

Numerical approximation of basic reproduction number for an age-structured HIV infection model with both virus-to-cell and cell-to-cell transmissions

Kangkang Chang^a, Qimin Zhang^{a,*}

^a*School of Mathematics and Statistics, Ningxia University, Yinchuan, 750021, P.R. China*

Abstract

In general, the basic reproduction number (\mathcal{R}_0) cannot be explicitly calculated for HIV(Human Immunodeficiency Virus) infection model with age-structured in a infinite dimensional spaces. To find \mathcal{R}_0 , we need to transform the HIV model into a finite-dimensional space. In this paper, we are absorbed in numerical approximation of \mathcal{R}_0 , which is the non-negative dominant eigenvalues of the positive irreducible matrices whose spectrum radius is defined as the next generation matrix. The linear operators generated by infected population are discretized into ordinary differential equations in a finite n-dimensional space. Thus, the abstract problem is transformed to find the positive dominant eigenvalues of the next generation matrix, we obtain a threshold $\mathcal{R}_{0,n}$. Based on the spectral approximation theory, we show that $\mathcal{R}_{0,n} \rightarrow \mathcal{R}_0$ as $n \rightarrow +\infty$. Finally, by virtue of a numerical simulation, we demonstrate the results of the theorem.

Keywords: Numerical approximation, Basic reproduction number, Age-structure HIV infection model, Spectral radius

1. Introduction

As far as we know, HIV is a malignant infectious disease with a very high fatality rate, which brings great harm to human life and health. When the body infected with HIV, the body's immune cells could be destroyed and the human immune system can be reduced, causing the infected person to gradually lose the ability to resist various diseases and eventually lead to death. Generally, HIV can be transmitted through two fundamental modes, the direct cell-to-cell transmission[1–4] and the classical virus-to-cell infection[5–7]. During both infection modes, the virus-to-cell transmission can occur from infected cells to healthy cells, for the cell-to-cell transmission, HIV infection be considered as uninfected cells are only infected by the movement of viruses. To analyze the pathogenesis of HIV infection, some people considered the HIV infection model with both virus-to-cell and cell-to-cell transmission[8–10], and using \mathcal{R}_0 to understand threshold dynamics

Email addresses: changkangkang86@sina.com (Kangkang Chang^a), zhangqimin64@sina.com (Qimin Zhang^{a,*})

* Author to whom any correspondence should be addressed.

of HIV infection model. In [8], on the basis of the basic reproduction number, Yang completed the global stability analysis of the model. In [9], Wang et al. proved the local stability of HIV infection model. In [10], Wang showed that the model has a threshold dynamics.

It is worth noting that the article mentioned above are based on the analysis of ordinary differential equation (ODE) model. In fact, the HIV infection model is also related to age, at the same time, the age structure makes the biological manifestation of HIV-1 infection more real [11]. Therefore, it is necessary to study HIV infection model with age structure. The literature [12] explored the effects of two infection patterns on virus generation and transmission by establishing a hybrid model of age-structure. In [13], Shen et al. investigated that the basic reproduction number is sensitive to some parameters and the effect of parameters on infected individuals. In [14], by constructing proper Lyapunov function, the dynamic properties of age structure model are established. The results show that the global asymptotic stability depends on the size of the basic reproduction number. Although they gave the expression form of the \mathcal{R}_0 , which is the non-negative dominant eigenvalues of the positive irreducible matrices whose spectrum radius is defined as the next generation matrix. On account of the partial differential equation contains the age structure and the integral terms, for example [14], $\mathcal{R}_0 = ks \int_0^{a+} p(a)\sigma(a)da/dc$, so that it is difficult to give the numerical solution of \mathcal{R}_0 . Therefore, it is more important to approximate the basic reproduction number by numerical methods.

In [15, 16], The author investigated the numerical approximation of the basic reproduction number for SIRS (Susceptible-Infective-Recovered-Susceptible) models. However, there are few studies on the calculation of the basic reproduction number of the HIV model. Therefore, in order to better understand the numerical solution of basic reproductive number. In this paper, our main goal is to give the numerical approximation of the basic reproduction number for an age-structured HIV infection model with both virus-to-cell and cell-to-cell transmissions, we use the backward Euler method to discretize the HIV model into a finite dimensional space, so that we can find the non-negative dominant eigenvalues of the positive irreducible matrices whose spectrum radius is defined as the next generation matrix. Subsequently, based on spectral approximation theory [17], we provide the next generation operator under relatively weak conditions and obtain the numerical solution of \mathcal{R}_0 .

