ ,  $T_A$  and  $T_M$  denote, respectively, the number of cells in the corresponding compartments. This model is formulated as follows:

$$\begin{aligned} \dot{T} &= A - \mu_T T - kT_A T, \\ \dot{T}_L &= kT_A T - (\mu_L + \alpha)T_L, \\ \dot{T}_A &= \alpha T_L - (\mu_A + \rho)T_A, \\ \dot{T}_M &= \rho T_A + \beta T_M \left(1 - \frac{T_M}{T_{Mmax}}\right) - \mu_M T_M, \end{aligned} \quad (1.1)$$

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where  $\Lambda$  is the source of CD4<sup>+</sup> T cells from precursors, the parameters  $\mu_T$ ,  $\mu_L$ ,  $\mu_A$  and  $\mu_M$  represent the death or removal rate of the uninfected, latent infected, actively infected CD4<sup>+</sup> T cells, and ATL cells, respectively. The parameter  $\alpha$  is the transmission rate at which latent infected CD4<sup>+</sup> T cells become actively infected,  $k$  is the infection rate,  $\rho$  is the transmission rate at which actively infected CD4<sup>+</sup> T cells converts to ATL cells. Thus,  $1/\alpha$  and  $1/\rho$  can be regarded as the mean latent and infectious periods, respectively. ATL cells proliferate at a rate  $\beta$  of a classical logistic growth function.  $T_{Mmax}$  is the maximal number that ATL cells proliferate. All parameters in model (1.1) are assumed to be positive constants. The global dynamics of system (1.1) have been further investigated by Wang et al. [4].

The bilinear incidence and the standard incidence (also called proportionate mixing incidence) are adopted by many authors. However, there are a variety of reasons that the above incidence rates may require modification (see, [5–12]). A non-linear incidence rate arising from saturation response of the infection in [13] has been incorporated into the above model. The model is presented in the following form:

$$\begin{aligned}\dot{T} &= \Lambda - \mu_T T - k \frac{T_A}{1 + \alpha_1 T_A} T, \\ \dot{T}_L &= k \frac{T_A}{1 + \alpha_1 T_A} T - (\mu_L + \alpha) T_L, \\ \dot{T}_A &= \alpha T_L - (\mu_A + \rho) T_A, \\ \dot{T}_M &= \rho T_A + \beta T_M \left(1 - \frac{T_M}{T_{Mmax}}\right) - \mu_M T_M.\end{aligned}\quad (1.2)$$

The dynamical behavior of the model (1.2) has been investigated by Song [13]. They observed that the basic reproduction number  $\mathfrak{R}_0$  can determine the global dynamics of T-cells infection, *i.e.*, if  $\mathfrak{R}_0 \leq 1$ , infected T-cells always die out; if  $\mathfrak{R}_0 > 1$ , the unique infected equilibrium is globally stable in the interior of the feasible region. In our model, it is assumed that the incidence rate is of form  $k f(T_A) T$ , where  $k$  is the infection rate which accounts for the overall effects of HTLV-I reproduction such as contact rate and infectivity. Thus, the model (1.2) can be modified into the following form:

$$\begin{aligned}\dot{T} &= \Lambda - \mu_T T - kf(T_A)T, \\ \dot{T}_L &= kf(T_A)T - (\mu_L + \alpha)T_L, \\ \dot{T}_A &= \alpha T_L - (\mu_A + \rho)T_A, \\ \dot{T}_M &= \rho T_A + \beta T_M \left(1 - \frac{T_M}{T_{Mmax}}\right) - \mu_M T_M,\end{aligned}\quad (1.3)$$

where the function  $f(T_A)$  satisfies the following properties:

$$f(0) = 0, \quad f'(T_A) > 0, \quad f''(T_A) \leq 0. \quad (1.4)$$

Obviously, the incidence rate with conditions (1.4) contains the bilinear and the saturation incidences. Thus, the model (1.3) is an extension of the model (1.2). In this paper, we shall perform global analysis for the model (1.3). Especially, we shall show the global stability of the equilibria for the model (1.3) by constructing a suitable Lyapunov function rather than utilizing geometric approach of Li and Muldowney [14].

The organization of this paper is as follows: In the next section, the existence and the local stability of the equilibria in system (1.3) are investigated. In Section 3, the global stability of the equilibria in system (1.3) is discussed. The paper ends with brief remarks.

## 2. Equilibria and their local stability

From the first three equations of the system (1.3), we have

$$\dot{T} + \dot{T}_L + \dot{T}_A = \Lambda - \mu_L T_L - \mu_T T - (\mu_A + \rho) T_A \leq \Lambda - \gamma(T + T_L + T_A),$$

where,  $\gamma = \min\{\mu_L, \mu_T, \mu_A + \rho\}$ . It follows that  $\limsup_{t \rightarrow \infty} (T + T_L + T_A) \leq \Lambda/\gamma$ . Thus, from the last equation of (1.3), we have

$$\dot{T}_M \leq \rho \Lambda/\gamma + \beta T_M (1 - T_M/T_{Mmax}) - \mu_M T_M,$$

which implies that  $\limsup_{t \rightarrow \infty} T_M(t) \leq \bar{T}_M$ . Here  $\bar{T}_M$  is the positive root of the following quadratic equation

$$\rho \Lambda/\gamma + \beta T_M (1 - T_M/T_{Mmax}) - \mu_M T_M = 0.$$

Let

$$\Gamma = \{(T, T_L, T_A, T_M) \in \mathbb{R}_+^4 : T + T_L + T_A \leq \Lambda/\gamma, T_M \leq \bar{T}_M\}.$$

It is easy to verify that the region  $\Gamma$  is positively invariant with respect to (1.3).