The structure of the article is as follows, next, we consider HIV transmission models of the age structure in virus-to-cell and cell-to-cell in Section 2, by the spectral radius of a linear operator, we obtain \mathcal{R}_0 . In Section 3, we apply the spectral approximation theory to present the convergence theorem of the basic reproduction ratio. While, we give an assumption to prove that the generation operator is compact. In Section 4, numerical simulation is given to prove the theoretical results. In Section 5 concluding remarks are given .

2. Model and basic reproduction number

Based on the work of Xu et al.[22], here, we add the effect of age after infection. In view of this, we consider the following HIV transmission models of the age structure in virus-to-cell and cell-to-cell.

$$\begin{cases} \frac{\partial U(a, t)}{\partial t} + \frac{\partial U(a, t)}{\partial a} = -u(a)U(a, t) - \beta_1 U(a, t)W(t) - U(a, t) \int_0^{a_{\dagger}} \beta(a, \varsigma)V(t, \varsigma)d\varsigma, \\ \frac{\partial V(a, t)}{\partial t} + \frac{\partial V(a, t)}{\partial a} = U(a, t) \int_0^{a_{\dagger}} \beta(a, \varsigma)V(t, \varsigma)d\varsigma - \mu(a)V(a, t), \\ \frac{dW(t)}{dt} = \int_0^{a_{\dagger}} l(a)V(a, t)da - cW(t), \end{cases} \quad (1)$$

with boundary condition

$$U(0, t) = s, \quad V(0, t) = \beta_1 U(0, t)W(t), \quad t > 0 \quad (2)$$

and initial condition

$$H_0 := (U(\cdot, 0), V(\cdot, 0), W(0)) = (U_0(\cdot), v_0(\cdot), W_0) \in \mathcal{F}, \quad (3)$$

In (1), $U(a, t)$ and $V(a, t)$ represent the concentration of uninfected cells and infected cells of age a at time t , respectively. $W(t)$ represents the concentration of infectious virus at time t . where $\mathcal{F} = L^1(0, a_{\dagger}) \times L^1(0, a_{\dagger}) \times \mathbb{R}^+$, $L^1(0, a_{\dagger})$ is the set of all integrable functions on $(0, a_{\dagger})$, and $\mathbb{R}^+ = [0, \infty)$. Other parameters are explained in Table 1.

Table 1: Definitions of all parameters

Parameters	Description
s	replacement rate of healthy cells
$u(a)$	natural death rate of uninfected cells with age a
β_1	transmission rate from infected cells to infected cells
$\beta(a, \varsigma)$	the age-dependent infection rate of productively infected cells
a_{\dagger}	maximum age
$\mu(a)$	per capita mortality rate of infected cells with age
$l(a)$	age-dependent viral production rate of infected cell
c	the clearance rate of virions

Clearly, system (1) always exists an infection-free steady state $E(se^{-\int_0^a u(s)ds}, 0, 0)$. We substitute $U(a, t) = se^{-\int_0^a u(s)ds}$ into the second equation of (1), then we define two linear operators on the space $X := L^1(0, a_{\dagger})$.

$$\begin{cases} \mathcal{A}\nu(a) := -\frac{d}{da}\nu(a) - \mu(a)\nu(a) \\ \mathcal{F}\nu(a) := se^{-\int_0^a u(s)ds} \int_0^{a_{\dagger}} \beta(a, \varsigma)\nu(\varsigma)d\varsigma, \end{cases} \quad (4)$$

$\text{Dom}(\mathcal{A})$ has the following definition

$$\text{Dom}(\mathcal{A}) := \left\{ \nu \in X : \nu \text{ is absolutely continuous on } [0, a_{\dagger}], \quad \frac{d}{da}\nu \in X \right\}.$$

Using operators \mathcal{A} and \mathcal{F} , we obtained the following abstract form of the second equation of system (1)

$$\frac{d}{dt}V(t) = \mathcal{A}V(t) + \mathcal{F}V(t), \quad V(0) = V_0. \quad (5)$$

By the method of variation of constant, we calculated that

$$-\mathcal{A}^{-1}\nu(a) := \int_0^a e^{-\int_{\varsigma}^a \mu(\eta)d\eta} \nu(\varsigma) d\varsigma, \quad \nu \in X,$$

where \mathcal{A}^{-1} is the inverse of \mathcal{A} . Thus, The next generation operator \mathcal{K} is defined as follows(see [18, 19])

$$\mathcal{K}\nu(a) := \mathcal{F}(-\mathcal{A})^{-1}\nu(a) = se^{-\int_0^a u(s)ds} \int_0^{a_{\dagger}} \beta(a, \varsigma) \int_0^{\varsigma} e^{-\int_{\rho}^{\varsigma} \mu(\eta)d\eta} \nu(\rho) d\rho d\varsigma.$$

Based on the definition in [20], \mathcal{R}_0 is defined as $r(\mathcal{K})$, where $r(\mathcal{K})$ is the spectral radius of the operator \mathcal{K} .

3. Main result

Since the form of $r(\mathcal{K})$ is abstract, we can not calculate \mathcal{R}_0 explicitly. To avoid misunderstanding, we let $\Delta a := a_{\dagger}/n$, $a_m := m\Delta a$, $\beta_{mj} := \beta(a_m, a_j)$, $u_m := u(a_m)$ and $\mu_m := \mu(a_m)$, $m, j = 1, 2, \dots, n$, Hence, we discretize the following equation

$$\frac{d}{dt}V(t) = A_n V(t) + F_n V(t), \quad V(0) = V_0 \in X_n \quad (6)$$

here $V(t)$ and V_0 denote n -column vectors, A_n and F_n are n -square matrices with the following form

$$A_n := \begin{bmatrix} -\mu_1 - \frac{1}{\Delta a} & 0 & \cdots & 0 \\ \frac{1}{\Delta a} & -\mu_2 - \frac{1}{\Delta a} & \cdots & 0 \\ \vdots & \ddots & \ddots & \vdots \\ 0 & \cdots & \frac{1}{\Delta a} & -\mu_n - \frac{1}{\Delta a} \end{bmatrix}_{n \times n},$$

$$F_n := \begin{bmatrix} se^{-u(a_1)\Delta a} \beta_{11} \Delta a & se^{-u(a_1)\Delta a} \beta_{12} \Delta a & \cdots & se^{-u(a_1)\Delta a} \beta_{1n} \Delta a \\ se^{-u(a_2)\Delta a} \beta_{21} \Delta a & se^{-u(a_2)\Delta a} \beta_{22} \Delta a & \cdots & se^{-u(a_2)\Delta a} \beta_{2n} \Delta a \\ \vdots & \vdots & \ddots & \vdots \\ se^{-u(a_n)\Delta a} \beta_{n1} \Delta a & se^{-u(a_n)\Delta a} \beta_{n2} \Delta a & \cdots & se^{-u(a_n)\Delta a} \beta_{nn} \Delta a \end{bmatrix}$$

Next, we define the next generation matrix $\mathcal{K}_n := \mathcal{F}_n(-\mathcal{A}_n)^{-1}$ and $\mathcal{R}_{0,n} := r(\mathcal{K}_n)$. While, we noticed that $r(\mathcal{K}_n) > 0$ with algebraic multiplicity 1 [21](Perron-Frobenius theorem). $\mathcal{P}_n : X \rightarrow X_n$ and $\mathcal{J}_n : X_n \rightarrow X$

are two bounded linear operators given as follows

$$\begin{cases} (\mathcal{P}_n \nu)_m := \frac{1}{\Delta a} \int_{a_m}^{a_{m+1}} \nu(a) da, & m = 1, 2, \dots, n-1, \quad \nu \in X, \\ (\mathcal{J}_n \psi)(a) := \sum_{m=1}^{n-1} \psi_k \chi_{(a_m, a_{m+1}]}(a), & \psi = (\psi_1, \psi_2, \dots, \psi_n)^\top \in X_n, \end{cases} \quad (7)$$

where m is the m th entry of a vector, ψ^\top is the transpose of matrix ψ , and $\chi_{(a_m, a_{m+1}]}(a)$ is the indicator function which implies that

$$\chi_{(a_m, a_{m+1}]}(a) = \begin{cases} 1, & a \in (a_m, a_{m+1}], \\ 0, & a \notin (a_m, a_{m+1}]. \end{cases}$$

From Section 4.1 in [23], we know that for all $n \in \mathbb{N}$, $\|\mathcal{P}_n\| \leq 1$ and $\|\mathcal{J}_n\| \leq 1$. We denote $\|\cdot\|_{X_n}$ is the norm in X_n , and

$$\|\psi\|_{X_n} := \Delta a \sum_{m=1}^n |\psi_m|, \quad \psi = (\psi_1, \psi_2, \dots, \psi_n)^\top \in X_n. \quad (8)$$

Next, we apply the spectral approximation theory to present the convergence theorem of the basic reproduction number.