Since the first three equations of the system (1.3) do not contain  $T_M$ , we first consider the following subsystem of (1.3).

$$\begin{aligned} \dot{T} &= \Lambda - \mu_T T - kf(T_A)T, \\ \dot{T}_L &= kf(T_A)T - (\mu_L + \alpha)T_L, \\ \dot{T}_A &= \alpha T_L - (\mu_A + \rho)T_A. \end{aligned} \tag{2.1}$$

The subsystem (2.1) describes the infection dynamics of T cells. Obviously, system (2.1) lies in the following feasible region.

$$\Gamma_0 = \{(T, T_L, T_A) \in R_+^3, T + T_L + T_A \leq \Lambda/\gamma\},$$

which is the projection of  $\Gamma$  onto the  $(T, T_L, T_M)$  subspace. System (2.1) obviously has always an infected free equilibrium  $E_0(\Lambda/\mu_T, 0, 0)$ . Now we find the other equilibria of system (2.1). Any equilibrium  $E(T, T_L, T_A)$  of system (2.1) satisfies the following equations:

$$\begin{aligned} \Lambda - \mu_T T - kf(T_A)T &= 0, \\ kf(T_A)T - (\mu_L + \alpha)T_L &= 0, \\ \alpha T_L - (\mu_A + \rho)T_A &= 0. \end{aligned} \tag{2.2}$$

From the second and third equations of (2.2), we obtain

$$T = \frac{(\mu_L + \alpha)T_L}{kf(T_A)}, \quad T_L = \frac{\mu_A + \rho}{\alpha} T_A. \tag{2.3}$$

After substituting (2.3) into the first equation of (2.2), we have

$$g(T_A) \stackrel{\text{def}}{=} \Lambda - \frac{\mu_T(\mu_L + \alpha)(\mu_A + \rho)T_A}{\alpha kf(T_A)} - \frac{(\mu_L + \alpha)(\mu_A + \rho)}{\alpha} T_A. \tag{2.4}$$

From (2.4), it can be easily seen that the function  $g(T_A)$  is negative for large positive  $T_A$ . Now we determine the sign of derivative of the function  $g(T_A)$

$$g'(T_A) = -\frac{\mu_T(\mu_L + \alpha)(\mu_A + \rho) f(T_A) - T_A f'(T_A)}{\alpha k f^2(T_A)} - \frac{(\mu_L + \alpha)(\mu_A + \rho)}{\alpha}. \tag{2.5}$$

From the properties of the function  $f(T_A)$ , in particular,  $f(0) = 0$ , and  $f'(T_A) \leq 0$ , it follows that  $f(T_A) - T_A f'(T_A) \geq 0$ . Consequently, from (2.5), we have  $g'(T_A) < 0$ , for all  $T_A > 0$ . Thus, when the function  $g(T_A)$  satisfies  $g(0) > 0$ , it follows from the above discussions that  $g(T_A) = 0$  has a positive root. Noticing that

$$g(0) = \lim_{T_A \rightarrow 0} g(T_A) = \Lambda - \frac{\mu_T(\mu_L + \alpha)(\mu_A + \rho)}{\alpha kf'(0)}.$$

Let

$$\mathfrak{R}_0 = \frac{\alpha kf'(0)\Lambda}{\mu_T(\mu_L + \alpha)(\mu_A + \rho)}.$$

Thus, we have  $g(0) = \Lambda(1 - \frac{1}{\mathfrak{R}_0})$ . Hence, if  $\mathfrak{R}_0 > 1$ , system (2.1) has a unique chronic-infection equilibrium  $E^*(T^*, T_L^*, T_A^*)$ . Thus, we first establish the following results:

**Theorem 2.1.** *If  $\mathfrak{R}_0 \leq 1$ , system (2.1) has only the infection-free equilibrium  $E_0(\Lambda/\mu_T, 0, 0)$ ; If  $\mathfrak{R}_0 > 1$ , system (2.1) has two equilibria: infection-free equilibrium  $E_0$  and a unique endemic equilibrium  $E^*(T^*, T_L^*, T_A^*)$  in the interior of  $\Gamma_0$ .*

Let  $P^*(T^*, T_L^*, T_A^*, T_M^*)$  be a chronic infection equilibrium of system (1.3), where  $T^*$ ,  $T_L^*$ , and  $T_A^*$  is given in (2.2),  $T_M^*$  satisfies the following quadratic equation

$$\beta T_M^2 - T_{M_{\max}}(\beta - \mu_M)T_M - \rho T_A^* T_{M_{\max}} = 0.$$

Similar to analysis of paper [4], we have following results

**Theorem 2.2.** *If  $\mathfrak{R}_0 \leq 1$ ,  $P_0(\Lambda/\mu_T, 0, 0, 0)$  is the only uninfected equilibrium of system (1.3) for  $\beta \leq \mu_M$ ;  $P_1(\Lambda/\mu_T, 0, 0, T_{M_{\max}}(\beta - \mu_M)/\beta)$  is a second uninfected equilibrium of system (1.3) for  $\beta > \mu_M$ . If  $\mathfrak{R}_0 > 1$ , there exists a unique chronic infection equilibrium  $P^*(T^*, T_L^*, T_A^*, T_M^*)$  in the interior of  $\Gamma$ .*

**Remark 1.**  $\mathfrak{R}_0$  can be regarded as a basic reproduction number or the contact number in the literature of epidemiological models [4,15]. It represents the average number of secondary infection caused by a single primary actively infected T cell introduced in a pool of susceptible T cells during its entire infection period.