Theorem 3.1. *Assuming that \mathcal{K} is compact, if for any $\nu \in X$, $\lim_{n \rightarrow +\infty} \|\mathcal{J}_n \mathcal{K}_n \mathcal{P}_n \nu - \mathcal{K} \nu\|_X = 0$, then $\mathcal{R}_{0,n} \rightarrow \mathcal{R}_0$ as $n \rightarrow +\infty$, preserving algebraic multiplicity 1.*

Proof. First, on the basis of [24] (Theorem 3) and [25] (Krein-Rutman theorem), we obtain \mathcal{K} is strictly positive and irreducible. Meanwhile, there is $r(\mathcal{K}) > 0$. By a simple calculation, the inverse matrix of $-A_n$ is shown as follows

$$(-A_n)^{-1} = \begin{bmatrix} \frac{1}{\mu_1 + \frac{1}{\Delta a}} & 0 & \cdots & 0 \\ \frac{\frac{1}{\Delta a}}{(\mu_1 + \frac{1}{\Delta a})(\mu_2 + \frac{1}{\Delta a})} & \frac{1}{\mu_2 + \frac{1}{\Delta a}} & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ \frac{(\frac{1}{\Delta a})^{n-1}}{\prod_{k=1}^n (\mu_k + \frac{1}{\Delta a})} & \frac{(\frac{1}{\Delta a})^{n-2}}{\prod_{k=2}^n (\mu_k + \frac{1}{\Delta a})} & \cdots & \frac{1}{\mu_n + \frac{1}{\Delta a}} \end{bmatrix}, \quad (9)$$

then we have

$$\|\mathcal{K}_n \psi\|_{X_n} = \|F_n(-A_n)^{-1} \psi\|_{X_n} \leq \Delta a \sum_{m=1}^n \frac{se^{-\underline{u}(a_1)\Delta a} \bar{\beta} \Delta a}{\underline{\mu}} \sum_{j=1}^m |\psi_j| \leq a_{\dagger} \frac{se^{-\underline{u}\Delta a} \bar{\beta}}{\underline{\mu}} \|\psi\|_{X_n}$$

here the upper bound of β is defined as $\bar{\beta}$. the lower bounds of u and μ are \underline{u} and $\underline{\mu}$, respectively. They are both finite positive. \square

In addition, we give a following assumption to make that \mathcal{K} is compact.

Assumption 3.2.

$$\lim_{g \rightarrow 0} \int_0^A |\pi(a+g)\beta(a+g, \varsigma) - \pi(a)\beta(a, \varsigma)| da = 0 \quad \text{uniformly for } \varsigma \in \mathbb{R}, \quad (10)$$

here $\pi^0 \beta$ is defined by $\pi^0(a)\beta(a, \varsigma) = 0$ for any $a, \nu \in (-\infty, 0) \cup (A, \infty)$.

Where

$$\pi(a) = e^{-\int_0^a \mu(\eta) d\eta} \quad \text{for } a \in R^\dagger$$

The above assumption implies that the operator \mathcal{K} keep the compactness [[19] Assumption 4.4]. In order to prove $\mathcal{J}_n \mathcal{K}_n \mathcal{P}_n$ converges to \mathcal{K} point by point, we provide the following lemma.

Lemma 3.3. *For all $\nu \in X$, $\lim_{n \rightarrow +\infty} \|\mathcal{J}_n \mathcal{K}_n \mathcal{P}_n \nu - \mathcal{K} \nu\|_X = 0$.*