We now investigate the local geometric properties of the equilibria in system (2.1).

Linearizing system (2.1) at equilibrium  $E_0\left(\frac{A}{\mu_T}, 0, 0\right)$ , we have

$$(\lambda + \mu_T)\left(\lambda^2 + (\mu_L + \alpha + \mu_A + \rho)\lambda + (\mu_L + \alpha)(\mu_A + \rho) - \alpha kf'(0)\frac{A}{\mu_T}\right) = 0. \tag{2.6}$$

Clearly, one root of the above Eq. (2.6) is  $\lambda_1 = -\mu_T$ , the other two roots are determined by the quadratic equation

$$\lambda^2 + (\mu_L + \alpha + \mu_A + \rho)\lambda + (\mu_L + \alpha)(\mu_A + \rho) - \alpha kf'(0)\frac{A}{\mu_T} = 0. \tag{2.7}$$

Since  $\mathfrak{R}_0 < 1$  is equivalent to  $(\mu_L + \alpha)(\mu_A + \rho) > \alpha kf'(0)\frac{A}{\mu_T}$ , hence all roots of Eq. (2.7) have negative real parts if and only if  $\mathfrak{R}_0 < 1$ . If  $\mathfrak{R}_0 > 1$ , the characteristic Eq. (2.6) has one eigenvalue with positive real part. So,  $E_0$  is unstable with  $\dim W^s(E_0) = 2$  and  $\dim W^u(E_0) = 1$ .

Now let us consider the stability of  $E_0$  for  $\mathfrak{R}_0 = 1$ . In fact, since  $\mathfrak{R}_0 = 1$  is equivalent to  $(\mu_L + \alpha)(\mu_A + \rho) = \alpha kf'(0)\frac{A}{\mu_T}$ , thus, from Eq. (2.7), we have

$$h(\lambda) = \lambda^2 + (\mu_L + \alpha + \mu_A + \rho)\lambda. \tag{2.8}$$

Obviously,  $\lambda = 0$  is one of roots of Eq. (2.8), the other root is  $\lambda = -(\mu_L + \alpha + \mu_A + \rho) < 0$ . Hence,  $E_0$  is stable for  $\mathfrak{R}_0 = 1$ . We now give the following stability results for  $E_0$ .

**Theorem 2.3.** *If  $\mathfrak{R}_0 < 1$ , the disease-free equilibrium  $E_0$  of system (2.1) is locally asymptotically stable. If  $\mathfrak{R}_0 = 1$ ,  $E_0$  is stable. If  $\mathfrak{R}_0 > 1$ ,  $E_0$  is a saddle point with  $\dim W^s(E_0) = 2$  and  $\dim W^u(E_0) = 1$ .*

Now we discuss local stability of the infected equilibrium  $E^*$  for  $\mathfrak{R}_0 > 1$ . Linearizing system (2.1), the jacobian matrix at  $E^*$  is given by

$$J = \begin{pmatrix} -\mu_T - kf(T_A^*) & 0 & -kf'(T_A^*)T^* \\ kf(T_A^*) & -\mu_L - \alpha & kf'(T_A^*)T^* \\ 0 & \alpha & -\mu_A - \rho \end{pmatrix}, \tag{2.9}$$

The characteristic equation associated with  $J$  is

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0, \tag{2.10}$$

where,

$$\begin{aligned} a_1 &= \mu_A + \rho + \mu_L + \alpha + \mu_T + kf(T_A^*) > 0, \\ a_2 &= (\mu_A + \rho + \mu_L + \alpha)(\mu_T + kf(T_A^*)) + (\mu_A + \rho)(\mu_L + \alpha) - \alpha kf'(T_A^*)T^*, \\ a_3 &= (\mu_T + kf(T_A^*))(\mu_L + \alpha)(\mu_A + \rho) - \alpha k\mu_T f'(T_A^*)T^*. \end{aligned}$$

Using  $0 < f'(T_A^*) \leq f(T_A^*)/T_A^*$ , and (2.3), we obtain

$$\begin{aligned} a_2 &\geq (\mu_A + \rho + \mu_L + \alpha)(\mu_T + kf(T_A^*)) + (\mu_A + \rho)(\mu_L + \alpha) - \alpha kf(T_A^*)/T_A^* T^* \\ &= (\mu_A + \rho + \mu_L + \alpha)(\mu_T + kf(T_A^*)) + (\mu_A + \rho)(\mu_L + \alpha) - (\mu_A + \rho)(\mu_L + \alpha) > 0, \\ a_3 &= (\mu_A + \rho)(\mu_L + \alpha)(\mu_T + kf(T_A^*)) - \alpha k\mu_T f'(T_A^*)T^* \geq (\mu_A + \rho)(\mu_L + \alpha)(\mu_T + kf(T_A^*)) - \alpha k\mu_T f(T_A^*)/T_A^* T^* \\ &= kf(T_A^*)(\mu_A + \rho)(\mu_L + \alpha) > 0. \end{aligned}$$

To finish the proof, we shall show that  $\Delta = a_1a_2 - a_3 > 0$  by using the Routh–Hurwitz criterion. In fact,

$$\begin{aligned} \Delta &= a_1(\mu_A + \rho)(\mu_T + kf(T_A^*)) + a_1[(\mu_A + \alpha)(\mu_L + \alpha) - \alpha kf'(T_A^*)T^*] + (\mu_A + \rho)(\mu_L + \alpha) \times (\mu_T + kf(T_A^*)) \\ &\quad + (\mu_L + \alpha + \mu_T + kf(T_A^*))(\mu_L + \alpha)(\mu_T + kf(T_A^*)) - (\mu_A + \rho)(\mu_L + \alpha)(\mu_T + kf(T_A^*)) + \alpha k\mu_T f'(T_A^*)T^* \\ &\geq a_1(\mu_A + \rho)(\mu_T + kf(T_A^*)) + a_1 \underbrace{\left[ (\mu_A + \alpha)(\mu_L + \alpha) - \alpha kf'(T_A^*)T^* \right]}_{=0} + (\mu_L + \alpha + \mu_T + kf(T_A^*))(\mu_L + \alpha)(\mu_T + kf(T_A^*)) \\ &\quad + \alpha k\mu_T f'(T_A^*)T^* > 0 \end{aligned}$$

(It is easy to calculate that the term in the bracket is zero by Eq. (2.3).)

By Routh–Hurwitz criterion, we have

**Theorem 2.4.** *If  $\mathfrak{R}_0 > 1$ , the unique equilibrium  $E^*$  of system (2.1) is locally asymptotically stable.*

By the above discussion, we have obtained that if  $\mathfrak{R}_0 > 1$ ,  $E_0$  is unstable. From the jacobian matrix  $J_0$  of system (2.1) at  $E_0$ , we obtain that  $J_0$  possesses one eigenvalue with positive real part and two eigenvalues with negative real part. Similar to the proof in [16], and by applying the Perron–Frobenius Theorem, we can show  $W^s(E_0) \cap \text{int}(R_+^3) = \emptyset$ , where  $W^s(E_0)$  denotes the

stable manifold of  $E_0$ . Thus, by applying Theorem 4.6 in [17], it is easy to show the uniform persistence of system (2.1). Therefore, system (1.3) is uniformly persistent. Biologically, the uniform persistence characterizes that a primary HTLV-I infection of T cells leads to chronic infection.

Therefore, we have the following result.

**Theorem 2.5.** *If  $\mathfrak{R}_0 > 1$ , then system (1.3) is uniformly persistent in Int  $\Gamma$ , i.e., there exists a constant  $0 < \eta < 1$  (independent of initial conditions), such that any solution  $(T(t), T_L(t), T_A(t), T_M(t))$  of (1.3) satisfies  $\liminf_{t \rightarrow +\infty} T(t) > \eta, \liminf_{t \rightarrow +\infty} T_L(t) > \eta, \liminf_{t \rightarrow +\infty} T_A(t) > \eta$ , and  $\liminf_{t \rightarrow +\infty} T_M(t) > \eta$ .*

### 3. The global stability of the equilibria

In this section, we shall provide a sufficient condition preventing oscillations, and lead to a globally asymptotically stable for chronic infection steady state. That is, if  $\mathfrak{R}_0 \leq 1$ , the infection-free equilibrium  $E_0$  is globally stable; and if  $\mathfrak{R}_0 > 1$ , the unique chronic-infection equilibrium  $E^*$  is globally stable in the feasible region. To do this, we first consider the following function

$$V_1(T, T_A, T_L) = T - T^* \ln T + \frac{\mu_L + \alpha}{\alpha} \left( T_A - f(T_A^*) \int_{T_A^*}^{T_A} \frac{d\tau}{f(\tau)} \right) + T_L - T_L^* \ln T_L. \tag{3.1}$$

It is obviously that  $V_1(T, T_A, T_L)$  is well defined and continuous for all  $T, T_A, T_L \geq 0$  in the feasible region  $\Gamma_0$ . From (3.1), we have the following facts:

$$\begin{aligned} \frac{\partial V_1}{\partial T} &= 1 - \frac{T^*}{T}, & \frac{\partial V_1}{\partial T_A} &= \frac{\mu_L + \alpha}{\alpha} \left[ 1 - \frac{f(T_A^*)}{f(T_A)} \right], & \frac{\partial V_1}{\partial T_L} &= 1 - \frac{T_L^*}{T_L}, \\ \frac{\partial^2 V_1}{\partial T^2} &= \frac{T^*}{T^2} > 0, & \frac{\partial^2 V_1}{\partial T_A^2} &= \frac{\mu_L + \alpha}{\alpha} \frac{f(T_A^*)f'(T_A)}{f^2(T_A)} > 0, & \frac{\partial^2 V_1}{\partial T_L^2} &= \frac{f(T^*)}{T_L^2} > 0, \\ \frac{\partial^2 V_1}{\partial T_A \partial T} &= \frac{\partial^2 V_1}{\partial T_L \partial T} = \frac{\partial^2 V_1}{\partial T_L \partial T_A} = 0. \end{aligned}$$

Hence, the existing unique equilibrium  $E^*$  (for  $\mathfrak{R}_0 > 1$ ) is the only extremum and global minimum of the function, and  $V_1(T, T_A, T_L) \rightarrow \infty$  at the boundary. So,  $V_1(T, T_A, T_L)$  is indeed a Lyapunov function.