Proof. For any $\nu \in X$, we obtain

$$\begin{aligned} & \|\mathcal{J}_n \mathcal{K}_n \mathcal{P}_n \nu - \mathcal{K} \nu\|_X \\ &= \|\mathcal{J}_n F_n (-A_n)^{-1} \mathcal{P}_n \nu - F(-A)^{-1} \nu\|_X \\ &\leq \|\mathcal{J}_n F_n (-A_n)^{-1} \mathcal{P}_n \nu - \mathcal{J}_n F_n \mathcal{P}_n (-A)^{-1} \nu\|_X + \|\mathcal{J}_n F_n \mathcal{P}_n (-A)^{-1} \nu - F(-A)^{-1} \nu\|_X \\ &\leq \|\mathcal{J}_n\| \|F_n\| \|(-A_n)^{-1} \mathcal{P}_n \nu - \mathcal{P}_n (-A)^{-1} \nu\|_{X_n} + \|\mathcal{J}_n F_n \mathcal{P}_n (-A)^{-1} \nu - F(-A)^{-1} \nu\|_X \\ &\leq a_\dagger s e^{-\underline{u} \Delta a} \|(-A_n)^{-1} \mathcal{P}_n \nu - \mathcal{P}_n (-A)^{-1} \nu\|_{X_n} + \|\mathcal{J}_n F_n \mathcal{P}_n (-A)^{-1} \nu - F(-A)^{-1} \nu\|_X. \end{aligned} \quad (11)$$

Since $\|\mathcal{J}_n\| \leq 1$, and for any $n \in \mathbb{N}$, $\|F_n\| \leq a_\dagger s e^{-\underline{u} \Delta a}$, Next we estimate the first item in the right-hand of (11), then

$$\begin{aligned} \|(-A_n)^{-1} \mathcal{P}_n \nu - (-A)^{-1} \mathcal{P}_n \nu\|_{X_n} &= \|(-A_n)^{-1} \mathcal{P}_n (-A) (-A)^{-1} \nu - (-A_n)^{-1} (-A_n) \mathcal{P}_n (-A)^{-1} \nu\|_{X_n} \\ &\leq \|(-A_n)^{-1}\| \|\mathcal{P}_n (-A) (-A)^{-1} \nu - (-A_n) \mathcal{P}_n (-A)^{-1} \nu\|_{X_n} \\ &\leq a_\dagger \|\mathcal{P}_n (-A) \vartheta - (-A_n) \mathcal{P}_n \vartheta\|_{X_n}, \end{aligned}$$

where $\vartheta := (-A)^{-1} \nu \in D(A)$, and for any $\psi = (\psi_1, \psi_2, \dots, \psi_n)^\top \in X_n$,

$$\|(-A_n)^{-1} \psi\|_{X_n} \leq \Delta a \sum_{m=1}^n \frac{1}{\underline{\mu} + \frac{1}{\Delta a}} \sum_{j=1}^m |\psi_j| \leq \Delta a \sum_{m=1}^n \Delta a \sum_{j=1}^m |\psi_j| = a_\dagger \|\psi\|_{X_n},$$

we obtain

$$\begin{aligned} & \|(-A_n)^{-1} \mathcal{P}_n \nu - (-A)^{-1} \mathcal{P}_n \nu\|_{X_n} \\ &\leq a_\dagger \Delta a \sum_{m=1}^n \left| \frac{1}{\Delta a} \int_{a_{m-1}}^{a_m} \left(\frac{d}{da} \vartheta(a) + \mu(a) \vartheta(a) \right) da - \frac{\frac{1}{\Delta a} \int_{a_{m-1}}^{a_m} \vartheta(a) da - \frac{1}{\Delta a} \int_{a_{m-2}}^{a_{m-1}} \vartheta(a) da}{\Delta a} - \frac{\mu_m}{\Delta a} \int_{a_{m-1}}^{a_m} \vartheta(a) da \right|, \end{aligned}$$

where $a_0 = a_{-1} = 0$. By the mean value theorem, we have

$$\begin{aligned} & \|(-A_n)^{-1} \mathcal{P}_n \nu - (-A)^{-1} \mathcal{P}_n \nu\|_{X_n} \\ &\leq a_\dagger \Delta a \sum_{m=1}^n \left| \frac{d}{da} \vartheta(\eta_m) + \mu(\eta_m) \vartheta(\eta_m) - \frac{1}{\Delta a} (\vartheta(\varepsilon_m) - \vartheta(\varepsilon_{m-1})) - \mu_m \vartheta(\varepsilon_m) \right| \\ &\leq a_\dagger \Delta a \sum_{m=1}^n \left(\left| \frac{d}{da} \vartheta(\eta_m) - \frac{d}{da} \vartheta(\zeta_m) \right| + \left| \mu(\eta_m) \vartheta(\eta_m) - \mu(m) \vartheta(\varepsilon_m) \right| \right) \\ &\leq a_\dagger^2 \left[\omega(\vartheta', 2\Delta a) + \omega(\mu, \Delta a) \omega(\vartheta, \Delta a) \right], \end{aligned}$$