Calculating the derivation of  $V_1$  along the solutions of (2.1) and using (2.2), we obtain that

$$\begin{aligned} \frac{dV_1}{dt} &= \dot{T} - \frac{T^*}{T} \dot{T} + \frac{\mu_L + \alpha}{\alpha} \left( \dot{T}_A - \frac{f(T_A^*)}{T_A} \dot{T}_A \right) + \dot{T}_L - \frac{T_L^*}{T_L} \dot{T}_L \\ &= \left( 1 - \frac{T^*}{T} \right) (\lambda - \mu_T T - kf(T_A)T) + \frac{\mu_L + \alpha}{\alpha} \left[ 1 - \frac{f(T_A^*)}{T_A} \right] [\alpha T_L - (\mu_A + \rho)T_A] - \left( 1 - \frac{T_L^*}{T_L} \right) (kf(T_A)T - (\mu_L + \alpha)T_L) \\ &= \mu_T T^* \left( 2 - \frac{T}{T^*} - \frac{T^*}{T} \right) - kf(T_A)T^* \left( \frac{T}{T^*} + \frac{T}{T^*} \frac{f(T_A)}{f(T_A^*)} \frac{T_L}{T_L} + \frac{f(T_A^*)}{f(T_A)} \frac{T_L}{T_L} - 2 \right) + kf(T_A^*)T^* \left( \frac{f(T_A)}{f(T_A^*)} - \frac{T_A}{T_A^*} + \frac{T_A}{T_A^*} \frac{f(T_A)}{f(T_A)} \right) \\ &= -\mu_T T^* \left( \frac{T}{T^*} + \frac{T^*}{T} - 2 \right) - kf(T_A)T^* \left( \frac{T^*}{T} + \frac{T}{T^*} \frac{f(T_A)}{f(T_A^*)} \frac{T_L}{T_L} + \frac{f(T_A^*)}{f(T_A)} \frac{T_L}{T_L} - 3 \right) \\ &\quad + kf(T_A^*)T^* \left( 1 - \frac{f(T_A^*)}{f(T_A)} \right) \left( \frac{f(T_A)}{f(T_A^*)} - \frac{T_A}{T_A^*} \right). \end{aligned} \tag{3.2}$$

Since the arithmetic mean is greater than or equal to the geometric mean, we have

$$\begin{aligned} \frac{T}{T^*} + \frac{T^*}{T} &\geq 2, \quad \text{for all } T \geq 0 \\ \frac{T^*}{T} + \frac{T}{T^*} \frac{f(T_A)}{f(T_A^*)} \frac{T_L}{T_L} + \frac{f(T_A^*)}{f(T_A)} \frac{T_L}{T_L} &\geq 3, \quad \text{for all } T, T_A, T_L \geq 0. \end{aligned} \tag{3.3}$$

Since the function  $f(T_A)$  is concave, it is easy to obtain the following inequalities,

$$\begin{aligned} \frac{f(T_A)}{f(T_A^*)} &\geq \frac{T_A}{T_A^*}, \quad \text{for } 0 \leq T_A \leq T_A^* \\ \frac{f(T_A)}{f(T_A^*)} &\leq \frac{T_A}{T_A^*} \quad \text{for } T_A > T_A^* \end{aligned}$$

So, we have

$$\left( 1 - \frac{f(T_A^*)}{f(T_A)} \right) \left( \frac{f(T_A)}{f(T_A^*)} - \frac{T_A}{T_A^*} \right) \leq 0, \tag{3.4}$$

with equality if and if  $T_A = T_A^*$ .

Hence, it follows from (3.2), (3.3) and (3.4) that  $\frac{dV_1(T, T_L, T_A)}{dt} \leq 0$ . The equality  $\frac{dV_1(T, T_L, T_A)}{dt} = 0$  holds if and only if  $T = T^*, T_A = T_A^*, T_L = T_L^*$ . Thus, the largest compact invariant set in  $\Gamma_0 = \{(T, T_L, T_A) \mid V_1(T, T_L, T_A) = 0\}$  is the singleton  $E^*$ . By LaSalle invariance principle [18] and Theorem 2.4, we can conclude that the infected equilibrium  $E^*$  of system (2.1) is globally asymptotically stable for  $\mathfrak{R}_0 > 1$ .

At last, we consider the global stability of the infection-free equilibrium  $E_0$ .

Let us consider the following Lyapunov function:

$$V_2(T, T_A, T_L) = T - \frac{A}{\mu_T} \ln T + \frac{\mu_L + \alpha}{\alpha} T_A + T_L. \tag{3.5}$$

Calculating the derivation of  $V_2$  along the solutions of (2.1), we have

$$\frac{dV_2}{dt} = \dot{T} - \frac{A}{\mu_T} \frac{\dot{T}}{T} + \frac{\mu_L + \alpha}{\alpha} \dot{T}_A + \dot{T}_L = -\frac{\mu_T}{T} \left(T - \frac{A}{\mu_T}\right)^2 + \frac{kA}{\mu_T} T_A \left(\frac{f(T_A)}{T_A} - \frac{(\mu_L + \alpha)(\mu_A + \rho)\mu_T}{\alpha k A}\right). \tag{3.6}$$