where $\omega(f, r)$ denotes the modulus of continuity. We know that $\omega(f, r)$ is defined by $\sup_{|y-z| \leq r} |f(y) - f(z)|$ with the following property

$$\omega(f, r) \rightarrow 0, \quad \text{as } r \rightarrow 0.$$

Hence, $\|(-A_n)^{-1}\mathcal{P}_n\nu - (-A)^{-1}\mathcal{P}_n\nu\|_{X_n} \rightarrow 0$ holds. Then we consider the second term of (11) as follows

$$\begin{aligned} & \|\mathcal{J}_n F_n \mathcal{P}_n (-A)^{-1}\nu - F(-A)^{-1}\nu\|_X = \|\mathcal{J}_n F_n \mathcal{P}_n \vartheta - F\vartheta\|_X \\ &= \sum_{m=1}^n \int_{a_m}^{a_{m+1}} \left| \sum_{j=1}^n s \pi_m \beta_{mj} \int_{a_{j-1}}^{a_j} \vartheta(\varsigma) d\varsigma - \int_0^{a_{\dagger}} s \pi(a) \beta(a, \varsigma) \vartheta(\varsigma) d\varsigma \right| da \\ &\leq s \sum_{m=1}^n \int_{a_m}^{a_{m+1}} \sum_{j=1}^n \int_{a_{j-1}}^{a_j} \left| \pi_m \beta_{mj} - \pi(a) \beta(a, \varsigma) \right| |\vartheta(\varsigma)| d\varsigma da \\ &\leq s a_{\dagger} \omega(\pi, \Delta a) \omega(\beta, \Delta a) \|\vartheta\|_X \rightarrow 0 \quad \text{as } n \rightarrow +\infty, \end{aligned} \tag{12}$$

where $\omega(\pi, \Delta a) \rightarrow 0 (\Delta a \rightarrow 0)$ and $\omega(\beta, \Delta a) \rightarrow 0 (\Delta a \rightarrow 0)$, respectively. Hence,

$$\|\mathcal{J}_n F_n \mathcal{P}_n (-A)^{-1}\nu - F(-A)^{-1}\nu\|_X \rightarrow 0.$$

Combine the above discussion, we have $\lim_{n \rightarrow +\infty} \|\mathcal{J}_n \mathcal{K}_n \mathcal{P}_n \nu - \mathcal{K} \nu\|_X = 0$. \square

As a result, from Assumption 3.2 and Lemma 3.3, we know that Theorem 3.1 holds. Namely, $\mathcal{R}_{0,n} \rightarrow \mathcal{R}_0$ as n converges to $+\infty$, preserving algebraic multiplicity 1[26].

4. Numerical simulations

To further illustrate the results of the theorem, we present a numerical simulation. At the moment, the values of these parameters in system (1) are as follows $a_{\dagger} = 100$, $s = 10^5$, $u(a) = 0.2(1 + \frac{a^3}{10^6})$, $\beta(a, \varsigma) = kJ(a - \varsigma)$, here $k=0.0003$ and $J(x) = 0.6(-x^2 + 100^2) \times 10^{-6} + 0.001$ ([15]) is a normalized distance function. $\mu(a) = 0.03 + 0.32(a - 5^2)$. Thus, we can easily verify that assumption 3.2 hold.

$$\begin{aligned} & |\pi(a+g)\beta(a+g, \varsigma) - \pi(a)\beta(a, \varsigma)| \\ &\leq 0.6k \times 10^{-6} |-\pi(a+g)(a+g-\varsigma)^2 + \pi(a)(a-\varsigma)^2 + 100^2(\pi(a+g) - \pi(a))| + 0.001k|\pi(a+g) - \pi(a)| \\ &\leq 0.6k \times 10^{-6} |(-\pi(a+g) + \pi(a))(a-\varsigma)^2 - \pi(a+g)2g(a-\varsigma) - g^2\pi(a+g)| + 0.0007k|\pi(a+g) - \pi(a)| \\ &\leq (0.6k \times 10^{-6}\omega^2 + 0.0007k)|\pi(a+g) - \pi(a)| + (2\omega g + g^2)\bar{\pi} \rightarrow 0 \text{ as } h \rightarrow 0 \text{ uniformly for } \varsigma \in R, \end{aligned}$$

Define the $\bar{\pi}$ is the upper bound of π . By calculating we get $\mathcal{R}_{0,1000} \approx 2.647322605581397 =: R^*$ as a threshold value for \mathcal{R}_0 . In Figure 1, we give the images of $\mathcal{R}_{0,n}$ and error $(R^* - \mathcal{R}_{0,n})$, respectively. From figure 1(a), we see that $\mathcal{R}_{0,n}$ increases as n increases. We note that diseases persist and eventually become endemic. From figure 1(b), we see that the error $(R^* - \mathcal{R}_{0,n}) \rightarrow 0$ as n increase. In table 2, we give the numerical value of $\mathcal{R}_{0,n}$, and we can see $\mathcal{R}_{0,n}$ converges to \mathcal{R}_0 as $n \rightarrow +\infty$.

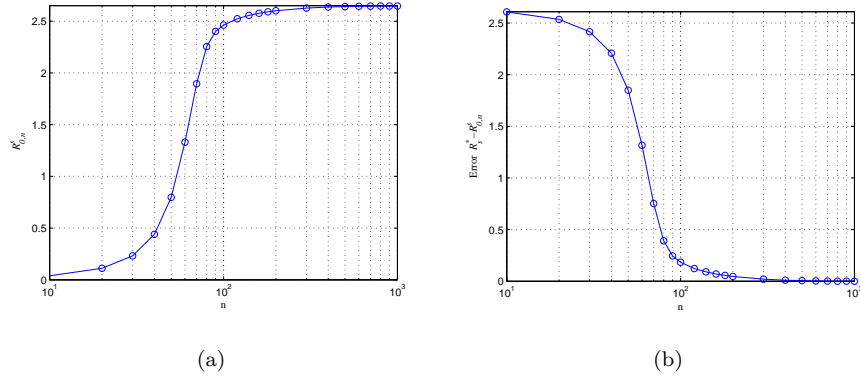


Figure 1: (a) Graphic of the threshold $R_{0,n}$; (b) the error $R^* - R_{0,n}$ in regard to the reference value $R^* = 2.647322605581397$

Table 2: Numerical value of $R_{0,n}$.

n	$R_{0,n}$
10	0.039168237289443
50	0.797849417727710
100	2.463366617482032
500	2.642085560275887
1000	2.647322605581397
R^*	2.647322605581397

5. Concluding remarks

Here, we consider HIV transmission models of the age structure. Generally, \mathcal{R}_0 cannot be explicitly calculated for an age-structured HIV infection model in an infinite dimensional space. Hence, we discretized the equation (6) into a finite space. Subsequently, we apply the spectral approximation theory to present the convergence theorem of the basic reproduction ratio. In addition, we proved that \mathcal{K} is compact. Finally, to verify the results of the theorem, we present a numerical simulation. In figure 1 and table 2, we see that \mathcal{R}_n increases as n increases, and the error $(R^* - \mathcal{R}_{0,n}) \rightarrow 0$ as n increases. For such problems, proof of pointwise convergence in Lemma 3.3 is still more challenging in future research.

Acknowledgments

The research was supported in part by the National Natural Science Foundation of China (No. 11661064).

Conflict of Interest

The authors declare that they have no conflict of interest.