Using the concavity of the function  $f(T_A)$ , it is easy to obtain that  $f'(0) \geq f(T_A)/T_A(t)$ . Hence, from (3.6), we have

$$\frac{dV_2}{dt} \leq -\frac{\mu_T}{T} \left(T - \frac{A}{\mu_T}\right)^2 + \frac{kA f'(0)}{\mu_T} T_A \left(1 - \frac{(\mu_L + \alpha)(\mu_A + \rho)\mu_T}{\alpha k A f'(0)}\right) \leq -\frac{\mu_T}{T} \left(T - \frac{A}{\mu_T}\right)^2 + \frac{kA f'(0)}{\mu_T} T_A \left(1 - \frac{1}{\mathfrak{R}_0}\right) \leq 0 \text{ (if } \mathfrak{R}_0 \leq 1\text{)}.$$

Thus, the maximal compact invariant set in  $\{(T, T_L, T_A) \in \Gamma_0 : dV_2/dt = 0\}$  is singleton  $\{E_0\}$  when  $\mathfrak{R}_0 \leq 1$ . The global stability of  $E_0$  follows from the LaSalle Invariant Principle [18].

In summary, we have the following conclusions.

**Theorem 3.1.** *If  $\mathfrak{R}_0 \leq 1$ , then the infection-free equilibrium  $E_0$  is globally asymptotically stable in  $\Gamma_0$ ; If  $\mathfrak{R}_0 > 1$ , then  $E_0$  is unstable and the unique chronic-infection equilibrium  $E^*$  is globally asymptotically stable in  $\text{int } \Gamma_0$ .*

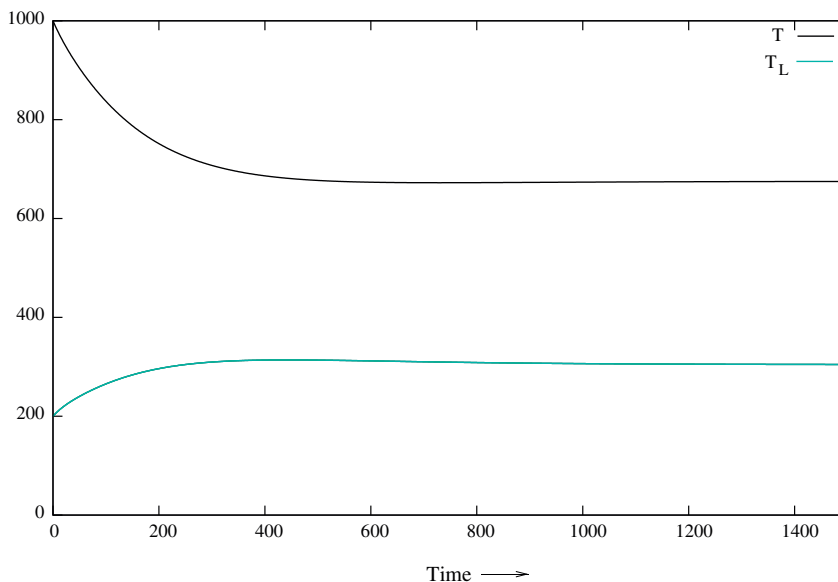
Finally, from systems (1.1), (1.2) and (1.3), we know that the proliferation of ATL cells is always determined by the following equation

$$\dot{T}_M = \rho T_A + \beta T_M \left(1 - \frac{T_M}{T_{M\max}}\right) - \mu_M T_M.$$

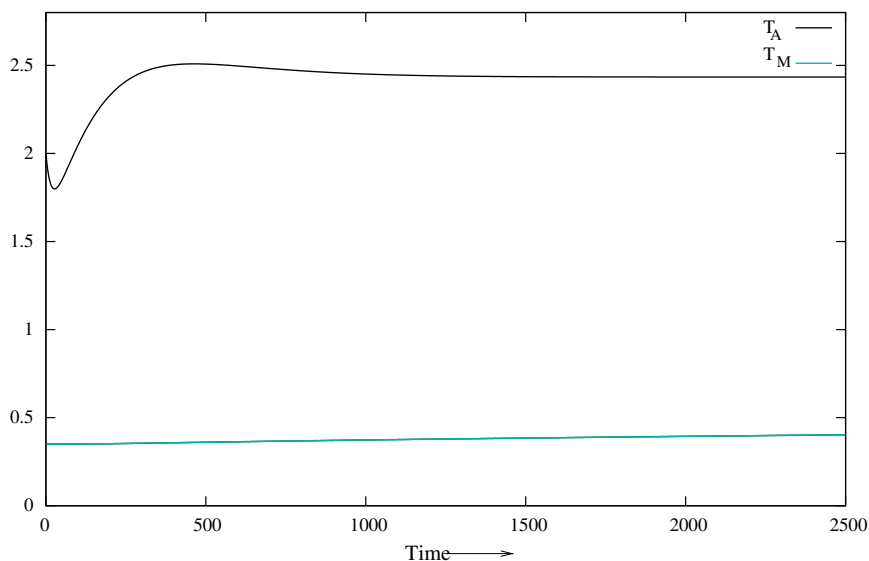
Hence, similar to discussions in [4,13], together with the information on the T-cell dynamics obtained in the previous sections, we obtain the following results on the global dynamics of (1.3).

**Theorem 3.2.** *Suppose that  $\mathfrak{R}_0 \leq 1$ . Then*

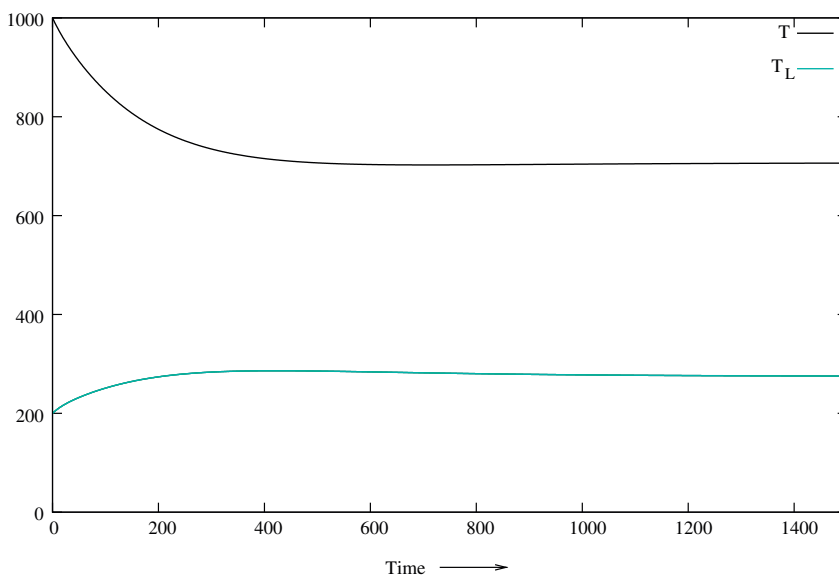
- (1) *If  $\beta \leq \mu_T$ , then the infection-free equilibrium  $P_0(A/\mu_T, 0, 0, 0)$  is globally stable in  $\Gamma_0$ ;*



**Fig. 1.** Variation of  $T, T_L$  with time showing the stability of the chronic-infection equilibrium for the parameter values  $A = 6, \mu_T = 0.006, k = 0.1, a = 0.1, b = 6, \mu_L = 0.006, \alpha = 0.0004, \mu_A = 0.05, \rho = 0.00004, \beta = 0.0003, \mu_M = 0.0005, T_{M\max} = 2200$ .



**Fig. 2.** Variation of  $T_A, T_M$  with time showing the stability of the chronic-infection equilibrium for the parameter values  $\lambda = 6, \mu_T = 0.006, k = 0.1, a = 0.1, b = 6, \mu_L = 0.006, \alpha = 0.0004, \mu_A = 0.05, \rho = 0.00004, \beta = 0.0003, \mu_M = 0.0005, T_{Mmax} = 2200$ .

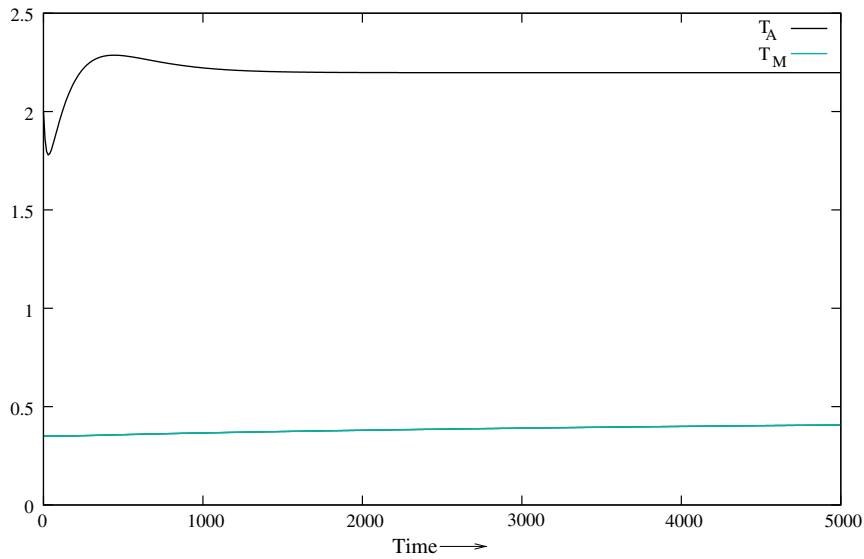


**Fig. 3.** Variation of  $T, T_L$  with time showing the stability of the chronic-infection equilibrium for the parameter values  $\lambda = 6, \mu_T = 0.006, k = 0.1, a = 0.07, b = 0.2, \mu_L = 0.006, \alpha = 0.0004, \mu_A = 0.05, \rho = 0.00004, \beta = 0.0003, \mu_M = 0.0005, T_{Mmax} = 2200$ .