References

- [1] Fan, Xiaoting, Yi Song, Wencai Zhao (2018) Modeling cell-to-cell spread of HIV-1 with nonlocal infections. *Complexity*. <http://doi.org/10.1155/2018/2139290>.
- [2] Lai, Xiulan, Xingfu Zou (2015) Modeling cell-to-cell spread of HIV-1 with logistic target cell growth. *Journal of Mathematical Analysis and Applications*. 426(1): 563-584.
- [3] Hattaf, Khalid, Noura Yousfi (2016) A generalized virus dynamics model with cell-to-cell transmission and cure rate. *Advances in Difference Equations*. <https://doi.org/10.1186/s13662-016-0906-3>.
- [4] Zhang, Tongqian, Xinzhu Meng, Tonghua Zhang (2015) Global dynamics of a virus dynamical model with cell-to-cell transmission and cure rate. *Computational and mathematical methods in medicine*. <http://dx.doi.org/10.1155/2015/758362>.
- [5] De Boer, Rob J., Alan S. Perelson (1998) Target cell limited and immune control models of HIV infection: a comparison. *Journal of theoretical Biology*. 190(3): 201-214.
- [6] Song, Xinyu, Xueyong Zhou, Xiang Zhao (2010) Properties of stability and Hopf bifurcation for a HIV infection model with time delay. *Applied Mathematical Modelling*. 34(6): 1511-1523.
- [7] Mller, Viktor, Athanasius FM Mare, Rob J. De Boer (2001) Small variations in multiple parameters account for wide variations in HIVC1 setCpoints: a novel modelling approach. *Proceedings of the Royal Society of London. Series B: Biological Sciences*. 268(1464): 235-242.
- [8] Yang, Yu, Lan Zou, Shigui Ruan (2015) Global dynamics of a delayed within-host viral infection model with both virus-to-cell and cell-to-cell transmissions. *Mathematical biosciences*. 270: 183-191.
- [9] Wang, Xia, Sanyi Tang, Xinyu song, Libin Rong (2017) Mathematical analysis of an HIV latent infection model including both virus-to-cell infection and cell-to-cell transmission. *Journal of biological dynamics*. 11(2): 455-483.
- [10] Lai, Xiulan, Xingfu Zou (2014) Modeling HIV-1 virus dynamics with both virus-to-cell infection and cell-to-cell transmission. *SIAM Journal on Applied Mathematics*. 74(3): 898-917.
- [11] P. W. Nelson, M. A. Gilchrist, D. Coombs, J. M. Hyman, A.S. Perelson; An age-structured model of HIV infection that allow for variations in the production rate of viral particles and the death rate of productively infected cells, *Math. Biosci. Eng.* 1(2) (2004) 267-288.

- [12] Wang, Jinliang, Jiying Lang, Xingfu Zou (2017) Analysis of an age structured HIV infection model with virus-to-cell infection and cell-to-cell transmission. *Nonlinear Analysis: Real World Applications*. 34: 75-96.
- [13] Mingwang Shen, Yanni Xiao, Libin Rong (2015) Global stability of an infection-age structured HIV-1 model linking within-host and between-host dynamics. *Mathematical Biosciences*. 263: 37C50.
- [14] Gang Huang, Xianning Liu, Yasuhiro Takeuchi (2012) Lyapunov functions and global stability for age-structured HIV infection model. *Society for Industrial and Applied Mathematics*. 72(1): 25C38.
- [15] Kuniya, Toshikazu (2017) Numerical approximation of the basic reproduction number for a class of age-structured epidemic models. *Applied Mathematics Letters*. 73: 106-112.
- [16] Guo, Wenjuan, Ming Ye, Xining Li, AnkeMeyer-Baese, Qimin Zhang (2019) A theta-scheme approximation of basic reproduction number for an age-structured epidemic system in a finite horizon. 16(5): 4107-4121.
- [17] Chatelin, F (1981) The spectral approximation of linear operators with applications to the computation of eigenelements of differential and integral operators. *SIAM review*. 23(4): 495-522.
- [18] Inaba H (2013) On the definition and the computation of the type-reproduction number T for structured populations in heterogeneous environments. *Journal of Mathematical Biology*. 66(4-5): 1065-1097.
- [19] Inaba H (1990) Threshold and stability results for an age-structured epidemic model. *Journal of Mathematical Biology*. 28(4): 411-434.
- [20] Diekmann, Odo, Johan Andre Peter Heesterbeek, Johan AJ Metz (1990) On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations. *Journal of mathematical biology*. 28(4): 365-382.
- [21] A. Berman, R.J. Plemmons, *Nonnegative Matrices in the Mathematical Sciences*, Academic Press, New York, 1979.
- [22] Xu R, Tian X, Zhang S (2018) An age-structured within-host HIV-1 infection model with virus-to-cell and cell-to-cell transmissions. *Journal of Biological Dynamics*. 12(1): 89-117.
- [23] Ito, Kazufumi, Franz Kappel (1998) The Trotter-Kato theorem and approximation of PDEs. *Mathematics of Computation of the American Mathematical Society*. 67(221): 21-44.
- [24] B. Pagter, Irreducible compact operators, *Math. Z.*, 192 (1986), 149C153.

- [25] M. Krein, Linear operators leaving invariant a cone in a Banach space, Amer. Math. Soc. Transl. 10 (1962), 3C95.
- [26] F. Chatelin, The spectral approximation of linear operators with applications to the computation of eigenvalues of differential and integral operators. SIAM Review. 23 (1981), 495-522.