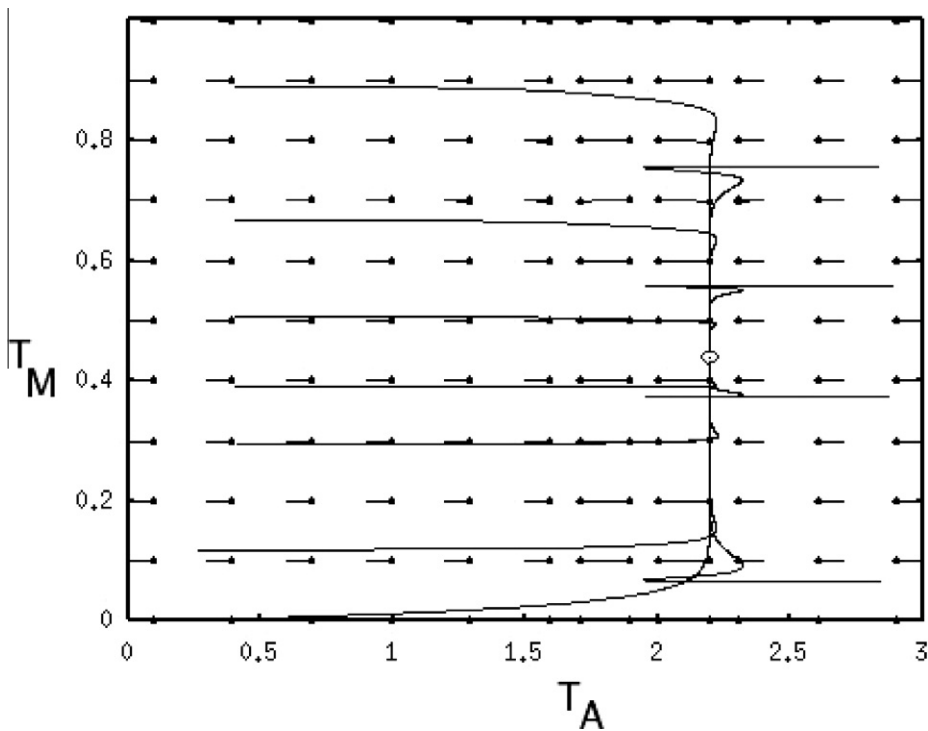
(2) If  $\beta > \mu_T$ , then the infection-free equilibrium  $P_0(\lambda/\mu_T, 0, 0, 0)$  is unstable and the second infection-free equilibrium  $P_1(\lambda/\mu_T, 0, 0, T_{Mmax}(\beta - \mu_M)/\beta)$  is globally stable in  $\Gamma/\{(T, 0, 0, 0): 0 \leq T(t) \leq \lambda/\mu_T\}$ .

**Theorem 3.3.** Suppose that  $\mathfrak{R}_0 > 1$ . Then  $E_0$  is unstable and the unique chronic-infection equilibrium  $P^*(T^*, T_L^*, T_A^*, T_M^*)$  is globally stable in  $\text{int } \Gamma$ .

This result is demonstrated in following Figures. Figs. 1, 2 are showing the stability of the chronic-infection equilibrium (675.24, 304.46, 2.4338, 0.48659) when the function  $f(T_A)$  is given by  $\frac{aT_A}{1+bT_A}$  and  $R_0 = 2.081668$ . Figs. 3,4 are demonstrating the same result for the function  $f(T_A)$  as  $a(1 - \exp(-b T_A))$ , when  $R_0 = 1.748601$  and chronic-infection equilibrium is given by (706.74, 274.93, 2.1977, 0.4394). Finally, Fig. 5 is showing the phase plot of  $T_M$  versus  $T_A$  which clearly shows that chronic-infection equilibrium is stable.



**Fig. 4.** Variation of  $T_A$ ,  $T_M$  with time showing the stability of the chronic-infection equilibrium for the parameter values  $\lambda = 6$ ,  $\mu_T = 0.006$ ,  $k = 0.1$ ,  $a = 0.07$ ,  $b = 0.2$ ,  $\mu_L = 0.006$ ,  $\alpha = 0.0004$ ,  $\mu_A = 0.05$ ,  $\rho = 0.00004$ ,  $\beta = 0.0003$ ,  $\mu_M = 0.0005$ ,  $T_{M\max} = 2200$ .



**Fig. 5.** Phase plot of  $T_M$  versus  $T_A$  showing the stability of the chronic-infection equilibrium for the parameter values  $\lambda = 6$ ,  $\mu_T = 0.006$ ,  $k = 0.1$ ,  $a = 0.07$ ,  $b = 0.2$ ,  $\mu_L = 0.006$ ,  $\alpha = 0.0004$ ,  $\mu_A = 0.05$ ,  $\rho = 0.00004$ ,  $\beta = 0.0003$ ,  $\mu_M = 0.0005$ ,  $T_{M\max} = 2200$ .

#### 4. Concluding remarks

In system (1.3), if we assume  $f(T_A) = \frac{T_A}{1 + \alpha_1 T_A}$ , the function  $f(T_A)$  obviously satisfies the conditions (1.4), and system (1.3) becomes system (1.2). Our results obtained in this paper have the same conclusions established in the paper [4,13], i.e., the global dynamics of system (1.1), (1.2) and (1.3) are completely determined by a basic reproduction number  $\mathfrak{R}_0$ . More specifically, if  $\mathfrak{R}_0 \leq 1$ , no chronic HLTV-I infection of T-cells is possible and ATL cells demonstrate a typical logistical behav-



our: if  $\beta \leq \mu_T$ , any ATL cells present will die out and the only uninfected equilibrium  $P_0(A/\mu_T, 0, 0, 0)$  is globally stable in the feasible region; if  $\beta > \mu_T$ , a second uninfected equilibrium  $P_1(A/\mu_T, 0, 0, T_{M_{\max}}(\beta - \mu_M)/\beta)$  exists and is globally stable in the feasible region; any existing ATL cells will proliferate to the carrying capacity  $T_{M_{\max}}(\beta - \mu_M)/\beta$ ; if  $\mathfrak{R}_0 > 1$ , a primary HTLV-I infection T-cells always leads to chronic infection, and the unique chronic-infection equilibrium  $P^*(T^*, T_L^*, T_A^*, T_M^*)$  exists and is globally stable in the feasible region. System (1.1) and (1.2) with the bilinear incidence and the saturation infection rate, respectively, can be regarded as special cases of system (1.3).

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